AstraZeneca

Externally Sponsored Research Handbook

Cross-TA AI/Digital

The aim of this Handbook is to provide Sponsors with guidance on how to **work successfully** with AstraZeneca and to provide advice on **key challenges** in Externally Sponsored Research

Get started >

Date preparation: 15 May 2024

This material is intended for use by potential Sponsors and Sponsors of Externally Sponsored Research

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Website hyperlinks

This guide contains links to online resources. Acrobat security preferences may ask you to permit access to these sites. If this is not an option, right click the link and select ‘Copy URL location’. You can then enter this URL into your browser address bar to access the website.

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Externally Sponsored Research at AstraZeneca

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What is Externally Sponsored Research?

Externally Sponsored Research (ESR) is research that is initiated, designed and conducted by an independent Sponsor
It can be broadly divided into two categories

1. **Investigator Initiated Sponsored Research (IISR)**
studies are unsolicited (unrequested) research that is planned, designed, initiated and conducted by a non-Company researcher (Sponsor).
AstraZeneca **does not assume legal and/or regulatory accountabilities, or assist** with research activities

2. **Externally Sponsored Collaborative Research (ESCR)**
studies are unsolicited (unrequested) or solicited (requested) research that is planned, designed, initiated and conducted by a non-Company researcher (Sponsor).
AstraZeneca **may assist** with some research activities

Within these categories are two types of research:

1. **Interventional clinical research (Phases 1–4)**
Clinical and/or methodology research involving authorised, unauthorised or discontinued Company compounds

2. **Observational research (i.e. real-world evidence)**
The product of interventional or non-interventional research, utilising data collected through observation of current clinical practice and/or patient-reported experience

Why does AstraZeneca support ESR?

AstraZeneca recognises the important role that ESR can play in expanding the knowledge related to a Company product and/or its associated disease area(s). This research can advance science and contribute to the development of better medicines for patients, consistent with the Company's overall research and global development strategies

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Important notices

- Invitation to submit a full protocol or approval of funding should not be interpreted as a suggestion that any product/compound is safe or effective for an investigational use or recommended for any use outside of approved labelling
- The consideration of support for the research project by the Company is not in exchange for, nor is it intended to induce the prescribing or recommending of, any Company product
- The Company does not guarantee that a proposal or protocol will be supported, or that funding will be provided. The decision to support a research project is subject to full execution of a written Externally Sponsored Research (ESR) Agreement.
- AstraZeneca can support AI/Digital ESR by providing funding only
- The Company considers submissions on a case by case basis according to the strength of the scientific rationale, and may not be able to support all requests received. Decisions regarding support for research are made at the sole discretion of the Company and are always subject to an ESR Agreement
- All requests for funding are subject to a fair market value (FMV) assessment
- The Company reserves the right to review all publications resulting from an approved ESR project, prior to submission to a journal or congress
- Receipt of this Handbook does not imply or guarantee that an ESR project will be funded or supported

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Who does what at AstraZeneca?

A number of functions at AstraZeneca are involved in Externally Sponsored Research (ESR)

Your Medical Science Liaison will help you to find the right contact at AstraZeneca

You may interact with different people at AstraZeneca depending on the development stage of a product

Product	Key contact	Local team	Global team
Marketed Products A product that has regulatory approval from the regulatory authority where the study is to take place	**Medical Science Liaison** ESR Manager	• Manages Veeva Clinical Vault system • Carries out local review of ESR • Handles communication • Primary contact with the Sponsor	• Owns product strategy • Approves ESR submissions
Development Products Products that **do not have** regulatory approval	**Medical Scientist** ESR Manager		

The Veeva Clinical Vault (VCV) platform will be the **main channel of communication** between you and AstraZeneca
You will submit all information relating to the ESR using the VCV platform
Learn more about VCV in Chapter 5

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Sponsor responsibilities

As a Sponsor you will have accountability for all aspects of the research, including the following:

Study design

- Submit a well-written proposal and protocol
- Submit all documents for Company review

Ensuring appropriate approvals

- Have the capabilities to conduct the research
- Submit and hold a medical device investigational approval in accordance with local requirements (as applicable)

Labelling and distribution of digital health technology

Study conduct

- Comply with the Externally Sponsored Research (ESR) Agreement
- Deliver to agreed timelines
- Provide project status updates (PSUs)

Analysis, interpretation and communication of the results

- Have expert statistical support

Posting your study on external websites

- Write the final report and publish the results

Please refer to **'E6 Good Clinical Practice'** on the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) website for additional information regarding Sponsor obligations for clinical studies
Please note that the Company reserves the right to **withdraw funding** in the event of **significant delays** to delivery

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ESR milestone definitions

AstraZeneca measures the performance of an Externally Sponsored Research (ESR) study by assessing adherence to key **milestones**

Clinical ESR milestones

First Subject In (FSI)
When the first subject in the study has signed the Informed Consent Form (ICF)

Sponsors will **start** being provided with patient safety information

50% enrolment
When 50% of the planned subjects in the study have given informed consent

Last Subject In
When the last subject in the study has entered treatment

Last Subject Last Visit (LSLV)
When the last subject has had their final visit assessment for the study

Sponsors will **stop** being provided with patient safety information

Completion of final study report and/or publications
When the final study deliverable (publication or report) detailed in the Research Agreement (RA) has been received by AstraZeneca

Observational/secondary data study milestones

Start of project
When the first subject in the study has given Informed Consent/Date of the Research Agreement execution (observational ESRs without subjects)

End of project
When the last subject has had their last visit or assessment for the study/When the last assessment for the study has been completed (observational ESRs without subjects)

Completion of final study report and/or publications
When the final study deliverable (publication or report) detailed in the Research Agreement (RA) has been received by AstraZeneca

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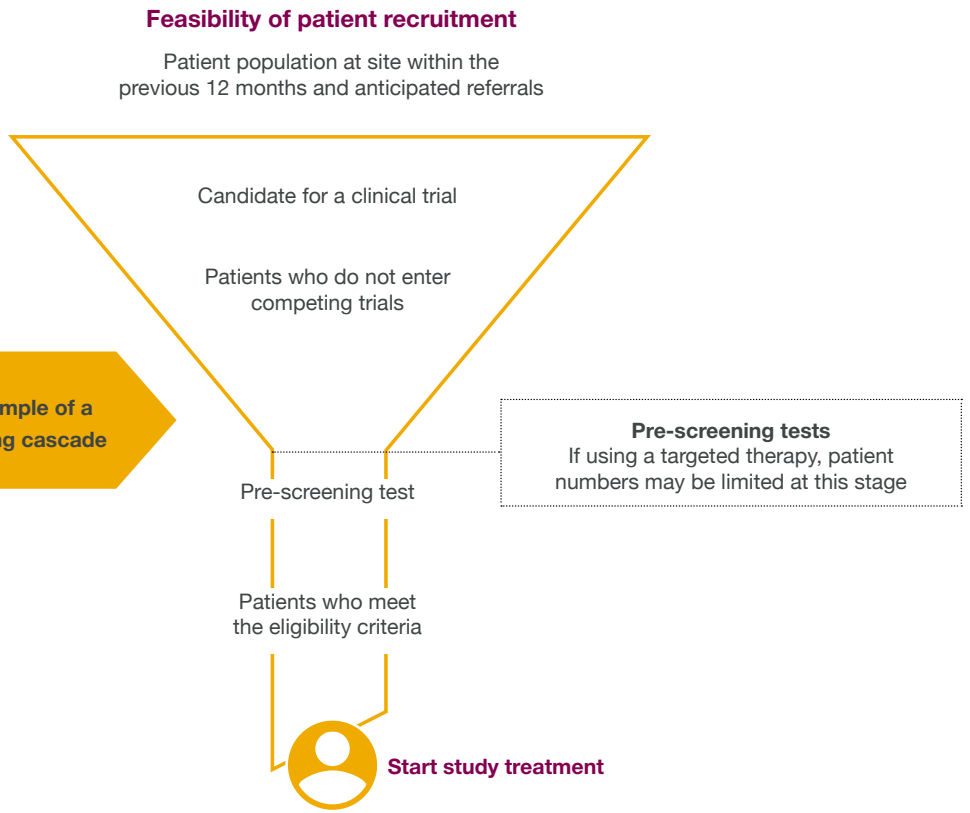
Design phase

Estimating study timelines

Please ensure that your proposal includes realistic and achievable timelines for study set-up, recruitment and reporting

Protocol writing	You are expected to submit a good draft protocol **within 90 days** of proposal approval
Set-up	Typically, it takes Sponsors approximately **9 months** from protocol approval until the first patient in a study receives treatment
Recruitment	When estimating how long it will take to recruit patients for a study, Sponsors should consider the number of patients available at each stage of the screening process
Data cut-off → Data available	Work with your **statistician** to estimate how long it will take until the data cut-off for your primary objective. Include the length of time to clean, validate and analyse your data

An example of a screening cascade



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Proposal submission and review & approval

When you are ready to submit your Externally Sponsored Research (ESR) proposal, ensure that you register for a Veeva Clinical Vault (VCV) account

Once submitted, your proposal will be reviewed by the AstraZeneca team(s) involved in your AI/Digital proposal

This process takes approximately **45 days**

Initial proposal submission (1 day)

Submit an ESR proposal via our submissions tool:

- VCV for clinical and observational ESR

You will need to provide the following information for your proposal submission:

Study design information

- Hypothesis and rationale
- Objective(s) and endpoint(s) (stated as measurable outcome variables)
- Treatment (if applicable)
- Sample size justification (based on the primary endpoint)
- Patient population (eligibility criteria)
- Statistical plan

Supporting documentation

- Your current CV
- Medical licence (if applicable)
- Budget requested (if applicable)
- Estimated timelines
- Study schematic

Review and approval (45 days)

Local and global review and approval decisions are typically communicated within 45 days of receipt of a complete submission

Please note that AstraZeneca will perform a detailed financial review and fair market value (FMV) analysis of the proposed budget

Next steps following proposal approval

Establish a confidentiality agreement (CDA). This is a legal contract between the Sponsor and AstraZeneca that outlines confidential material, knowledge or information to be shared between the two parties for the purpose of the ESR study

Draft **Research Agreement (RA)** to initiate contract negotiations

If more details or clarifications are needed, AstraZeneca will request additional information from the Sponsor
The 45-day review target does not include time taken to provide additional information

You will be **notified** of the decision regarding your ESR proposal by your AstraZeneca contact and through VCV
Please ensure that **high-quality proposals** are submitted because AstraZeneca will carry out a thorough cross-functional review

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Protocol review and approval

Protocol submission

If your proposal is approved, a full study protocol should be submitted to Veeva Clinical Vault within 90 days

Review and approval (45 days)

Your study protocol will be reviewed:

- against the previously approved ESR proposal
- against the ESR AI/Digital strategy

Next steps following protocol approval

- Execution of the research agreement
- Regulatory/IRB/IEC approvals
- Study set-up **(see details in the 'Set-up phase' section)**

If more details or clarifications are needed, AstraZeneca will request additional information from the Sponsor
The 45-day review target does not include time taken to provide additional information

Good submissions **involve input from key disciplines** at your institution (statistician, research nurse, pharmacist etc.)

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Set-up phase

- Contracting
- Informed Consent Form
- Regulatory and other approval steps

Contracting

An Externally Sponsored Research (ESR) **Research Agreement (RA)** that complies with local laws and regulations must be negotiated and signed by AstraZeneca and the Sponsor
This occurs after protocol approval but prior to AstraZeneca providing funding, and before research can begin

Once the ESR proposal has been approved your ESR Manager will send you a draft RA
- If funding is to be provided, this may include a **draft payment schedule** that does not exceed the approved amount
- Scheduled payments will be linked to ESR milestones, such as study activation, First Subject In (FSI), 50% Subject Enrolment, Last Subject In, Last Subject Last Visit (LSLV) and publication

Please note that changes to **indemnity**, **confidentiality**, and/or **intellectual property** will require review by AstraZeneca's Legal Department and will cause delay

An **RA amendment** may be negotiated to reflect scope changes throughout the study, or prior to study closure, if the full scope is not likely to be executed upon closure

Please also consider **other contracts** that you may need for the study as all third-party contracts are your institution's responsibility to negotiate
- Contracts for additional sites if you are running a multi-site study
- Contracts for other vendors
  - E.g. contract research organisation (CRO), if applicable

Contracting is a frequent cause of significant delay in the set-up of ESR studies –
we strongly recommend that you **liaise with your contracting department early in the process**

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Informed Consent Form

You are responsible for developing an **Informed Consent Form (ICF)** that complies with all applicable regulation(s) on data protection.

- For Externally Sponsored Collaborative Research (ESCR), we strongly recommend that language is included in the ICFs to enable the transfer of the clinical data/samples to AstraZeneca and/or any third party contracted by AstraZeneca or the Sponsor (with no restriction on geographical location)
- Such transfers will only be made when they are agreed between AstraZeneca and the Sponsor, and specified in the Research Agreement (RA) contract

Please ensure that there are **no references to AstraZeneca as the Sponsor** included in the language of the ICF

Regulatory and other approval steps

Once the Externally Sponsored Research (ESR) protocol is approved by AstraZeneca,
the Sponsor is responsible for obtaining all necessary approvals for the clinical trial as per local regulations

Generally, this includes submitting a **Clinical Trial Application (CTA)** to both **Ethics Committees** or **Institutional Review Boards (IRBs)** and **Regulatory Authorities**

Contact your ESR Manager if you receive questions from your IRB or Regulatory Authority that require AstraZeneca's support to be answered

Be aware that there may be additional committee reviews at your institution (e.g. R&D Boards)

Once you have obtained all relevant approvals, upload the approval documentation to Veeva Clinical Vault

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Delivery phase

- Patient recruitment
- Safety reporting
- Changes during study conduct
- Project Status Updates
- Statistical analysis
- Study publication(s)

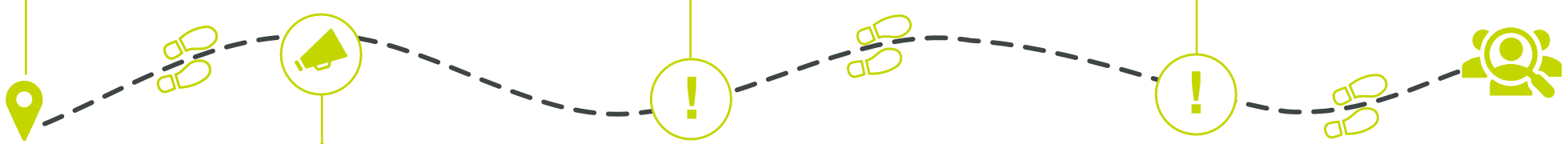
Patient recruitment

Be aware of the **recruitment rate** needed to achieve planned study timelines
- Keep track of how recruitment is progressing compared with the plan
- Recruitment often starts slowly and increases over time as more sites are set-up

Ensure that **potential referrers** are aware of your study
- Referral networks
- ClinicalTrials.gov

Keep track of reasons for **pre-screen failure**

Keep track of reasons for **screening failure**
- Are there specific eligibility criteria that are causing issues?



Inform AstraZeneca if the **recruitment rate** is **slower than expected**

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Safety reporting

As a Sponsor of AI/Digital-driven Externally Sponsored Research (ESR), you will be responsible for informing the Company, Health Authorities and Ethics Committees of any adverse experience as per local requirements

At the end of the study, the Sponsor is responsible for sending a comprehensive list of all relevant safety reports to the mailbox stated in the Research Agreement (RA)

- The **safety collection vendor** is accountable for issue resolution and may contact the Sponsor as needed

The Sponsor completes **Project Status Updates (PSUs)** in Veeva Clinical Vault (VCV) as stated in the RA

- State whether any safety reports were submitted within a particular time period
- No individual reports or safety listings are to be uploaded to VCV at any time

Changes during study conduct

AstraZeneca and the Sponsor are both responsible for updating the other party regarding **any changes** that may occur during the course of an Externally Sponsored Research (ESR) study

Protocol amendments

- Please ensure that all protocol amendments are submitted to Veeva Clinical Vault (VCV) for AstraZeneca approval prior to submitting to the relevant Health Authority and/or Ethics Committee

Changes to timelines

- Milestones for ESR studies are documented in a Research Agreement (RA) prior to First Subject In (FSI)
- Sponsors are expected to deliver to their committed milestones
- However, milestones may occasionally need to be re-agreed with AstraZeneca
- If you identify a risk that your study will not deliver to the agreed milestones, please discuss this with your AstraZeneca contact and agree an action plan
  - This plan will then be discussed with the Global Team at AstraZeneca

Please note that the Company reserves the right to **withdraw funding** in the event of **significant delays** to delivery

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Project Status Updates

Once an Externally Sponsored Research (ESR) study is active, the Sponsor is required to submit Project Status Updates (PSUs) at the frequency defined in the Research Agreement (RA)

All PSUs are submitted via Veeva Clinical Vault

As a Sponsor, you will need to ensure that the Company is informed of progress and is promptly provided with the following

Recruitment progress update (if applicable)
Summarises the work performed and the results achieved, including number of participants (screened, enrolled, completed, withdrawn and/or in follow-up)

Milestone updates
Confirms milestones achieved (First Subject In, 50% Subject Enrolment, Last Subject In, Last Subject Last Visit) or newly proposed milestones

Safety updates (if applicable)
Identifies emerging safety-related issues and reports all adverse experience

Publication activity
Updates the plan for any study publications

After updating the relevant information, the Sponsor should navigate to the menu and submit the PSU in order to notify the ESR AstraZeneca manager

Why are PSUs important?

- Provides AstraZeneca with a full picture of ESR performance
- Helps to identify performance issues and facilitates implementation of corrective actions
- Ensures the timely delivery of expected study data
- Allows AstraZeneca to manage budget more efficiently

The AstraZeneca Global ESR Team can request **more frequent updates** if the study is not progressing according to agreed milestones

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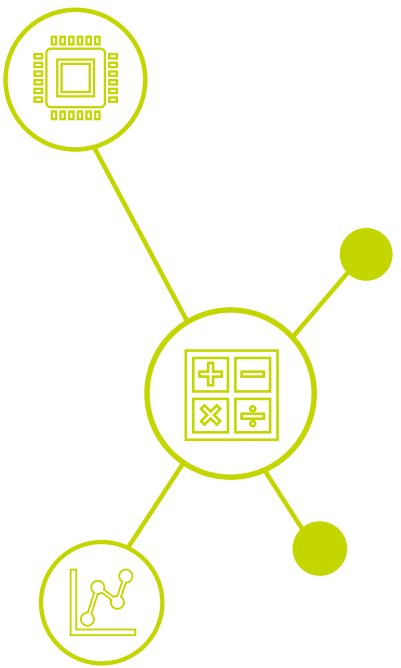
Statistical analysis

Plan your statistical analysis in advance and prespecify it as much as possible – do not leave it until the end of the study before planning how the data should be analysed

- Define data cut-off for **interim analysis** (if applicable)
- Define data cut-off for **final analysis**
- Specify the **end of the study**
- Specify **all planned analyses**
- Specify whether patients will be followed up for **survival (if applicable)**
  - Even if the primary endpoint is safety and tolerability



Involve a **statistician** in all aspects of data analyses

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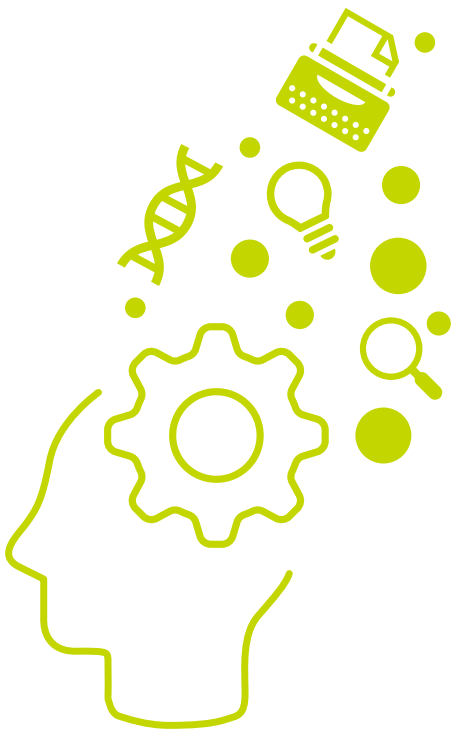
Study publication(s)

Publications resulting from Externally Sponsored Research (ESR) must abide by **Good Publication Practice** (GPP) guidelines and the **International Committee of Medical Journal Editors** (ICMJE) recommendations



- Register the study on a public clinical trial registry, post the results in the registry and publish the analyses in an appropriate scientific journal
- **Do not** include any confidential Company information in a clinical trial registry or publication
- Send all publications to the Company for review prior to submission (e.g. to a journal or conference) by uploading the publication to Veeva Clinical Vault (VCV)
- Final-stage draft publications from ESR undergo review by AstraZeneca for medical/scientific accuracy, disclosure and intellectual property (IP), using the **publication sign-off (PSO)** procedure
  - PSO takes a minimum of 30 days

Investigator Initiated Sponsored Research (IISR)

- Publications must be developed independently of Company influence
- No Company authors or co-authors
- Final-stage draft publications from IISR require only PSO review

Externally Sponsored Collaborative Research (ESCR)

- The Company's employees may be involved in:
  - planning and developing ESCR publications
  - editing and medical writing assistance
  - authorship
- Final-stage draft publications from ESCR that involve Company author(s) require both PSO review and PSO approval signature

! Please also submit a copy of the **final version of the publication** to AstraZeneca

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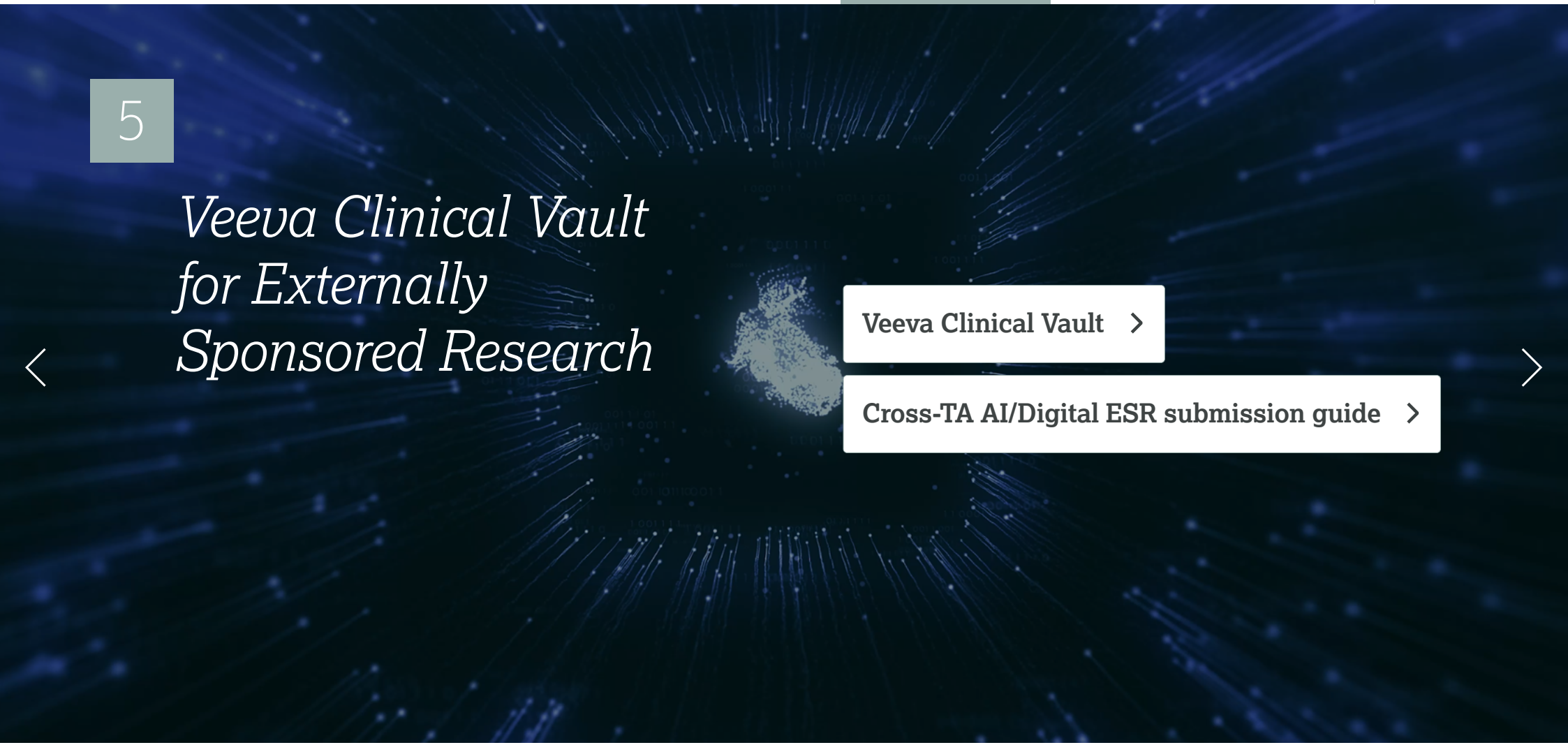
Veeva Clinical Vault for Externally Sponsored Research



Veeva Clinical Vault >

Cross-TA AI/Digital ESR submission guide >

Veeva Clinical Vault

The **Veeva Clinical Vault (VCV) for Externally Sponsored Research (ESR)** platform is AstraZeneca's electronic system for processing ESR submissions, and for tracking and managing ongoing ESR studies

- The VCV platform has been designed to offer Sponsors a fast, user-friendly and secure way to submit and to track ESR studies
- VCV is the main channel of communication between you and AstraZeneca
- Please note that submissions to VCV must be made in English
  - For help with how to use VCV, please refer to the VCV External Partner User Guide

- Before accessing VCV for the first time, make sure to register for a new account through the Externally Sponsored Scientific Research Partner Portal, and watch the video trainings on the Externally Sponsored Scientific Research Partner Training Centre
- Then follow the **'make a submission'** link to access VCV and submit a new ESR study proposal

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Cross-TA AI/Digital ESR submission guide

Guidelines on creating cross-TA AI/Digital ESR submission in Veeva Clinical Vault (General Information section):
To ensure that your submission is reviewed by the AI/Digital AstraZeneca Global Team, please follow the steps below
For all other steps please follow the general ERS submission guidelines

Step 1
Therapeutic Area – "Across TAs [AT]"

1

Step 2
Indication – "Other Diseases"

2

Step 3
Primary Product – "None"

3

Step 4
Direct to AI/Digital Team? – "Yes"

4

This field will only be available when the previous three options are selected together

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