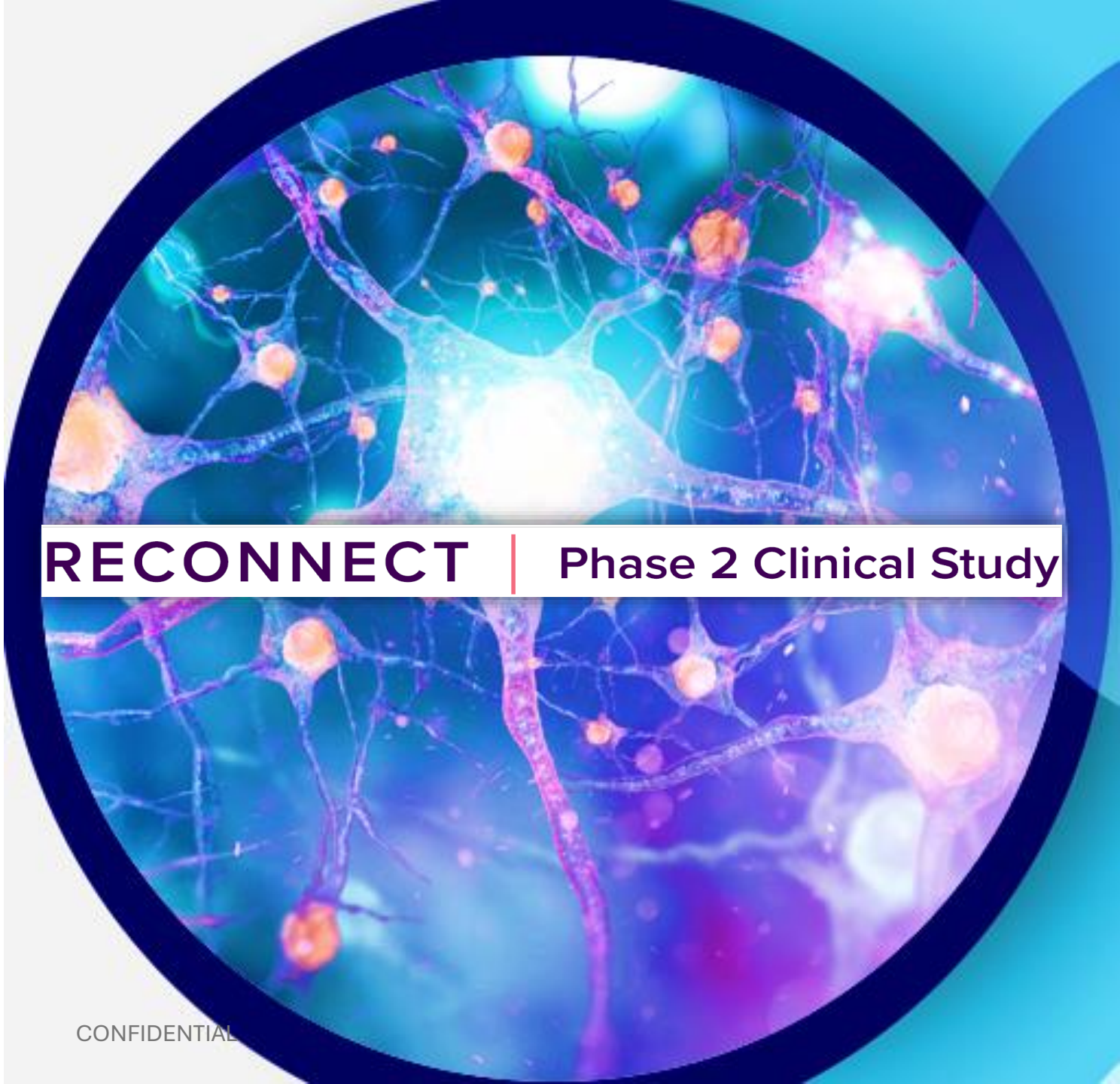
RE104-201-PPD
Investigator Meeting Slides



reunion NEUROSCIENCE

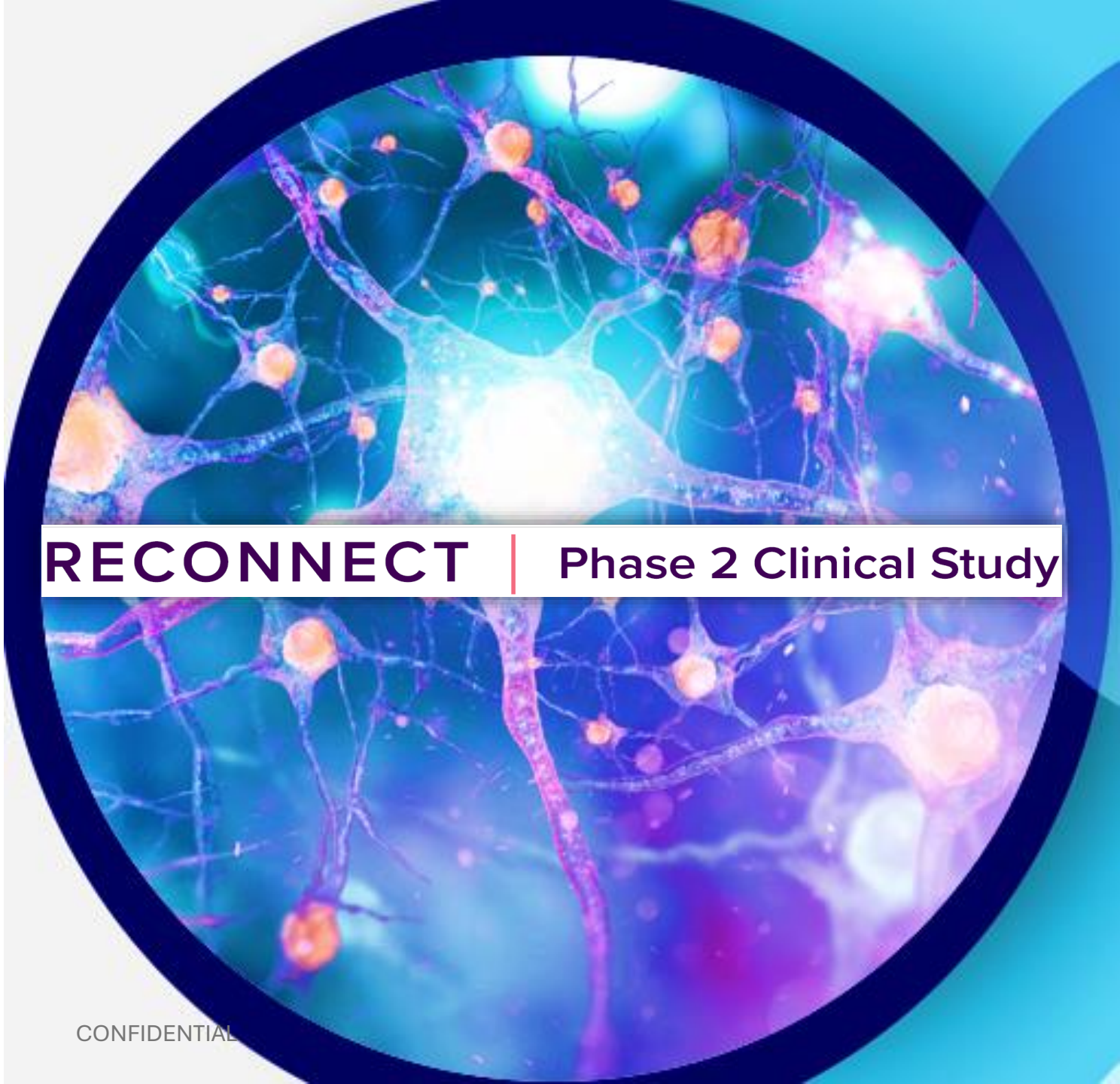
WORLDWIDE CLINICAL TRIALS

CONFIDENTIAL

Disclaimer

These slides are provided exclusively for the Investigator Meeting and are confidential. They must not be shared outside the study team. Please be aware that these slides are not intended for formal training purposes; all official training will be conducted using the SIV (Site Initiation Visit) slides.

Site Responsibilities & Roles



reunion NEUROSCIENCE

WORLDWIDE CLINICAL TRIALS

CONFIDENTIAL

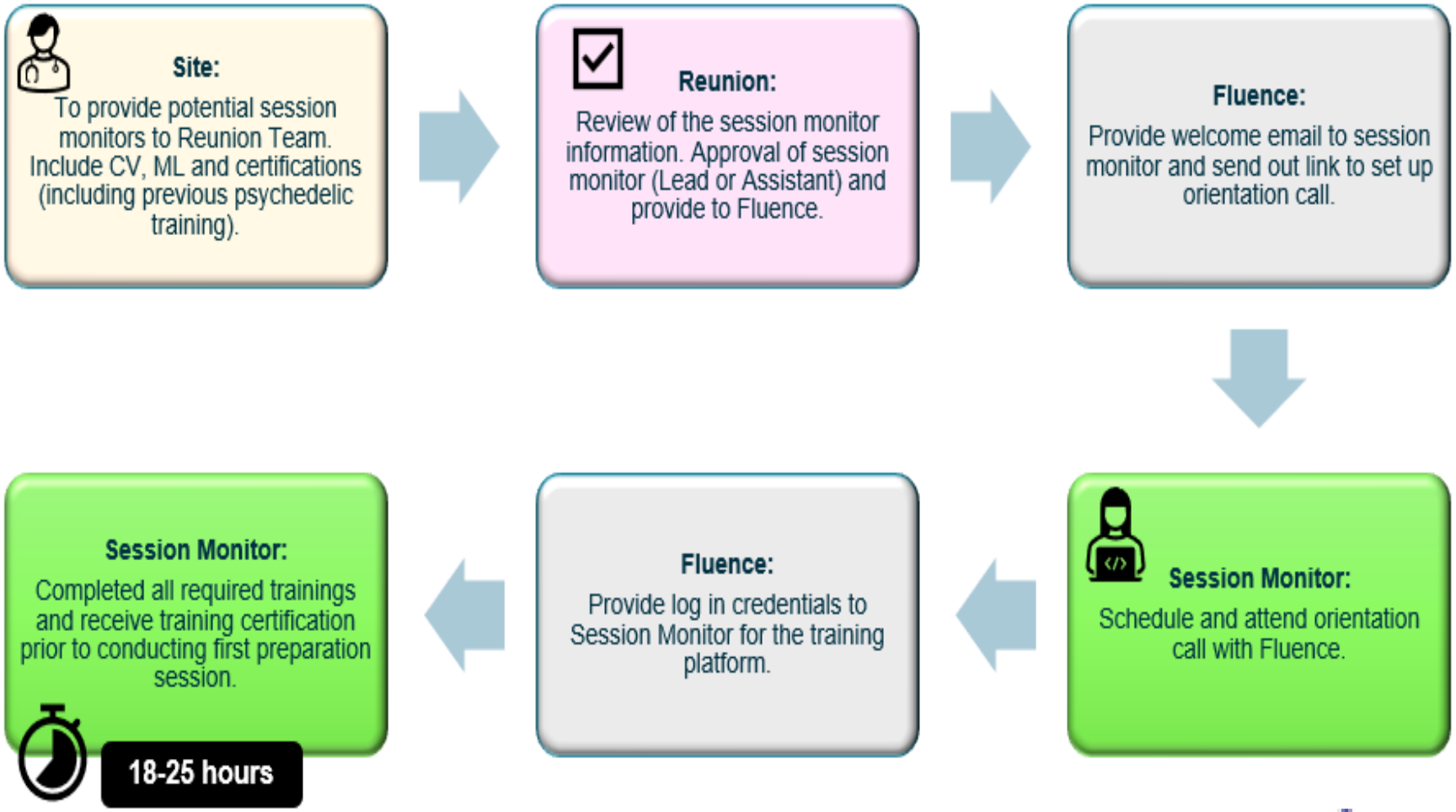
Agenda

- Training Expectations- Fluence & Raters
- Blinded vs Unblinded Staff
- Lessons Learned
- Site Management Team
- On-site monitoring

Fluence

Session Monitor Training

Fluence Session Monitor Training



Reunion Neuroscience

RE104-Assisted Treatment for Post-Partum Depression Study Monitor Training

A 9-Part Training with Self-Paced and Live Online Components to Prepare Therapists for work on Clinical Research Trials

About this Training

This therapist training portal includes:

- Background on RE104 and anticipated user experiences
- Current research relevant to psychedelic therapy in clinical trials
- Therapy manual background and knowledge checks
- MAPS Ethical Guidelines and knowledge checks
- Therapy Manual review and Adherence Criteria
- Video lectures and demonstrations
- Live-online instruction and role-plays
- Therapist competency assessment

reunion NEUROSCIENCE

Training Program Overview

- The following 5 live-online training sessions must be scheduled in order to complete the training. (**refer to the training portal for more detailed information about each session**):

  - **Orientation-** Complete an orientation to receive more information about the overall training process and have the opportunity to ask any questions.

  - **Role Play Practice Sessions 1 & 2-** Identify a practice partner. This should be a site colleague or other fellow trainee. If you do not have a practice partner, Fluence will assist in providing one for you.
    - Sign up for two role play practice sessions

  - **Trainer Feedback Session-** Complete a trainer feedback session after completion of your second role play practice session. Allow a period of 3 business days between your second role play practice session and your feedback session to allow the trainer to review your role plays.

  - **Competency Assessment-** Your competency assessment should be the final task you complete in the training.

Recommendation:
Zoom meetings will be scheduled via Calendly.
Schedule your 4 zoom meetings ahead of time, in parallel to your portal training.

Lessons Learned

Properly follow Fluence Instructions for live trainings

Do not wait to complete Fluence Training

Encourage your site Session Monitors to review what is expected and to plan it out

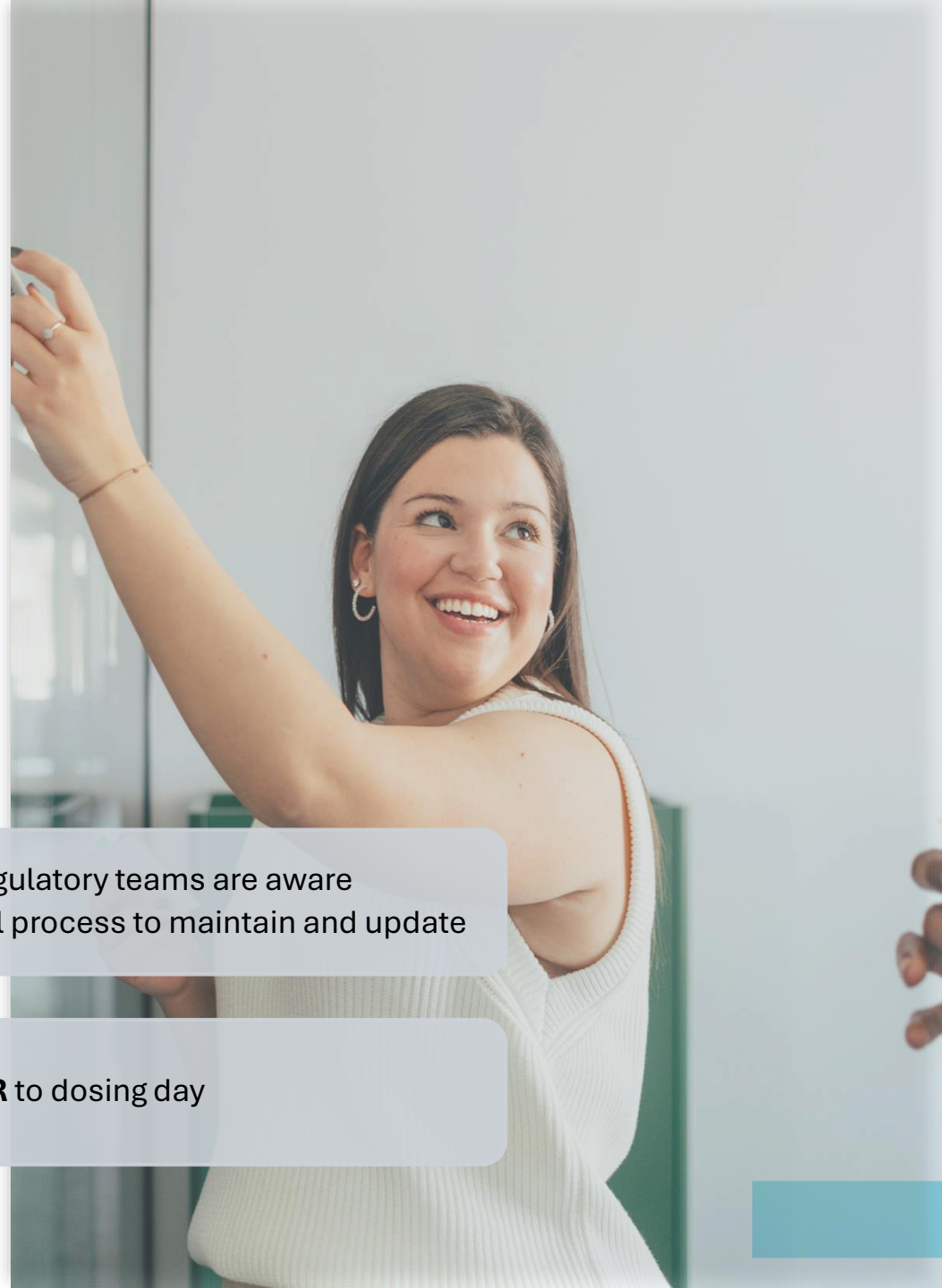
Sites that completed Fluence training in advance were able to activate in timely fashion

All Session Monitors and Raters must be listed on 1572

- Ensure your regulatory teams are aware
- Ensure internal process to maintain and update

When eCOA is live, it will be important to ensure raters have appropriate access

- Confirm **PRIOR** to dosing day



CONFIDENTIAL

RE104-201: Rater and Certification Process Program Overview

1. Sites Identify Raters

2. Trainee Experience Questionnaire (TEQ)

3. CAT Experience Review

4. Didactic Training* + Applied Skills Assessment

5. Certification

** External training certificate required for C-SSRS as applicable to role*

1. Identifying Site Raters: 3 Rater Roles

Blinded Independent Site Rater

Blinded to IP assignment and all other study assessments

Trained and certified to rate:

- SIGMA/MADRS
- SIGH-A/ HAM-A
- Blinding Assessment

Blinded Site Rater

blinded to IP assignment

Trained and certified to rate:

- SCID-5-CT
- SIGH-D/HAM-D 17
- CGI- I/S
- BPRS+
- C-SSRS

Can be same, "Dual Rater" role

PRO Administrator

blinded to IP assignment

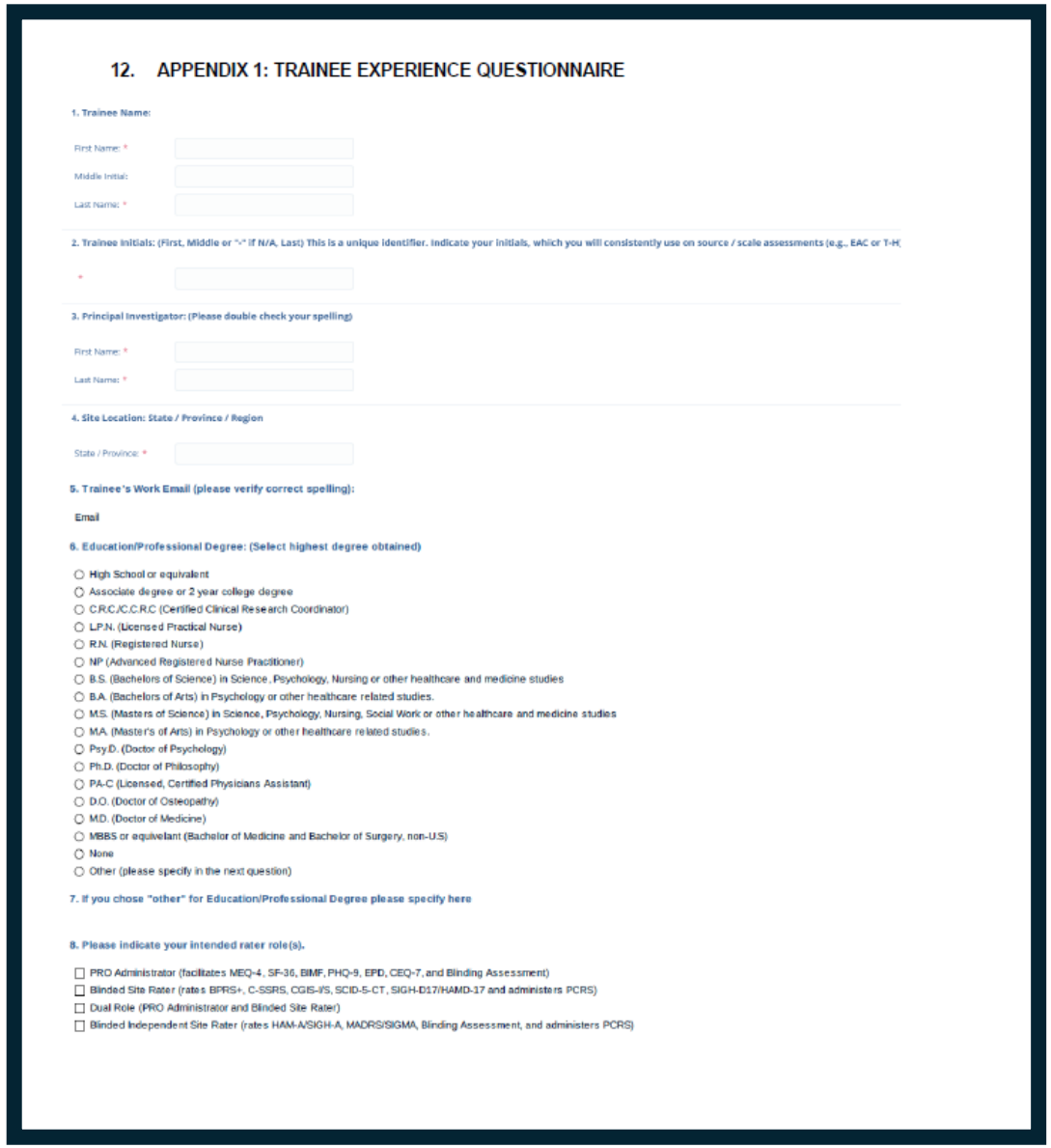
Trained and Certified to train and facilitate study participant ratings:

- MEQ-4
- CEQ-7
- PHQ-9
- BIMF
- SF-36
- EPDS
- Blinding Assessment

reunion NEUROSCIENCE

2. Trainee Experience Questionnaire (TEQ)

- All potential Trainees will be required to submit experience information via a Trainee Experience Questionnaire (TEQ)
- Up to 4 Trainees per site will be granted access to the TEQ via an emailed link requesting to submit



12. APPENDIX 1: TRAINEE EXPERIENCE QUESTIONNAIRE

1. Trainee Name:

First Name: *

Middle Initial:

Last Name: *

2. Trainee Initials: (First, Middle or "-" if N/A, Last) This is a unique identifier. Indicate your initials, which you will consistently use on source / scale assessments (e.g., EAC or T-H

*

3. Principal Investigator: (Please double check your spelling)

First Name: *

Last Name: *

4. Site Location: State / Province / Region

State / Province: *

5. Trainee's Work Email (please verify correct spelling):

Email

6. Education/Professional Degree: (Select highest degree obtained)

- ○ High School or equivalent
- ○ Associate degree or 2 year college degree
- ○ C.R.C./C.C.R.C (Certified Clinical Research Coordinator)
- ○ L.P.N. (Licensed Practical Nurse)
- ○ R.N. (Registered Nurse)
- ○ NP (Advanced Registered Nurse Practitioner)
- ○ B.S. (Bachelors of Science) in Science, Psychology, Nursing or other healthcare and medicine studies
- ○ B.A. (Bachelors of Arts) in Psychology or other healthcare related studies.
- ○ M.S. (Masters of Science) in Science, Psychology, Nursing, Social Work or other healthcare and medicine studies
- ○ M.A. (Master's of Arts) in Psychology or other healthcare related studies.
- ○ Psy.D. (Doctor of Psychology)
- ○ Ph.D. (Doctor of Philosophy)
- ○ PA-C (Licensed, Certified Physicians Assistant)
- ○ D.O. (Doctor of Osteopathy)
- ○ M.D. (Doctor of Medicine)
- ○ MBBS or equivelant (Bachelor of Medicine and Bachelor of Surgery, non-U.S)
- ○ None
- ○ Other (please specify in the next question)

7. If you chose "other" for Education/Professional Degree please specify here

8. Please indicate your intended rater role(s).

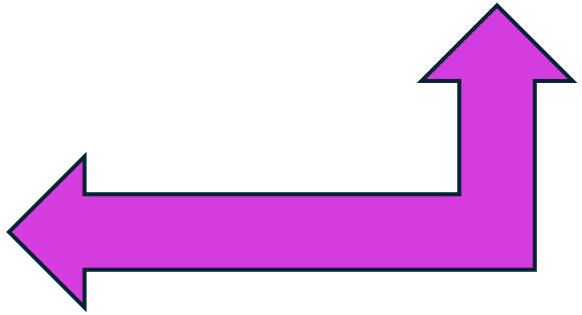
- ☐ PRO Administrator (facilitates MEQ-4, SF-36, BIMF, PHQ-9, EPD, CEQ-7, and Blinding Assessment)
- ☐ Blinded Site Rater (rates BPRS+, C-SSRS, CGIS-I/S, SCID-5-CT, SIGH-D17/HAMD-17 and administers PCRS)
- ☐ Dual Role (PRO Administrator and Blinded Site Rater)
- ☐ Blinded Independent Site Rater (rates HAM-A/SIGH-A, MADRS/SIGMA, Blinding Assessment, and administers PCRS)

3. CAT Experience Review

Experience Criteria			
Role/ Assessment	**Degree**	**Clinic or Research Experience with Postpartum Depression (PPD) or Major Depressive Disorder (MDD)**	**Experience with Assessment Measure**
Clinician Rated Scales			
Blinded Site Rater • SCID-5-CT • SIGH-D/HAM-D 17 • CGI- I/S • BPRS+ • C-SSRS	Medical Doctor (M.D) Doctor of Osteopathy (D.O) or medical doctor equivalent (i.e., Bachelor of Medicine Bachelor of Surgery (MBBS) Doctor of Philosophy (PhD, PsyD) Certified Physician's Associate (PA-C) Nurse Practitioner (ARNP) Master's Degree in Science, Psychology, Nursing or Social Work (MA/MS/MSW)	3 years	3 years
Blinded Independent Site Rater • SIGMA/MADRS • SIGH-A/ HAM-A	Medical Doctor (M.D) Doctor of Osteopathy (D.O) or medical doctor equivalent (i.e., Bachelor of Medicine Bachelor of Surgery (MBBS) Doctor of Philosophy (PhD, PsyD) Certified Physician's Associate (PA-C) Nurse Practitioner (ARNP) Registered Nurse (RN) Master's Degree in Science, Psychology, Nursing or Social Work (MA/MS/MSW)	3 years	3 years
Study Participant Rated Scales			
PRO Administrator • MEQ-4 • CEQ-7 • PHQ-9 • BIMF • SF-36 • EPD	Medical Doctor (M.D) Doctor of Osteopathy (D.O) or medical doctor equivalent (i.e., Bachelor of Medicine Bachelor of Surgery (MBBS) Doctor of Philosophy (PhD, PsyD) Certified Physician's Associate (PA-C) Nurse Practitioner (ARNP) Registered Nurse (RN) Master's or Bachelor Degree in Science, Psychology or Nursing (MA/MS BA/BS) Clinical Research Coordinator (CCRC)	1 year	1 year*

*Note: the experience of 1 year on at least one of the listed PROs will be accepted to qualify trainees for this role.

- CAT Team will review experience and follow-up with training material if approved.
- CAT recommends the following educational and experience criteria for the protocol assessments:



reunion NEUROSCIENCE

4. Didactic Training + Applied Skills Assessment

Rating Scale/ Training Program	Training Method	Approximate Time (minutes)
Blinded Site Rater/ Blinded Independent Site Rater, PRO Administrator	Didactic, vIM /webinar or self-paced online training portal	**Total 30 minutes**
• CAT Rater Training & Certification Process Overview	Didactic, vIM /webinar or self-paced online training portal (WLC)	30 minutes
Blinded Site Rater		**Total 2 hours**
• CGI-I/ S • SCID-5-CT • SIGH-D17/HAM-D • C-SSRS Overview • BPRS+	Didactic, vIM /webinar or self-paced online training portal (WLC)	90 minutes
• Placebo Control Reminder Script (PCRS)	Didactic, vIM /webinar or self-paced online training portal (WLC)	30 minutes
PRO Administrator		**Total 30 minutes**
• MEQ-4 • SF-36 • BIMF • PHQ-9 • EPD • CEQ-7 • Blinding Assessment	Didactic, vIM /webinar or self-paced online training portal (WLC)	30 minutes
Blinded Independent Site Rater		**Total 110 minutes**
• SIGMA • HAM-A/SIGH-A • Blinding Assessment	Didactic, vIM /webinar or self-paced online training portal (WLC)	40 minutes
• Applied Skills Assessment (ASA)	Self-paced ASA exercise	40 minutes
• Placebo Control Reminder Script (PCRS)	Didactic, vIM /webinar or self-paced online training portal (WLC)	30 minutes

reunion NEUROSCIENCE

Certificate of Achievement

presented to

WORLDWIDE
CLINICAL TRIALS

YOUR NAME

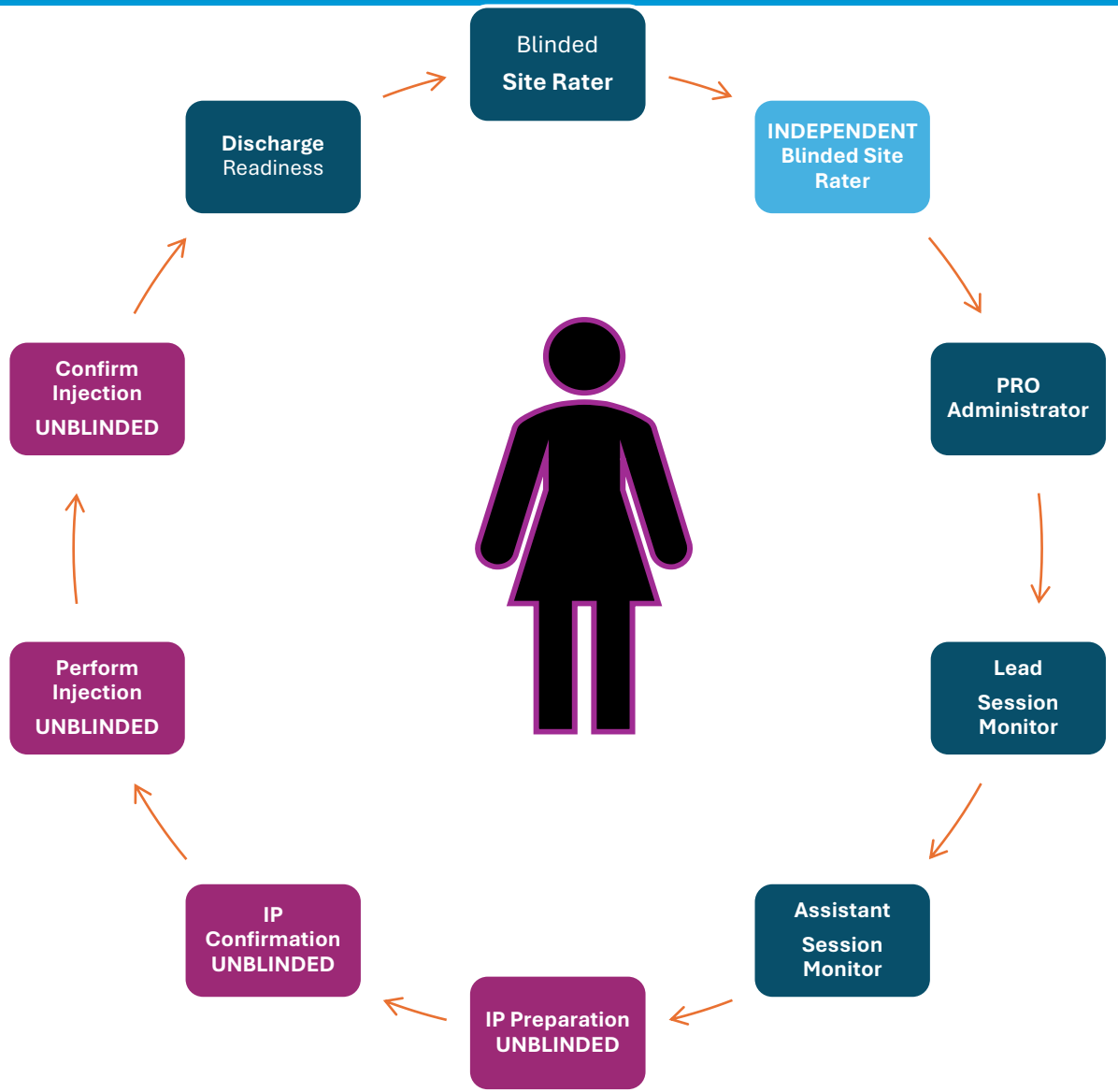
for the completion of

Study Role/Course Name

Completed on XX-XXX-XXXX

Blinded vs Unblinded Staff

Dosing Day Roles



Site Personnel Assignment Worksheet

WORLDWIDE CLINICAL TRIALS	Reunion Neuroscience	RE104-201-PPD V1.0 17May2024

SITE PERSONNEL ASSIGNMENT WORKSHEET

Principal Investigator:		Site Number:	
Subject ID:		Dosing Date:	

The purpose of this worksheet is to assist sites and CRAs with the identification of site personnel and the roles they will take for the subject. Please ensure that only delegated and appropriately trained personnel are completing their assigned task. File this worksheet in the subject's source documents.

Role	Name of Site Personnel
Blinded Site Rater (*Clinician Rater*)	
Blinded Independent Rater (*Efficacy Rater*)	
PRO Administrator	
Lead Session Monitor	
Assistant Session Monitor	
IMP Administrator (Unblinded)	
IMP Confirmation (Unblinded)	

If possible, all scales should be completed by a consistent rater. Assigned Session Monitors should also remain consistent for an individual throughout the study. Please document if there was a change in a rater or a Session Monitor from the names listed above during the subject's participation. Include role, visit, name of the site team member, and reason for change.

Role	Visit	Name of Site Personnel	Reason for Change

CONFIDENTIAL

Reminders

Unblinded Team

- Register in IRT as Unblinded
- Confirm IP receipt
- IP Preparation
- IP Preparation Confirmation
- Dosing Administration
- Dosing Confirmation
- IP Accountability
- Assist in Unblinded IMV
- Only access to Pharmacy ISF
- May be utilized to assist with uploading data to eCOA once live (if applicable)

Blinded Team

- Will not conduct IP accountability
- Will not be present for dosing
- Only register patient in IRT
- Will not access pharmacy ISF
- May not perform any unblinded tasks

IP Dose Formulation Worksheet

Unblinded

reunion NEUROSCIENCE | IP Dose Formulation Worksheet for RE104-201-PPD

Subject Number:		Subject Date of Birth: (MM/DD/YYYY)	
Site Number:		Preparation Date: (MM/DD/YYYY)	

Obtain IP vials as listed in IRT Unblinded Dispensation Confirmation (Randomization) e-Mail Notification Details and acclimate to room temperature for at least 30-60 minutes.

RE104 for Injection Vial ID (Drug Unit):		Time Out of Freezer: (HH:MM):	
RE104 Diluent Vial IDs (Drug Units):	1:	2:	

!IMPORTANT! This preparation must be done following site aseptic procedure:

IP Preparation Steps	Completed by (Initials)
Read and understand the detailed preparation instructions listed in Appendix 2 of the Pharmacy Manual before initiating this preparation.	
Ensure that appropriate aseptic conditions and necessary material and equipment are in place before initiating this preparation.	
Confirm that the RE104 Diluent vials are clear and essentially free of visible particles or foreign material.	
Document start time of preparation. Note: Start Time of Preparation - Time out of Freezer > 30 min.	Time (HH:MM):
Pull approximately 0.6 mL from each diluent vial using the 3mL syringe and expel the excess volume to 1.1mL. Confirm the volume of RE104 Diluent is 1.1mL	
Transfer the 1.1mL of RE104 Diluent into the RE104 for Injection vial by carefully injecting the content of the syringe into the RE104 for Injection vial. **DO NOT** release the plunger, hold it down while removing the needle from the vial.	
Swirl the vial for a minimum of 30 seconds and invert 5 times until the solution is essentially clear and free of any particles. Document the time of reconstitution. **!IMPORTANT!** IP must be administered within **4 hours** of reconstitution.	Time (HH:MM):
Confirm that the reconstituted RE104 vial is clear, colorless to slightly yellow to yellow-brown solution, essentially free of visible particles or foreign material.	

reunion NEUROSCIENCE | IP Dose Formulation Worksheet for RE104-201-PPD

IP Preparation Steps	Completed by (Initials)
Write the subject ID and site number in the space provided on the vial label.	
Complete randomization and Drug Accountability documentation.	
Without hiding the graduated marks, label the 1mL syringe and transport box in accordance with the Pharmacy Manual section 8.3	
Package the labeled transport box with: 1- Reconstituted RE104 vial 2- Labelled 1 mL dosing syringe 3- Sterile alcohol prep pad 4- Sterile gauze pad 5- Adhesive bandages	

Completed By:

		Date

Reviewed By

		Date

reunion NEUROSCIENCE
CONFIDENTIAL

IP Administration Worksheet

Source Document Worksheet created to document IP administration
(maintain in subject's source)

Blinded

reunion NEUROSCIENCE

IP Administration Worksheet for RE104-201-PPD

DOCUMENT TO BE FILED IN THE SUBJECT'S SOURCE DOCUMENTATION

Subject Number:		Subject Date of Birth: (MM/DD/YYYY)	
Site Number:		Administration Date: (MM/DD/YYYY)	

IP must be administered **subcutaneously** by an appropriately qualified unblinded nurse or designated staff as documented on the Delegation of Authority Log. The following are requirements to maintain blind, during the administration process.

	Completed by (Initials)	Date
Administrator ensures all blinding precautions are in place, documents are shielded, preparation of the dosing syringe and study drug administration are blinded to the patient (e.g.: participant is behind a blinding curtain or places eye mask over their eyes). **Remove any blinded staff from the dosing area**		
Administrator ensures the required amount of RE104 solution (please reference Pharmacy Manual) has been drawn into the dosing syringe per treatment assignment. For reference: Low Dose: 1.5 mg RE104 (0.05 mL) High Dose: 30 mg RE104 (1.0 mL)		
Administrator will present the vial to a second unblinded person. The second unblinded person will confirm the volume of RE104 aligns with the treatment assignment prior to administration.		

Administered By:

Print **Sign** **Date**

Confirmed By:

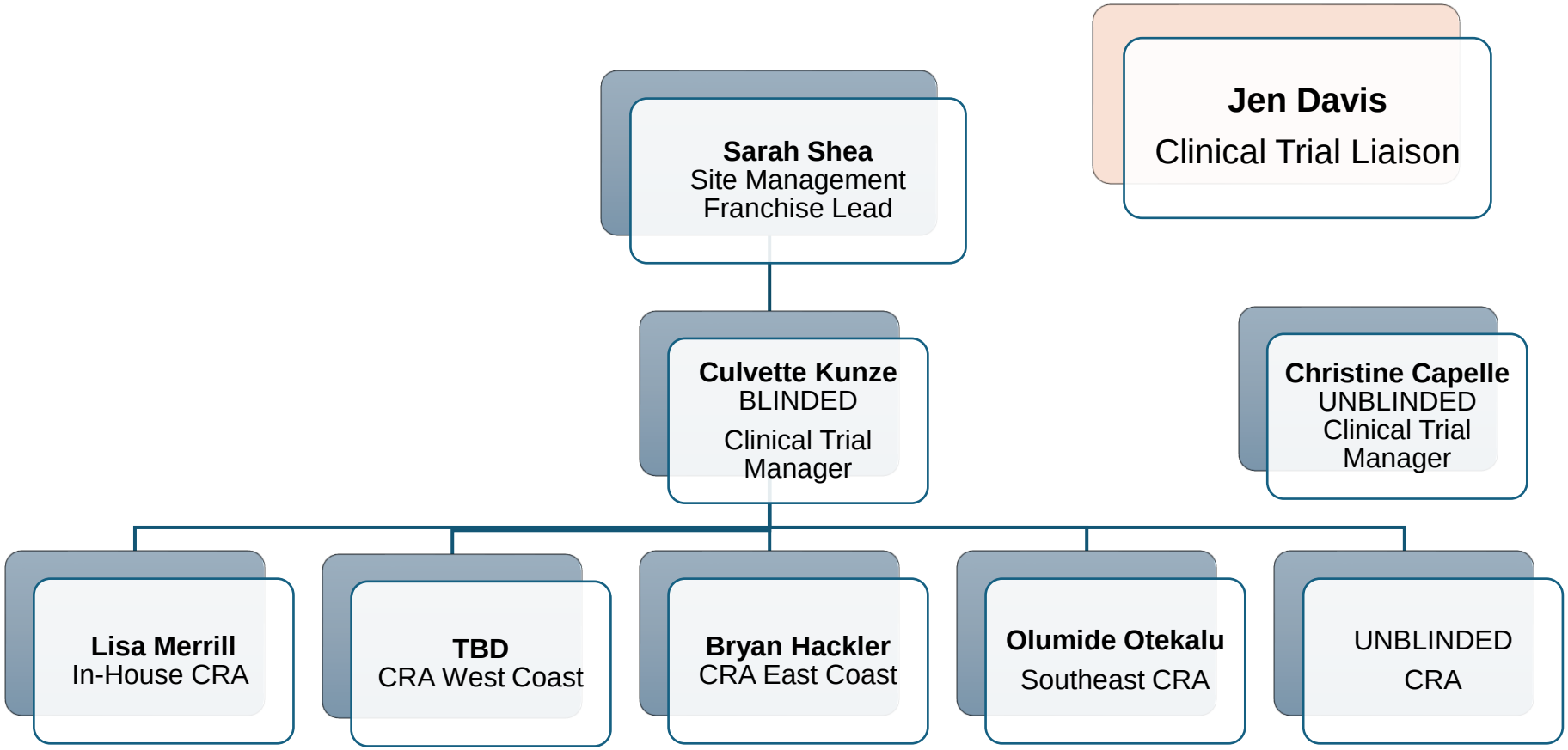
Print **Sign** **Date**

Effective Date: 2024-06-12
Version Number 01

CONFIDENTIAL

Page 1 of 1

Worldwide Site Management Team



CONFIDENTIAL

Contacts

Your **In-house CRA** is your primary contact for

- Operational questions
- Data query follow-up
- Access and training requests for vendor portals

Your **field CRA** is your contact for

- Monitoring visits
- Protocol deviation management
- Action Item follow up & resolution

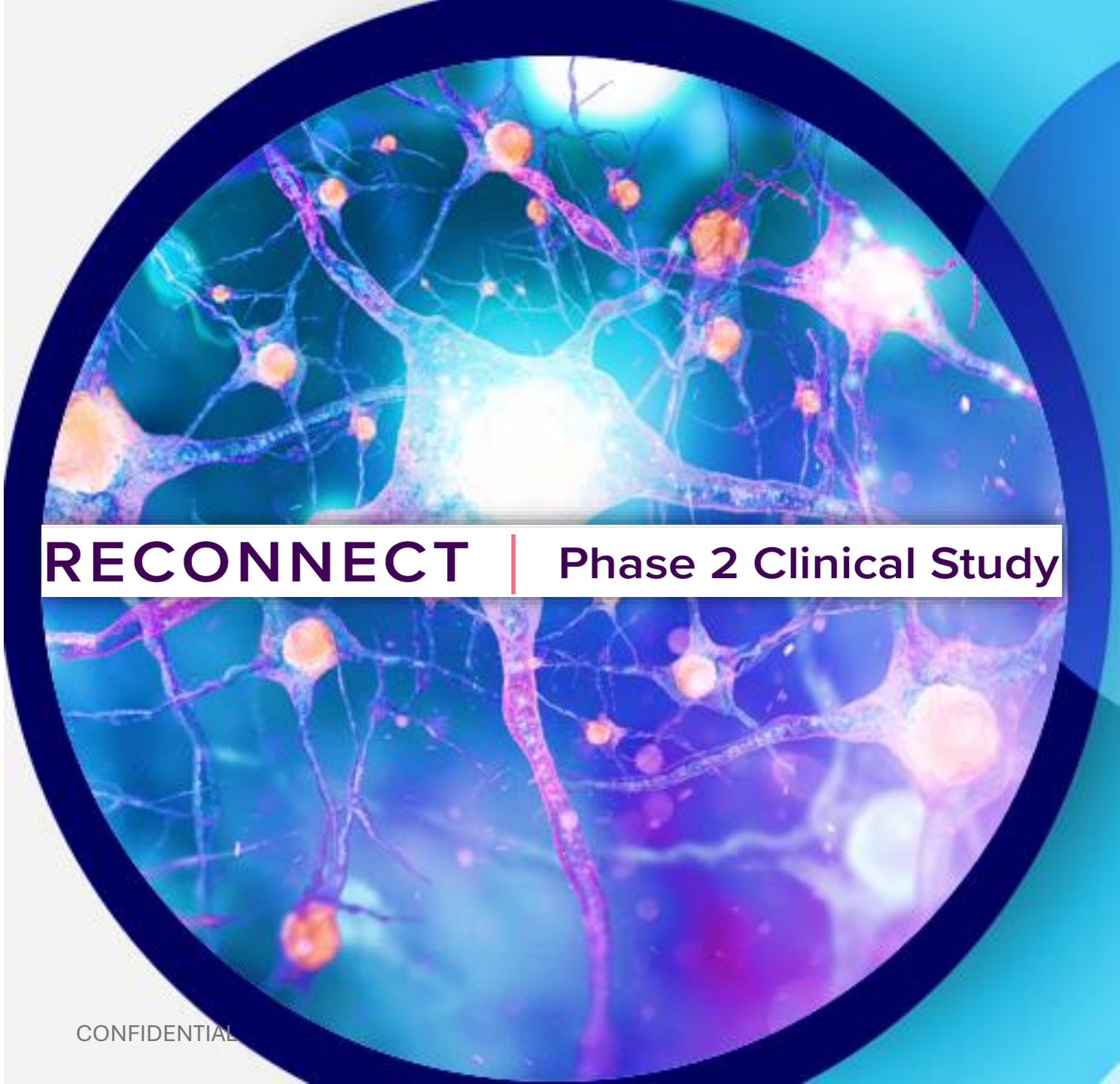
Vendors provide technical support for their **portals** and **equipment** (Zelta, Suvoda*, ACM)

*Suvoda access requests- CTM

On-site monitoring visit frequency will be dependent upon:

- First IMV expected to occur within 2 weeks of first subject dosing.
- Site recruitment and enrollment progress.
- Specific site issues, protocol adherence, data quality and central monitoring findings.
- Continuously evaluated by the Global Project Lead (GPL) and Clinical Trial Manager (CTM).

RE104-201-PPD
Investigator Meeting Slides



reunion NEUROSCIENCE

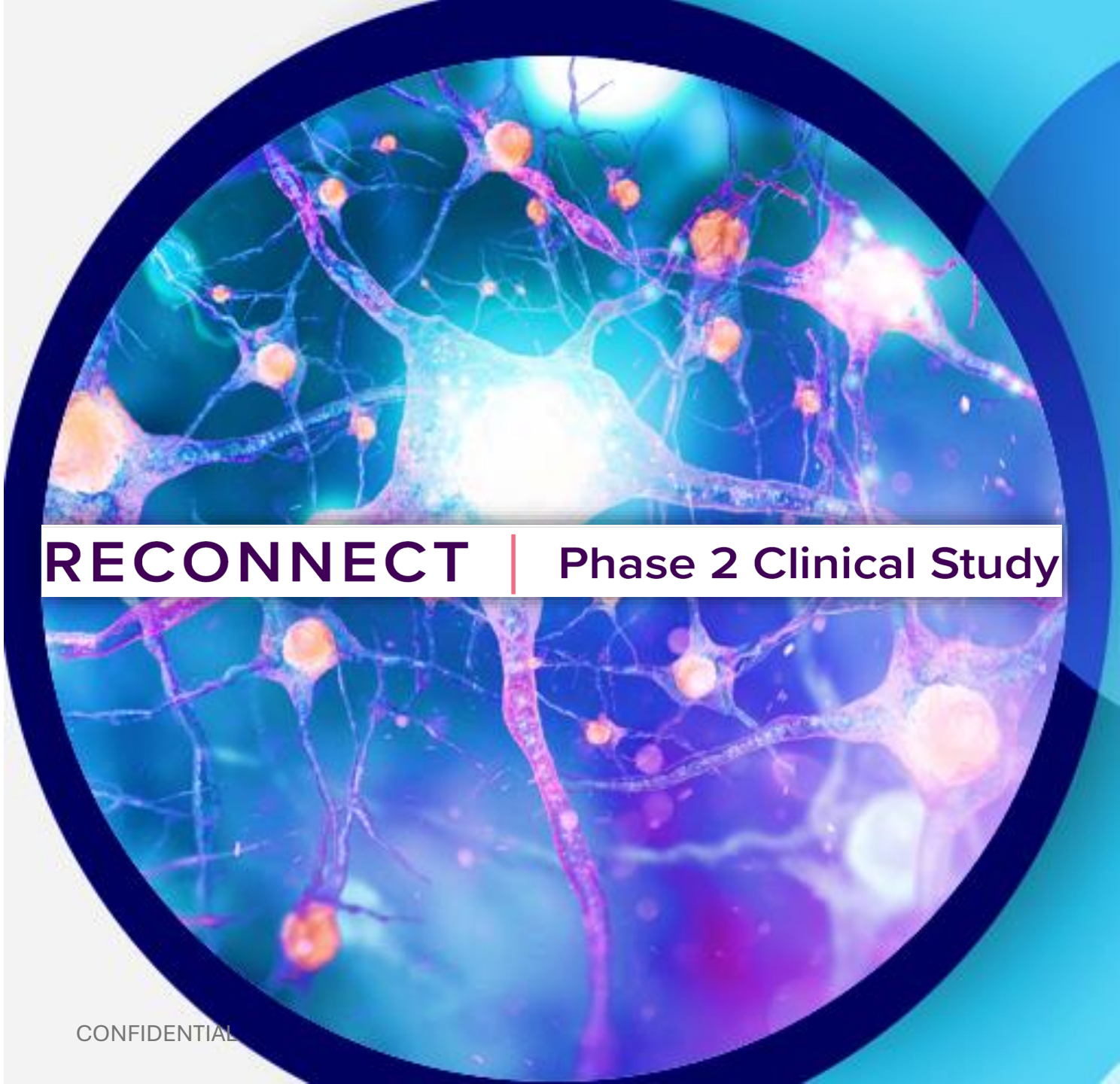
WORLDWIDE CLINICAL TRIALS

CONFIDENTIAL

Disclaimer

These slides are provided exclusively for the Investigator Meeting and are confidential. They must not be shared outside the study team. Please be aware that these slides are not intended for formal training purposes; all official training will be conducted using the SIV (Site Initiation Visit) slides.

Eligibility Process Overview



reunion NEUROSCIENCE

WORLDWIDE CLINICAL TRIALS

CONFIDENTIAL

Agenda

- Screening Visit overview
- Eligibility Review Roadmap
- Medical Records Expectation
- Trial Interactive & EDC
- Site Initiation to Activation

The goal of this session is to provide:

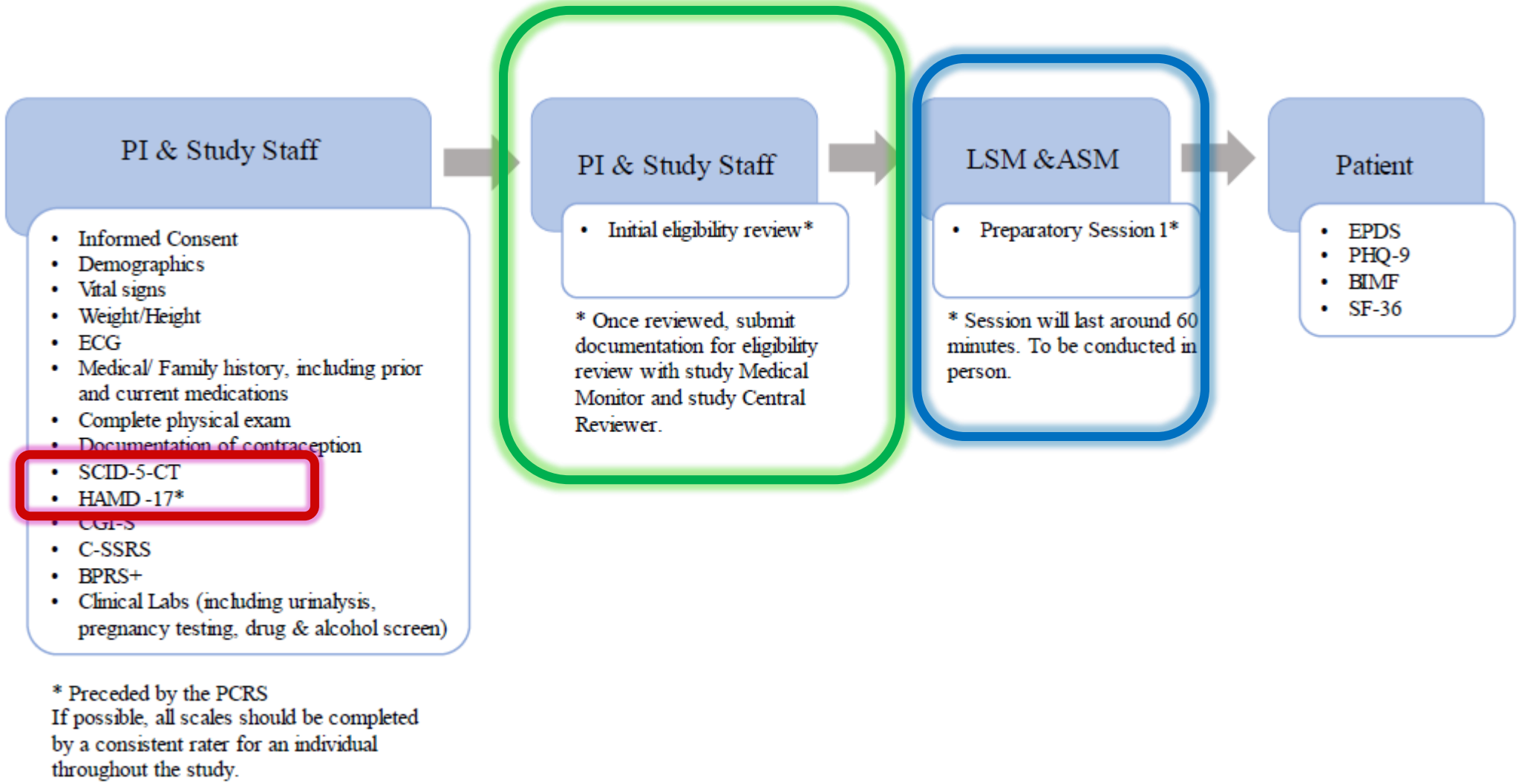
- High-level overview of the targeted eligibility process
- Discuss required medical records

NOTE: Targeted eligibility process training will be provided during the SIV please refer to SIV slides for more details about related systems and processes

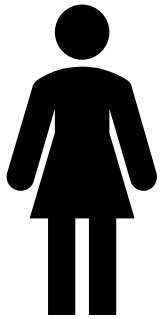
- Walk through from screening to dosing
- Discuss what is needed for SIV
- Pathway to Activation
- Q + A

CONFIDENTIAL

Screening Visit



Eligibility Review Process



SCREENING VISIT
Data entry, Labs, ECG, Scales

Schedule planned dosing day, provide date to Worldwide team member

Labs, ECG, additional information reviewed by Site Investigator.

Site Investigator determines and confirms eligibility.

Uploaded to Trial Interactive
Subject Eligibility Checklist +
Medical records (redacted) +
SCID-5-CT & Audio*

Clinical Assessment & Technology (CAT) team reviews subject for eligibility.

Not Eligible:
Site is notified by Medical Monitor.

Site files all correspondence in subject's source documents.

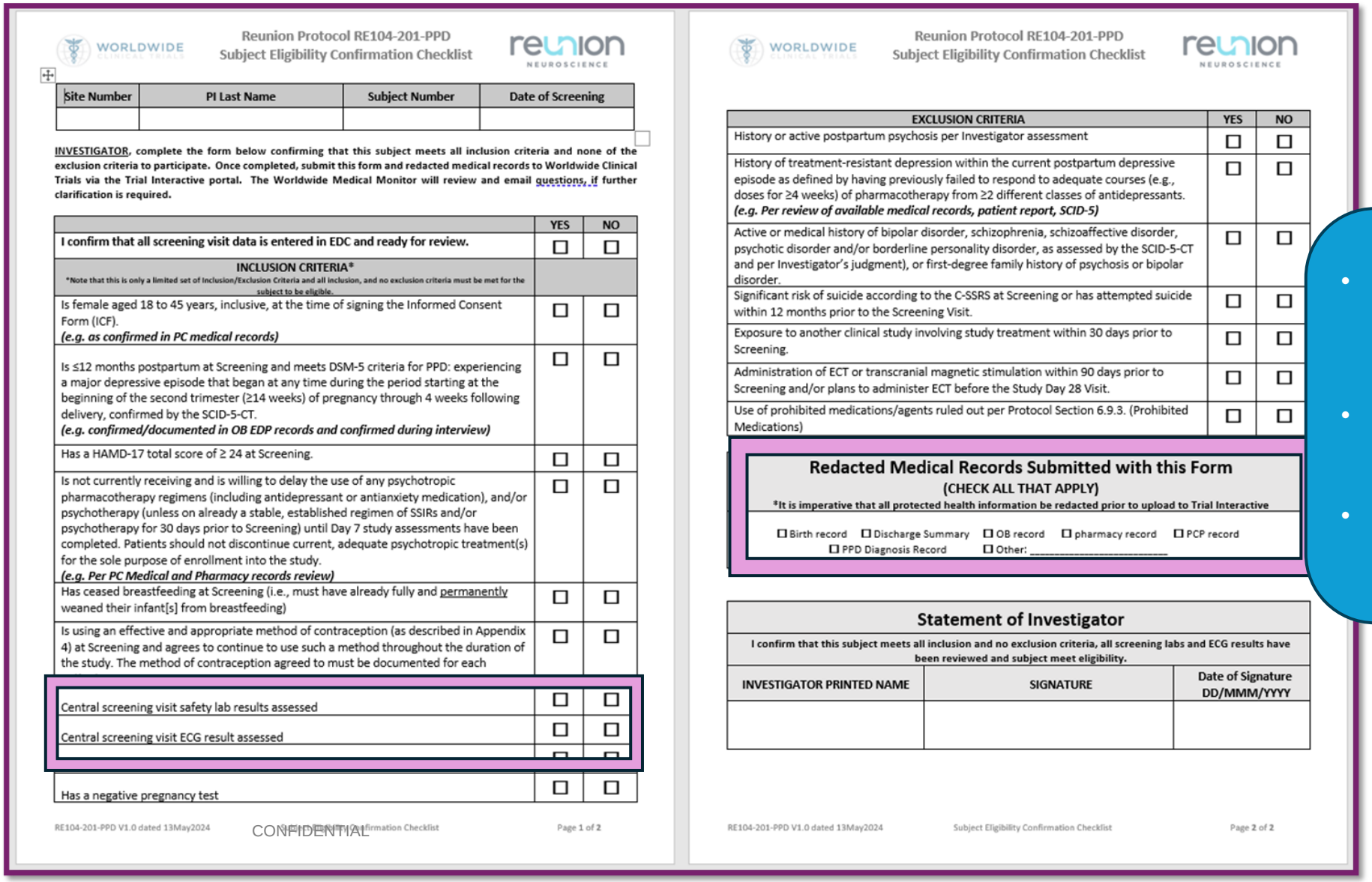
Medical Monitor reviews for eligibility (EDC data, Eligibility Checklist, Medical records)

ELIGIBLE
Site is notified. May enroll at Investigator's discretion

Site files all correspondence in subject's source documents

* Additional scales to be uploaded when using paper.

Subject Eligibility Confirmation Checklist



Reunion Protocol RE104-201-PPD
Subject Eligibility Confirmation Checklist

Site Number	PI Last Name	Subject Number	Date of Screening

INVESTIGATOR, complete the form below confirming that this subject meets all inclusion criteria and none of the exclusion criteria to participate. Once completed, submit this form and redacted medical records to Worldwide Clinical Trials via the Trial Interactive portal. The Worldwide Medical Monitor will review and email questions, if further clarification is required.

	YES	NO
I confirm that all screening visit data is entered in EDC and ready for review.	☐	☐
INCLUSION CRITERIA* *Note that this is only a limited set of Inclusion/Exclusion Criteria and all inclusion, and no exclusion criteria must be met for the subject to be eligible.*		
Is female aged 18 to 45 years, inclusive, at the time of signing the Informed Consent Form (ICF). ***(e.g. as confirmed in PC medical records)***	☐	☐
Is ≤12 months postpartum at Screening and meets DSM-5 criteria for PPD: experiencing a major depressive episode that began at any time during the period starting at the beginning of the second trimester (≥14 weeks) of pregnancy through 4 weeks following delivery, confirmed by the SCID-5-CT. ***(e.g. confirmed/documented in OB EDP records and confirmed during interview)***	☐	☐
Has a HAMD-17 total score of ≥ 24 at Screening.	☐	☐
Is not currently receiving and is willing to delay the use of any psychotropic pharmacotherapy regimens (including antidepressant or antianxiety medication), and/or psychotherapy (unless on already a stable, established regimen of SSIRs and/or psychotherapy for 30 days prior to Screening) until Day 7 study assessments have been completed. Patients should not discontinue current, adequate psychotropic treatment(s) for the sole purpose of enrollment into the study. ***(e.g. Per PC Medical and Pharmacy records review)***	☐	☐
Has ceased breastfeeding at Screening (i.e., must have already fully and permanently weaned their infant[s] from breastfeeding)	☐	☐
Is using an effective and appropriate method of contraception (as described in Appendix 4) at Screening and agrees to continue to use such a method throughout the duration of the study. The method of contraception agreed to must be documented for each	☐	☐
Central screening visit safety lab results assessed	☐	☐
Central screening visit ECG result assessed	☐	☐
	☐	☐
Has a negative pregnancy test	☐	☐

RE104-201-PPD V1.0 dated 13May2024 Subject Eligibility Confirmation Checklist Page 1 of 2

Reunion Protocol RE104-201-PPD
Subject Eligibility Confirmation Checklist

EXCLUSION CRITERIA	YES	NO
History or active postpartum psychosis per Investigator assessment	☐	☐
History of treatment-resistant depression within the current postpartum depressive episode as defined by having previously failed to respond to adequate courses (e.g., doses for ≥4 weeks) of pharmacotherapy from ≥2 different classes of antidepressants. ***(e.g. Per review of available medical records, patient report, SCID-5)***	☐	☐
Active or medical history of bipolar disorder, schizophrenia, schizoaffective disorder, psychotic disorder and/or borderline personality disorder, as assessed by the SCID-5-CT and per Investigator's judgment), or first-degree family history of psychosis or bipolar disorder.	☐	☐
Significant risk of suicide according to the C-SSRS at Screening or has attempted suicide within 12 months prior to the Screening Visit.	☐	☐
Exposure to another clinical study involving study treatment within 30 days prior to Screening.	☐	☐
Administration of ECT or transcranial magnetic stimulation within 90 days prior to Screening and/or plans to administer ECT before the Study Day 28 Visit.	☐	☐
Use of prohibited medications/agents ruled out per Protocol Section 6.9.3. (Prohibited Medications)	☐	☐

Redacted Medical Records Submitted with this Form
(CHECK ALL THAT APPLY)
It is imperative that all protected health information be redacted prior to upload to Trial Interactive

☐ Birth record ☐ Discharge Summary ☐ OB record ☐ pharmacy record ☐ PCP record
☐ PPD Diagnosis Record ☐ Other: _____

Statement of Investigator

I confirm that this subject meets all inclusion and no exclusion criteria, all screening labs and ECG results have been reviewed and subject meet eligibility.

INVESTIGATOR PRINTED NAME	SIGNATURE	Date of Signature DD/MMM/YYYY

RE104-201-PPD V1.0 dated 13May2024 Subject Eligibility Confirmation Checklist Page 2 of 2

- PI to complete checklist, include confirmation on the review of central lab results and central ECG result.
- Include medical records that will be provided.
- Send in with eligibility documents to Trial Interactive.

CONFIDENTIAL

Medical records – Expectations

Utility of Expected Medical Records

- **Delivery Hospital Discharge, Birth Certificate** – *to provide confirmation of infant's DOB & mother's age, Delivery history*
- **Edinburgh Postnatal Depression Scale (EPDS)**- *can confirm time of onset of depressive* symptoms
- **Primary Care records**- *Med History*
- **Pharmacy records**–Prior and ConMed review
- **OB Records-** *additional check on any diagnosis, conmeds during pregnancy*

Patients with NO PPD Diagnosis or Treatment
No prior Psych History

- Delivery Hospital Discharge and Birth Certificate
- **EPDS** (provided by OB or Pediatrician)
- Pharmacy records
- PCP records
- OB records

Patients with PPD Diagnosis or Treatment
and/or Prior Psych History

- All records listed for patients with NO PPD or Psych Hx

+

- **Treating physician records (for minimum last year of OB, therapist, or other as applicable)**

- For patients with incomplete or inadequate hospital records, additional steps of eligibility will be implemented, e.g., review of diagnostic interview (SCID-CT) or severity assessment (HAM-D) audio recordings to confirm the diagnosis

Medical Records Review Process

The purpose of the targeted eligibility process is to ensure the **safety and quality** of the subjects that are being considered for enrollment

Sites will be required to send the following to Worldwide for Eligibility Review:

- ✓ Redacted medical records
- ✓ All available sources of medical history (including external and historical medical records) should be reviewed as sources of data (original data source)
- ✓ Subject Eligibility Confirmation Checklist, signed by treating Investigator (physician)
  - ❖ Purpose is to document subject's eligibility
  - ❖ Confirm his/her review of this information
  - ❖ Agreement that the subject is eligible to participate in the trial

CAT Data Surveillance: Screening Eligibility Review

CAT Study eMailbox:
smp_re104-201_cat@worldwide.com

ALL screening assessments completed on paper prior to the CLARIO eCOA being available are to be submitted to CAT for review and eligibility confirmation. This includes audio recordings as well.

Once CLARIO eCOA is live:

- **Upload to Trial Interactive Portal (TI)** within 2 business days of the screening visit
  - **SCID paper administration**
  - **Scanned copy of the SCID-CT scale source documents**

  All other scales will be reviewed in the CLARIO portal

Ensure submitted documents do not contain any patient identifying information (e.g. Name, DOB, address, etc.)

- ✓ Access to the portal and upload instructions will be provided separately to identified site personnel ahead of site activation
- ✓ In the rare event, any other scales were administered using a paper emergency back-up, these are to be uploaded to the TI portal for review as well when applicable

Data Surveillance Process for Screening Visit

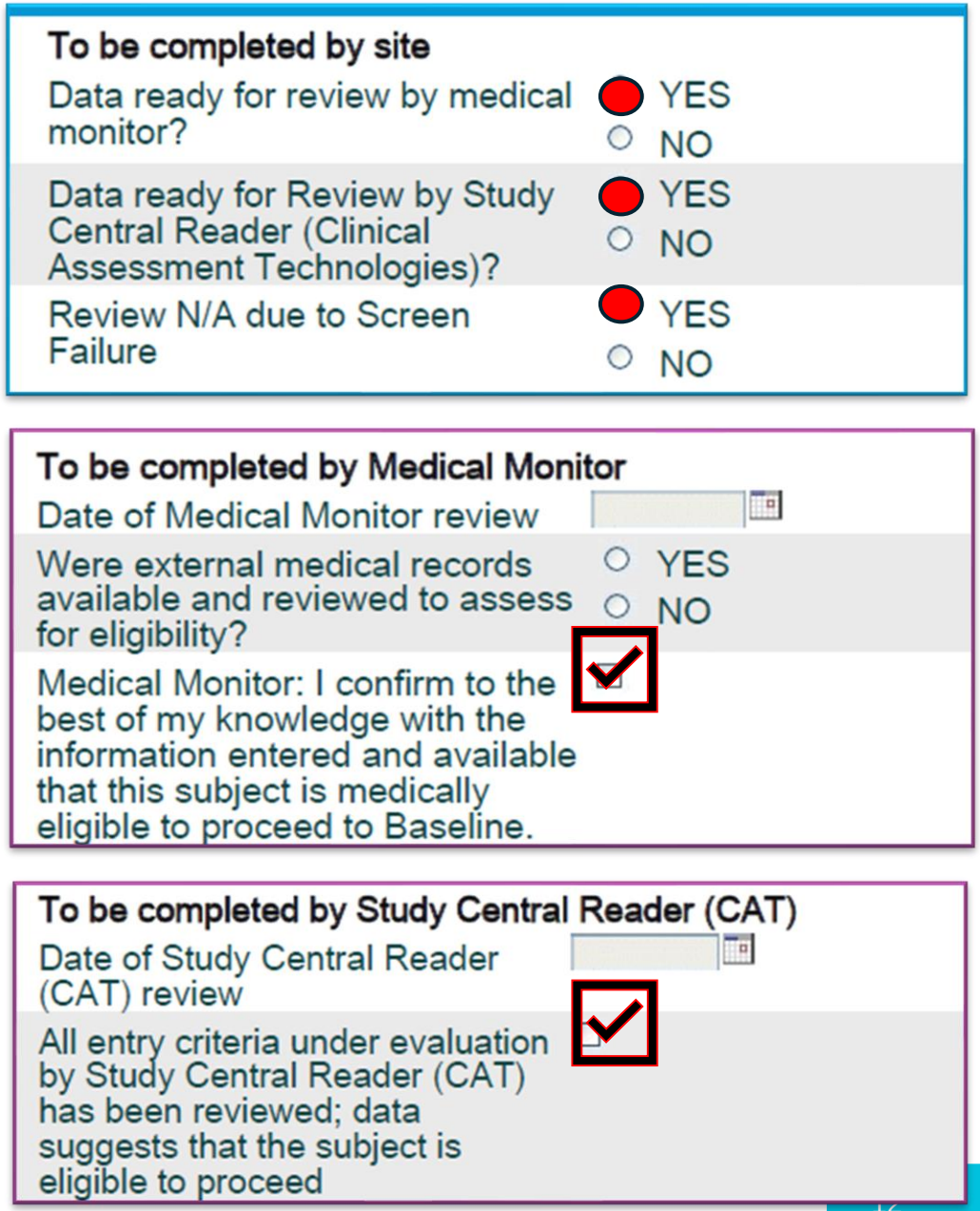
Sites must first check data is ready to be reviewed by CAT & MM in the EDC

CAT & MM are notified data is ready for review

CAT & MM complete eligibility review and determination is entered in the EDC
[Screening Visit folder]

- Queries may be entered if CAT/ MM have questions regarding data.
- Additional questions may be sent via email if not easily resolved via EDC query

☑ Sites must confirm subject is eligible via EDC page before proceeding to Baseline Visit. <u>If check is not present for both MM & CAT, **do not proceed**</u>

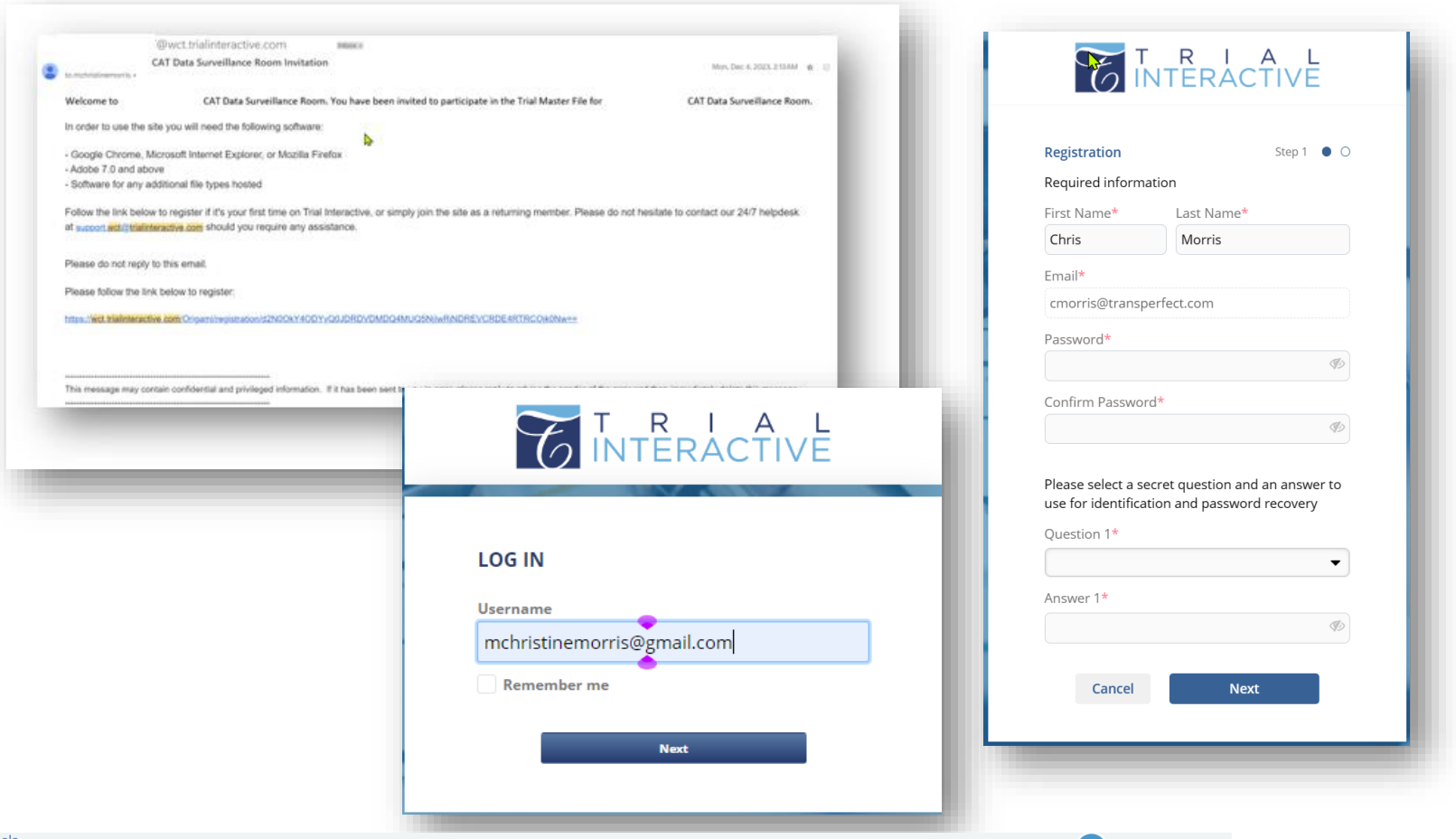


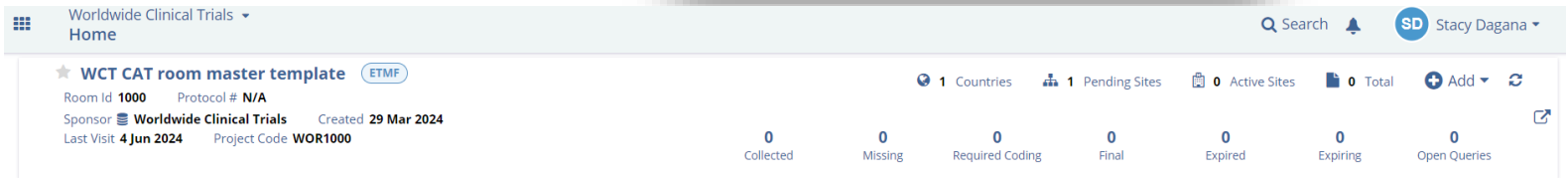
Trial Interactive

- Worldwide's Clinical Assessment Technologies (CAT) team will be performing eligibility review on the SCID-5-CT paper scale.
- Sites are requested to provide CAT with a scanned copy of the completed SCID-5-CT scale within 2 business days of each visit.
- Scale source documents are submitted via email to the Trial Interactive platform.
  - Create New Email
  - Attach Documents
  - Submit to room email address: RE104-201-PPD_CAT@wct.trialinteractive.com
- File attachments up to 100mb can be submitted.
- If the CAT team has questions about your submission, they will send you a query through the workflow.
- You will receive an email notification with a link to respond, or you can reply directly via email.
- For troubleshooting or assistance, please contact your CAT team at RE104-201-PPD_CAT@wct.trialinteractive.com

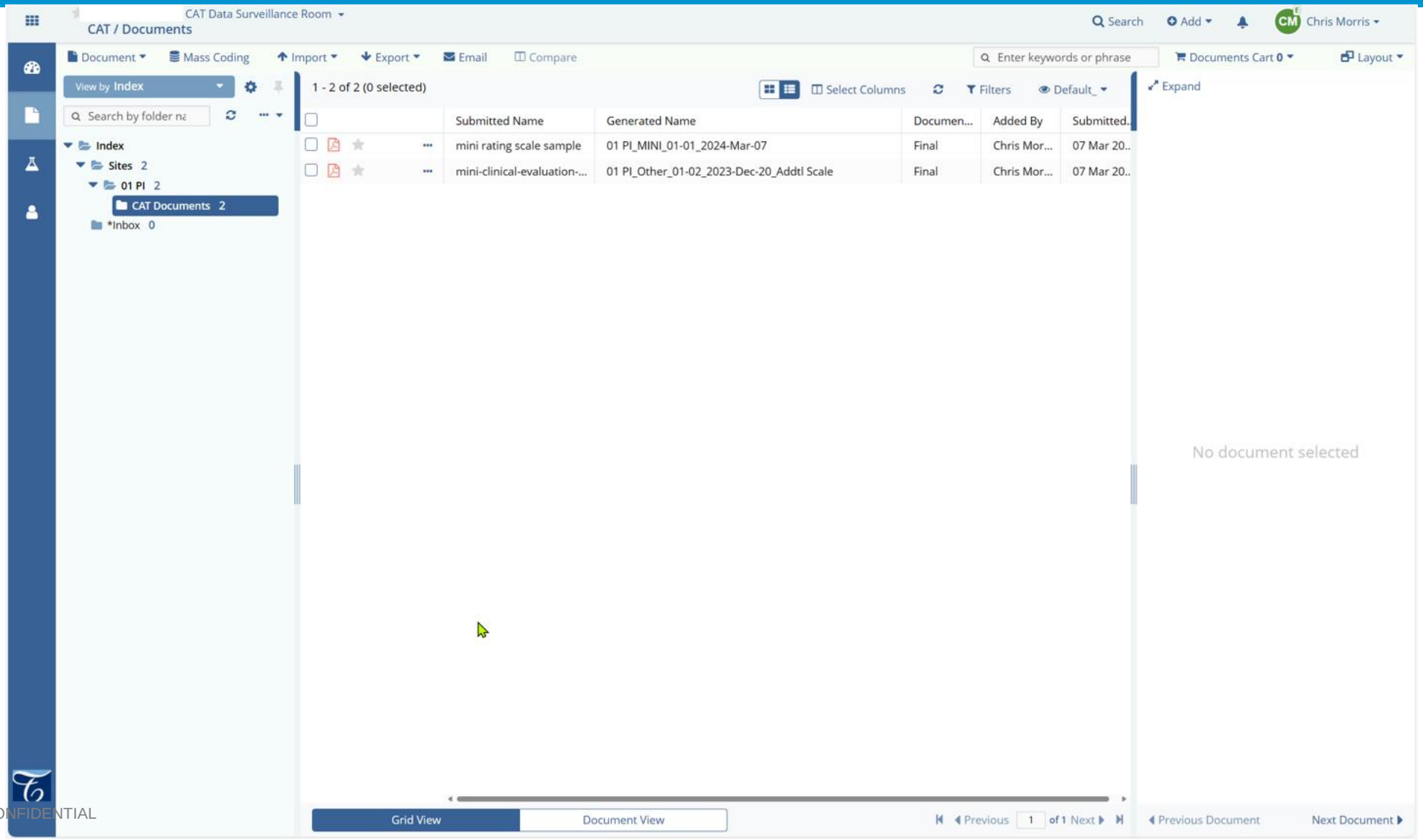
Logging Into The System

- Go to https://wct.trialinteractive.com
- Log in using your credentials
  - Email Address
  - Password
- Note: The first time you log into TI, you will click on the registration link you received via email, and be asked to create a password recovery question
- Subsequent logins, you may bookmark the room directly, or navigate to it from the main page after logging into the system.



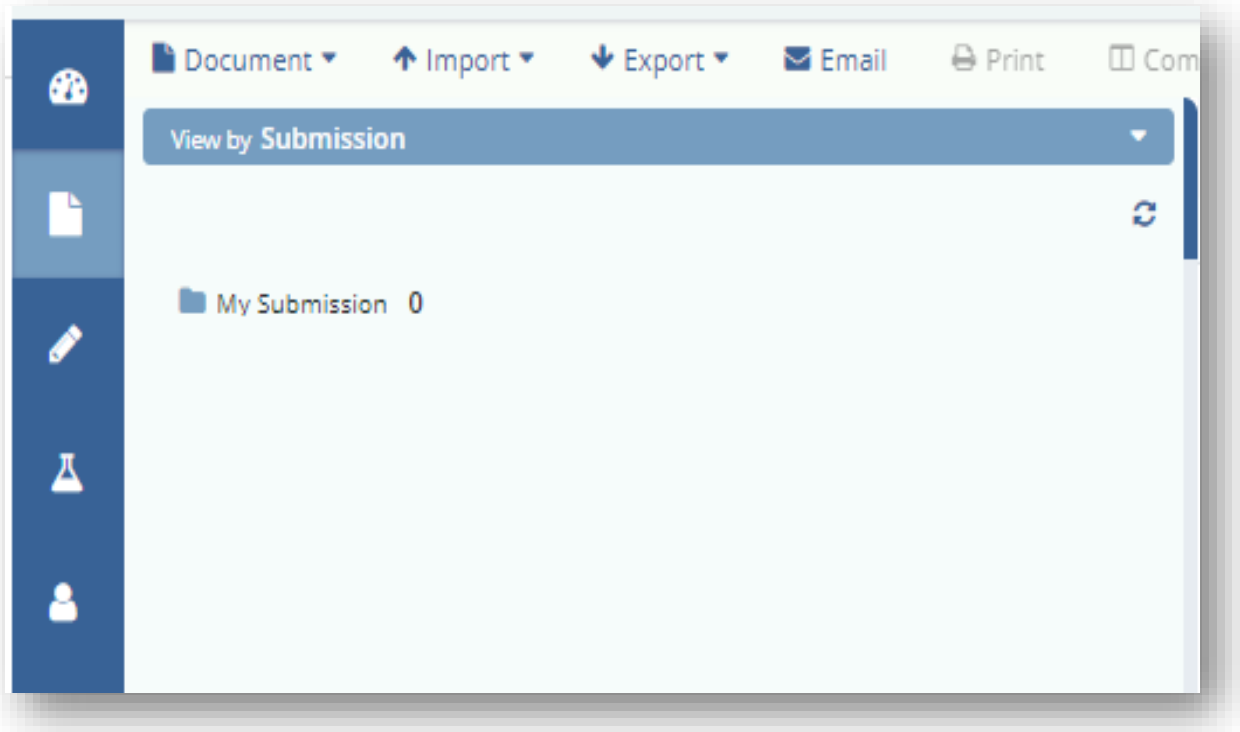


Basic Navigation

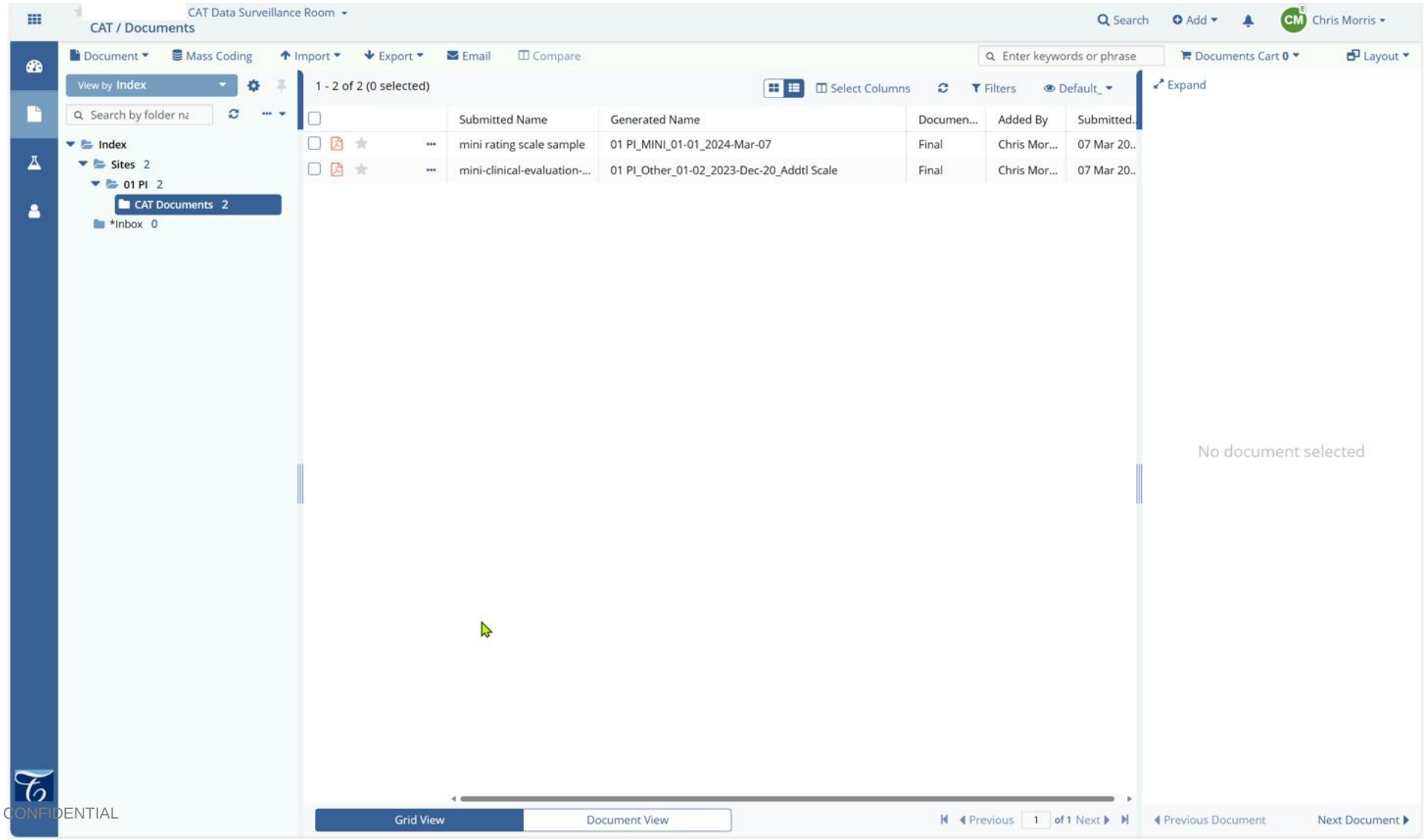


Document Library – Initial View

- Clicking on the small paper icon on the left-hand side of the screen will bring you to the "**Document Library**"
- The initial view is usually set up for "**My Submissions**," which shows all the documents that you have personally submitted to the room.



Document Library – Interface

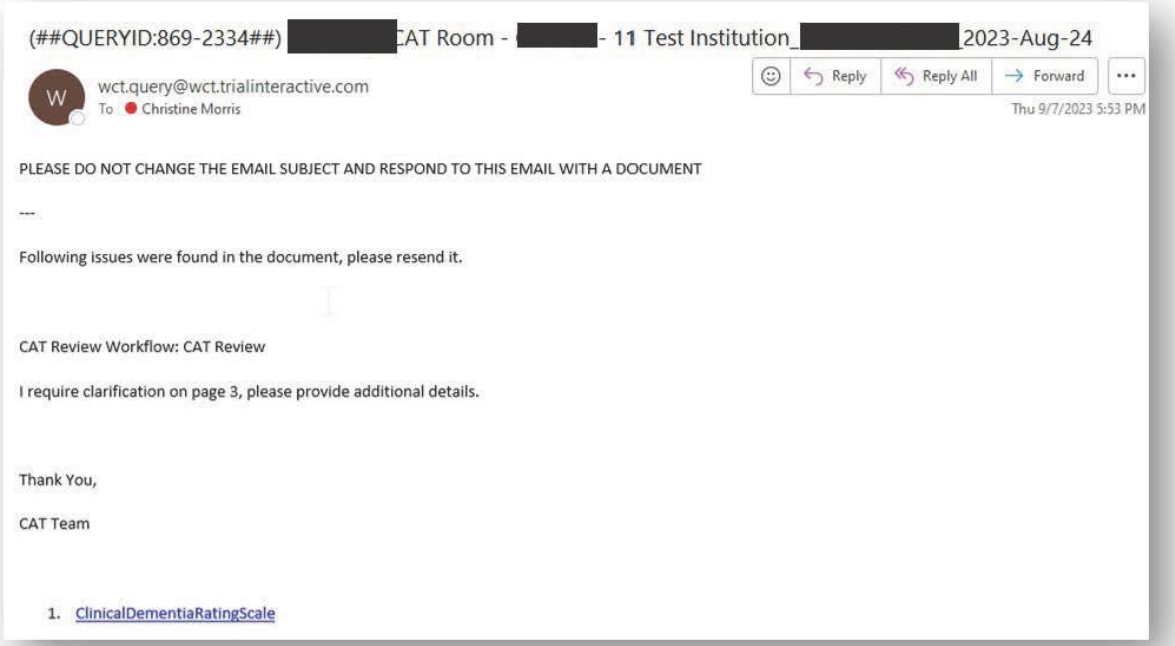


Documents – Email submission

1. Open email (Outlook)
2. Create new email
3. Attach document(s)
4. Submit to room email address **RE104-201-PPD_CAT@wct.trialinteractive.com**

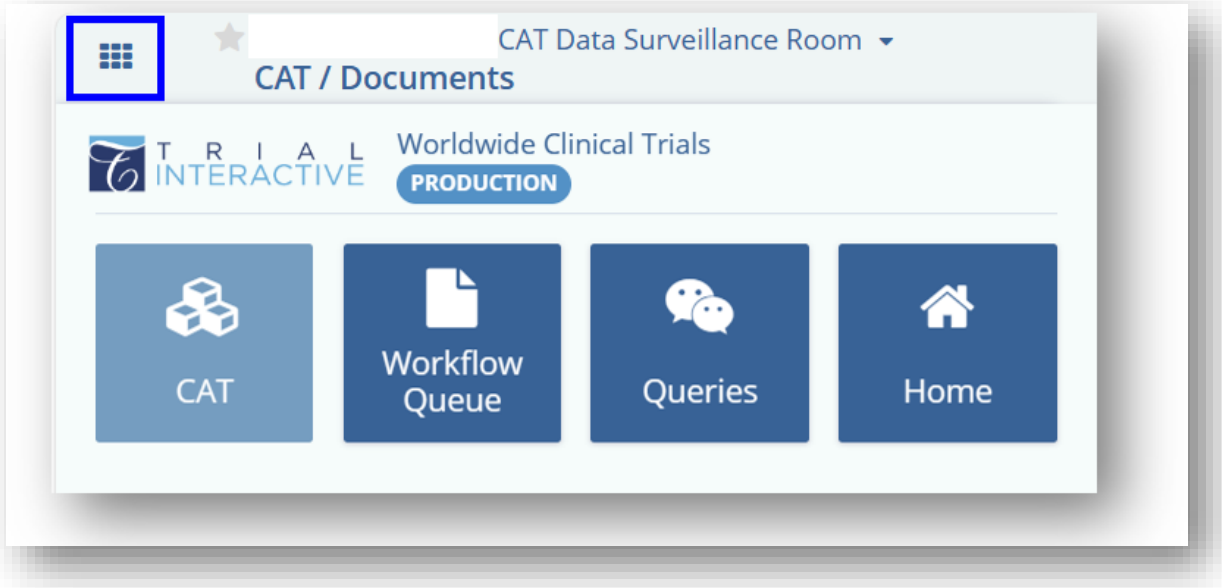
Responding to Queries from the CAT TEAM

- If the CAT team has questions about your submission upon review, they will send you a query through the workflow.
- You will receive an **email notification**
  - Click on the link within the email to view the document associated with the query.
  - Reply to the query directly from this email, providing a response



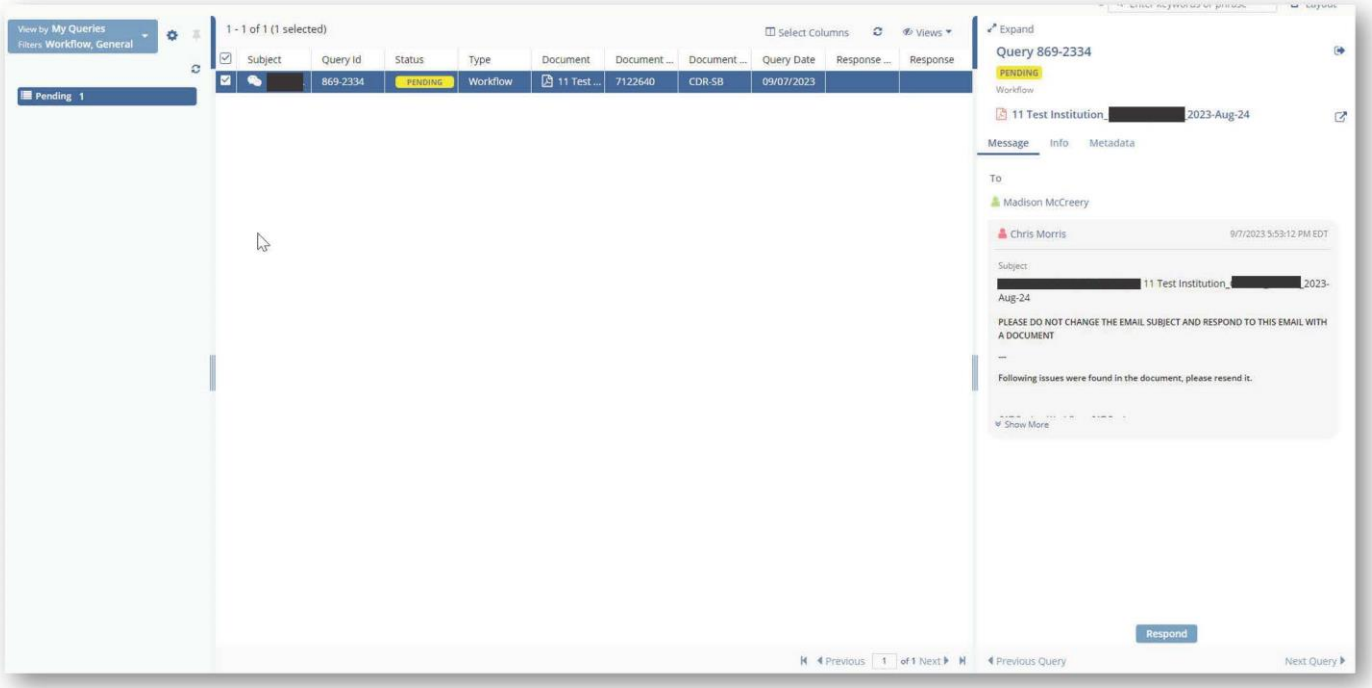
Responding to Queries in Portal

Use the Waffle menu to navigate to the **Queries** module.

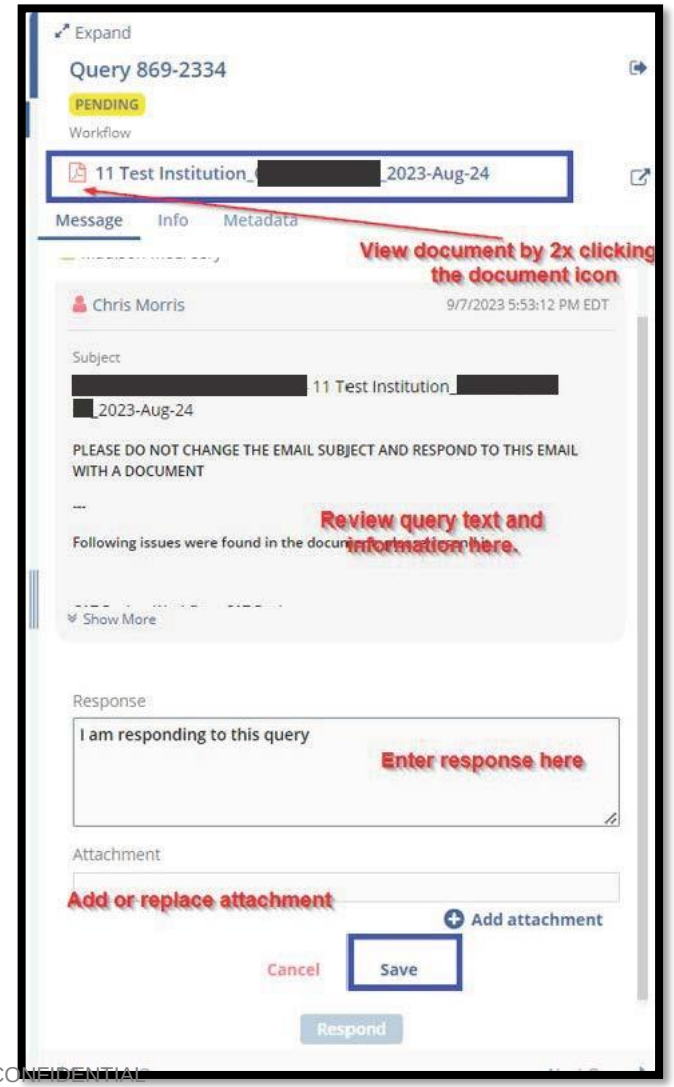


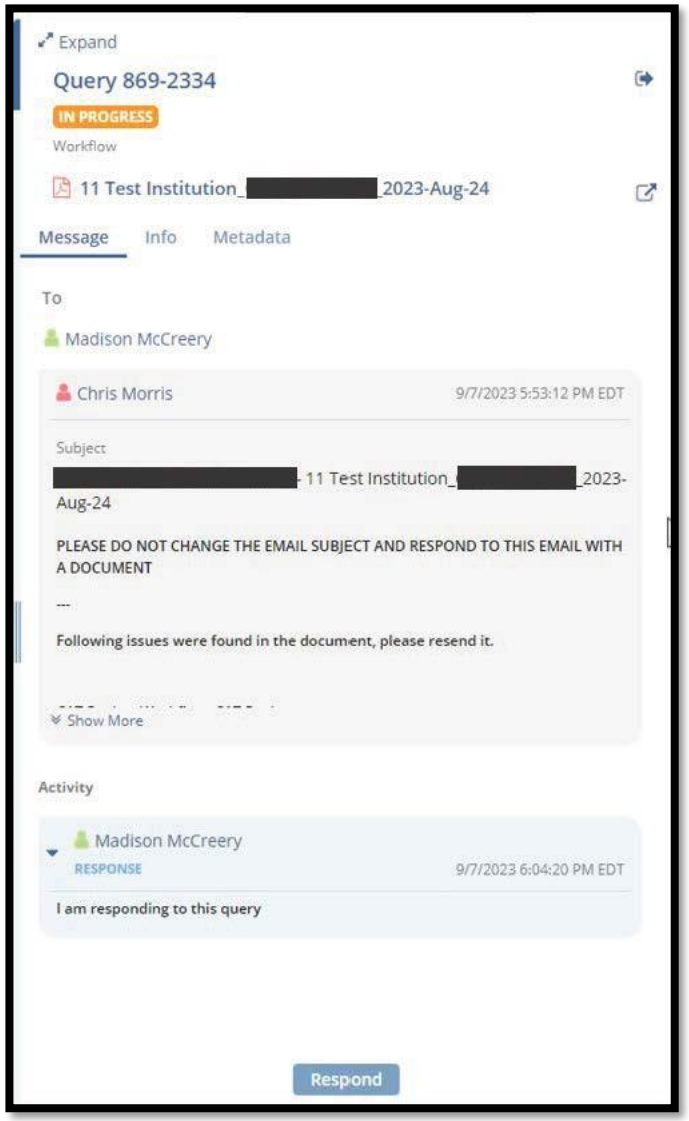
Query Module- Responding to Queries

- Queries will be organized by *status*
- *Grid* will display all queries with the selected status
- Query details will be in the *metadata panel*.
- Use the “**Respond**” option at the bottom of the panel to respond to the query.

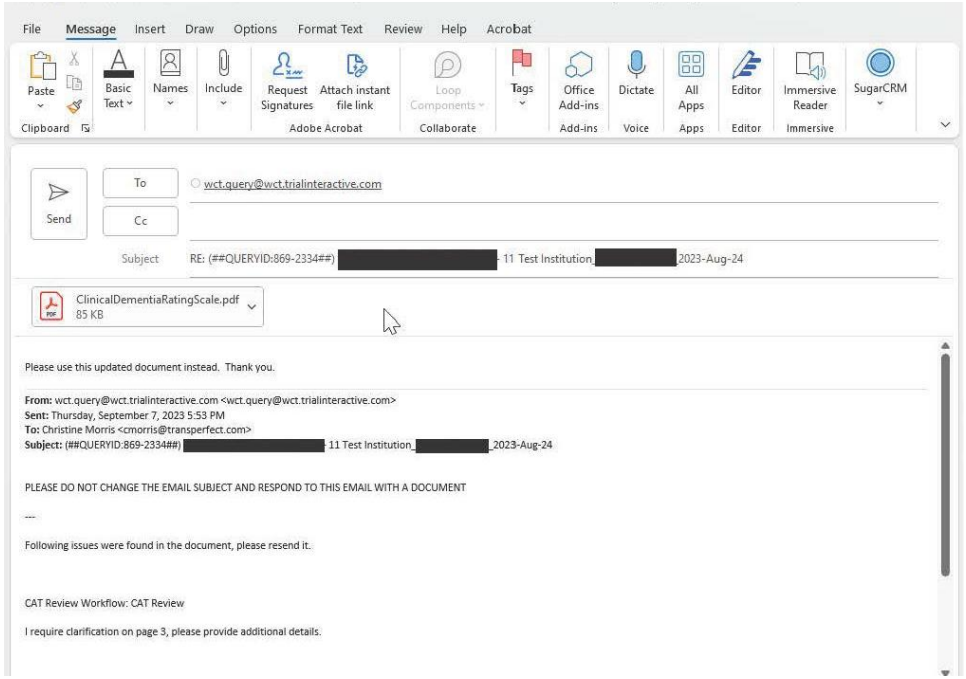


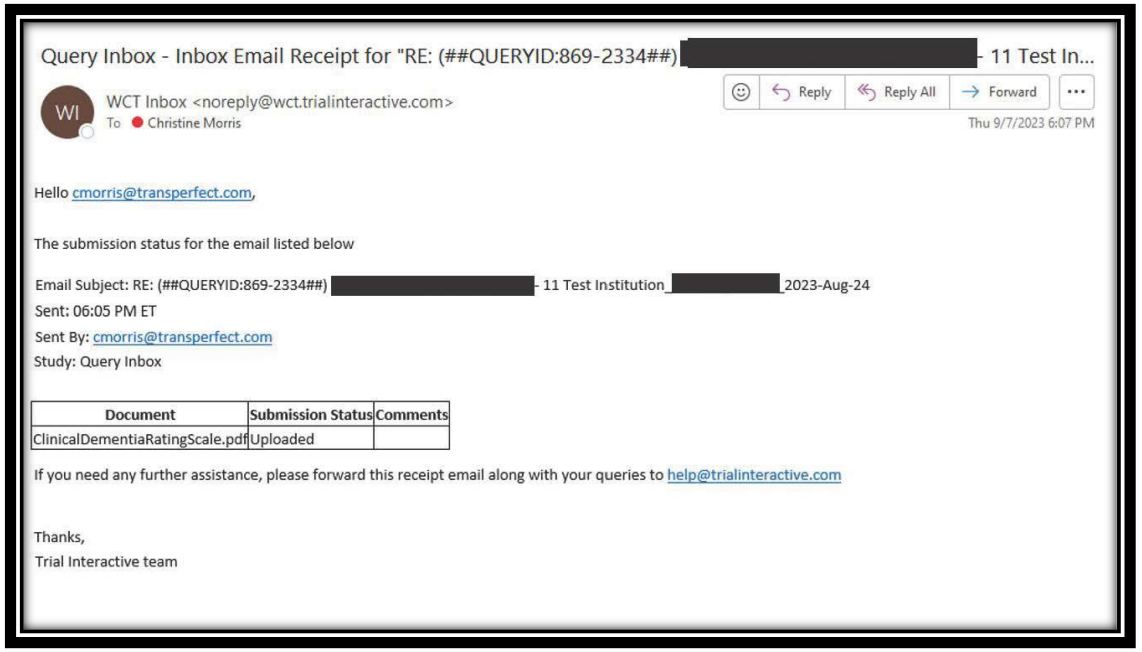
Query Response in System- Example





Site Email Response & Confirmation to Query





Help & Support

- Training Handout
- Please reach out to your CAT Team for study questions.
- If you experience technical difficulties, please reach out to support.wct@trialinteractive.com and copy your CAT Lead.

CONFIDENTIAL

Electronic Data Capture (EDC)

- Direct data entry of assessments/scales on devices to vendor portal.
- Worldwide Clinical Trials (Worldwide) is providing an online electronic data capture (EDC) system for use
- **This system is known as Zelta**
- Zelta has been chosen and designed to make life as easy as possible for the end user:
  - Intuitive page layouts & functionality
  - Quick load times
  - Real time system query fire

EDC Access and Training Requirements

To gain access there are two steps for site staff:

1. Create your Zelta General Account

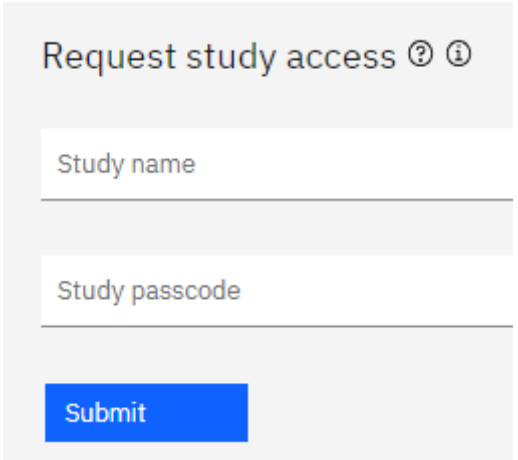
2. Study Access Request

The Worldwide study team will follow-up internally to ensure access is granted

You will be required to complete on-line training before gaining access to the EDC

EDC Access and Training Requirements

- Log in with your general Zelta Clinical Development account
- Locate the Request Study Access box. On the landing page, it is at the top of the right column.
- Enter the text RE104-201-PPD into both the boxes and click Submit.



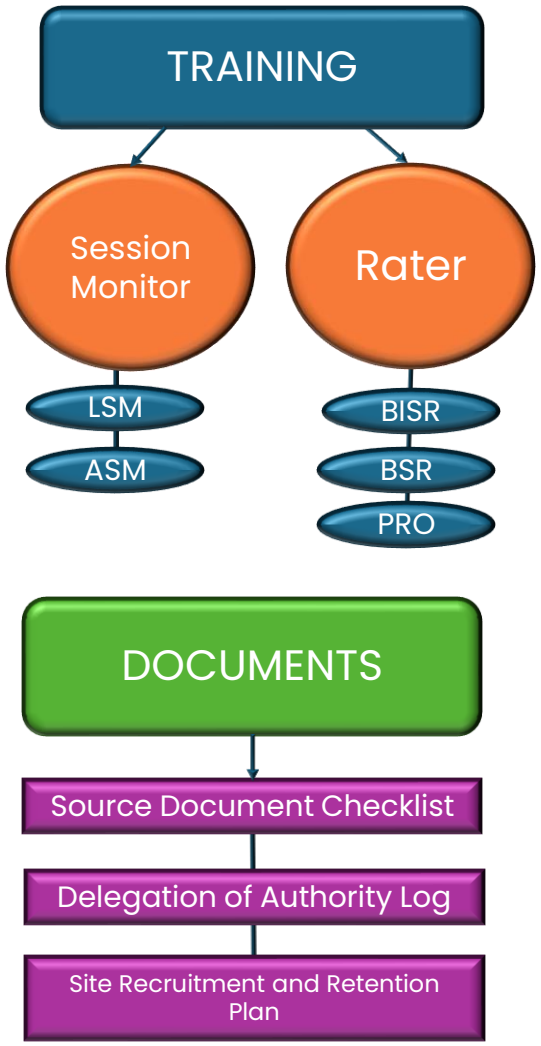
- On the review request screen, select a role. If applicable, select the site you will be accessing from.
- Click Submit.
- Once the study team approves your request, you will receive a welcome email to the study and be able to proceed into the study.
- If you have forgotten your login details, use the 'Forgot your password?' link to answer your secret questions and get a user ID reminder or password reset.

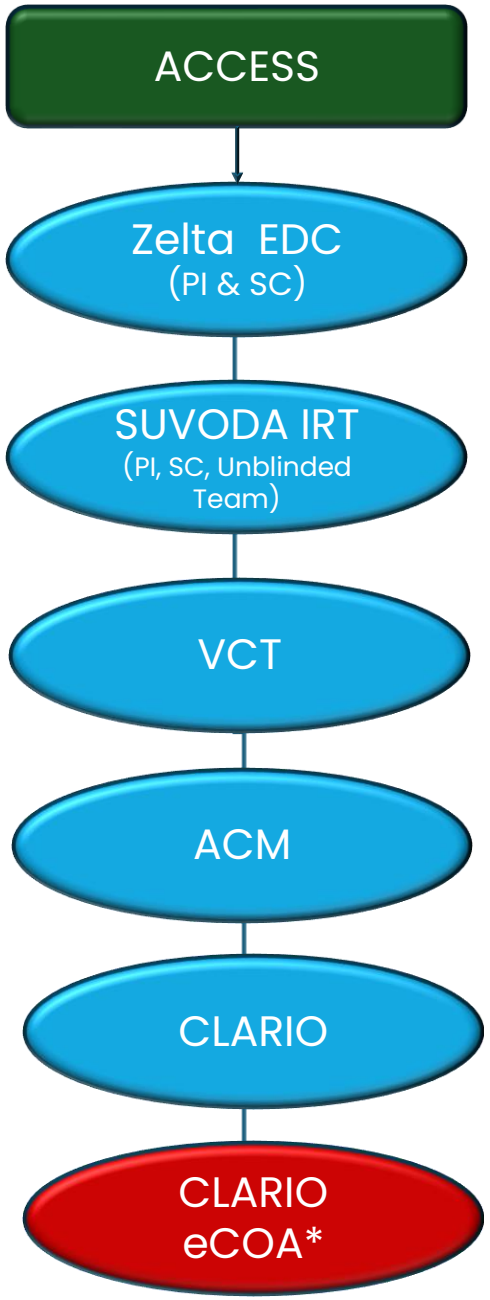
Reminders:

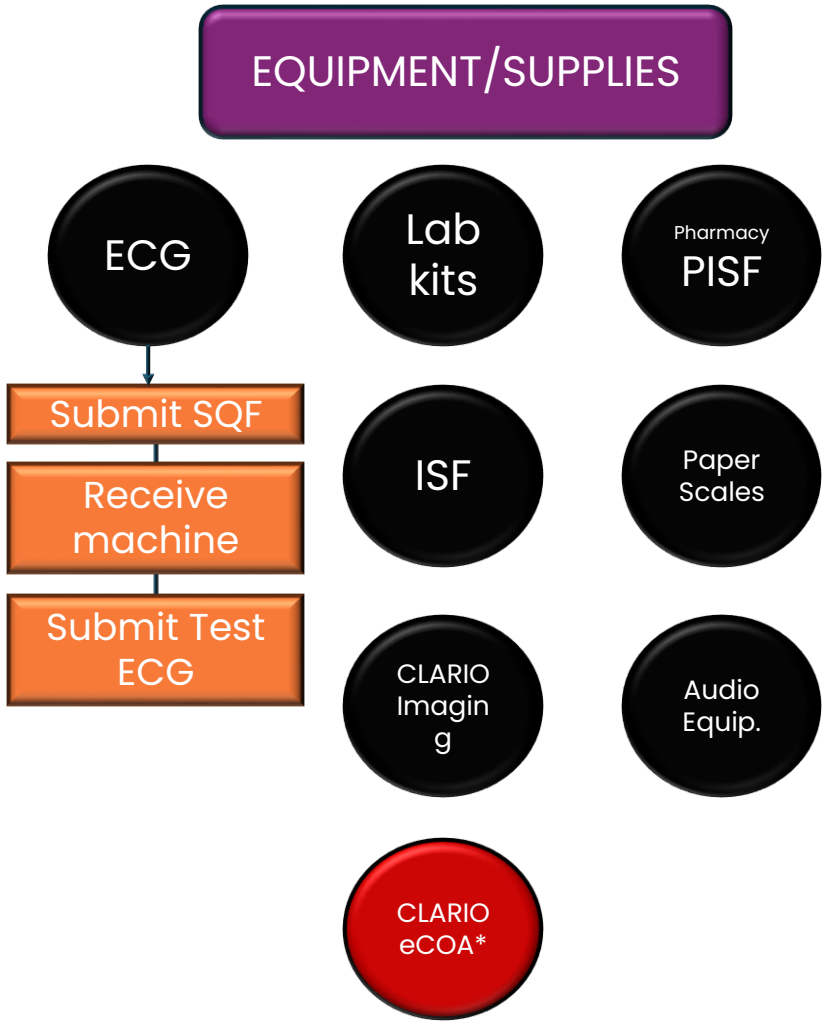
- **SCID-5-CT and HAM-D** will be audio recorded
  - ➢ Upload for CAT team to review for Eligibility
- Utilize the CLARIO Imaging tablet for audio recording (*until eCOA tablet is provided*)
  - *Password for CLARIO imaging tablet: Site0009*
- Until eCOA is live, place completed assessment scales in sealed envelope
- Ensure completeness of assessments

CONFIDENTIAL

SIV Preparation



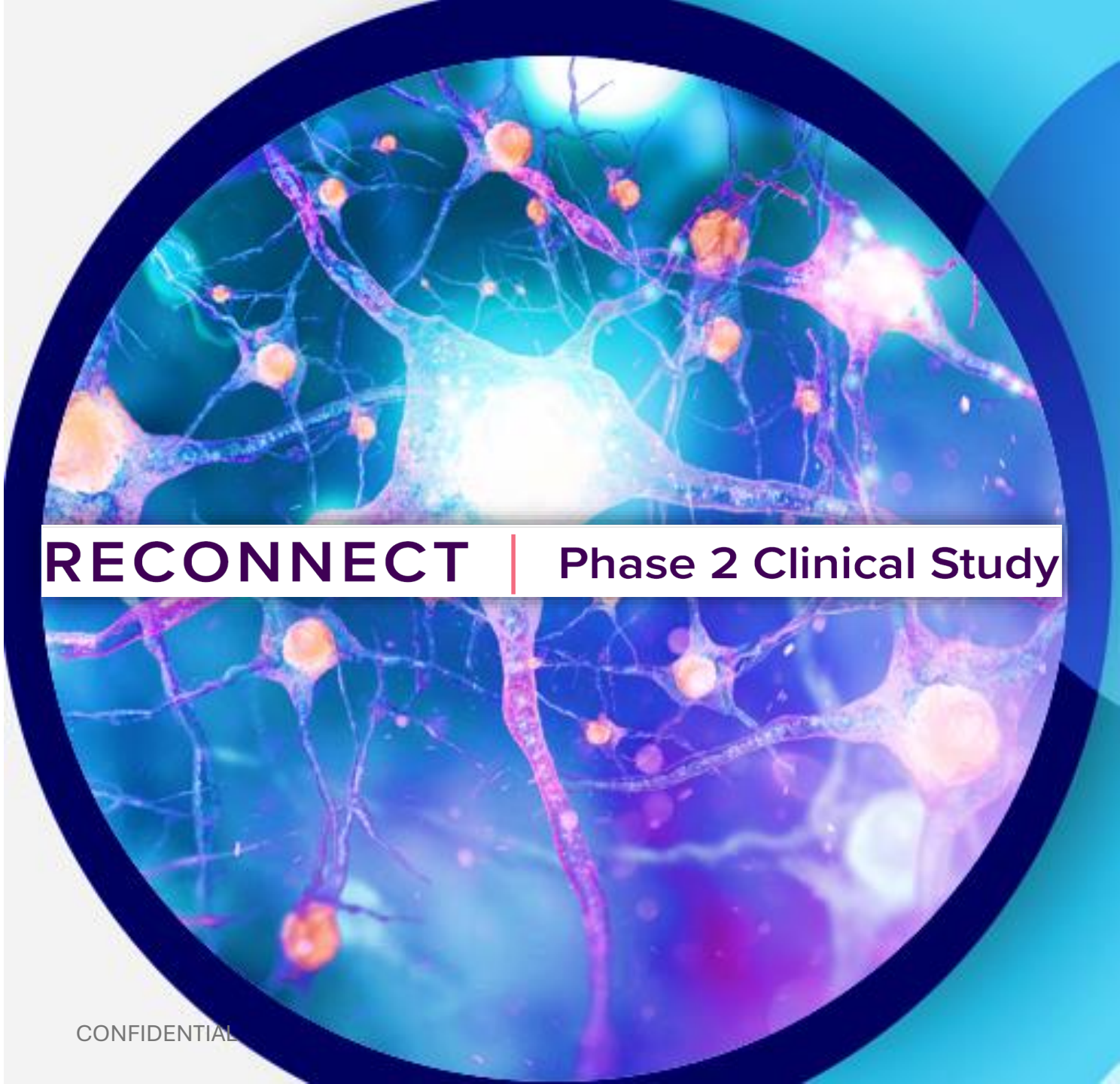




Pathway to Site Activation for Screening

- Site Regulatory Package complete and approved
  - Fully executed CTA
  - Regulatory approvals
  - Schedule I DEA 223 License (if applicable)
  - Ensure all Session Monitors and Raters are listed on your Form 1572
- Rater training complete
- Session Monitor training complete
- Access to:
  - Zelta EDC
  - Suvoda IRT
  - VCT
- Submit test ECG
- Study supplies and equipment on site
  - Lab kits
  - Investigator Site File
  - Clario Imaging Tablet
  - Paper rating scales
- SIV is complete
- Delegation of Authority Log complete
- CRA will notify CTM when all requirements are met
- CTM will open for screening in the IRT

Questions?



reunion NEUROSCIENCE

WORLDWIDE CLINICAL TRIALS

CONFIDENTIAL

RE104-201-PPD
Day 0
Dosing Day Walk Through

PROTOCOL VERSION 4.0, 10MAY2024

Disclaimer

These slides are provided exclusively for the Investigator Meeting and are confidential. They must not be shared outside the study team. Please be aware that these slides are not intended for formal training purposes; all official training will be conducted using the SIV (Site Initiation Visit) slides.

CONFIDENTIAL

Study Assignments

1. Principal Investigator
2. Study Coordinator, trained as PRO Administrator
3. Study Nurse
4. Blinded Site Rater (Clinician Rater) *Can be the PI*
5. Blinded Independent Site Rater (Efficacy Rater)
6. Lead Session Monitor *(Session monitors can collect vitals during the dosing session if medically qualified)*
7. Assistant Session Monitor
8. Unblinded Pharmacist
9. Unblinded Site Staff
10. Participant
11. Participant's family member, friend, caregiver

Roles listed from #1-7 can have a bit of overlap with assessments that are completed on the day of dosing. Best to speak with the Reunion team if you have any questions.

CONFIDENTIAL

Disclaimer:

These images have been created using artificial intelligence to provide you with the best overview of the day of dosing events. Please note that none of these images depict actual patients, and there may be some inaccuracies or distortions in the details.

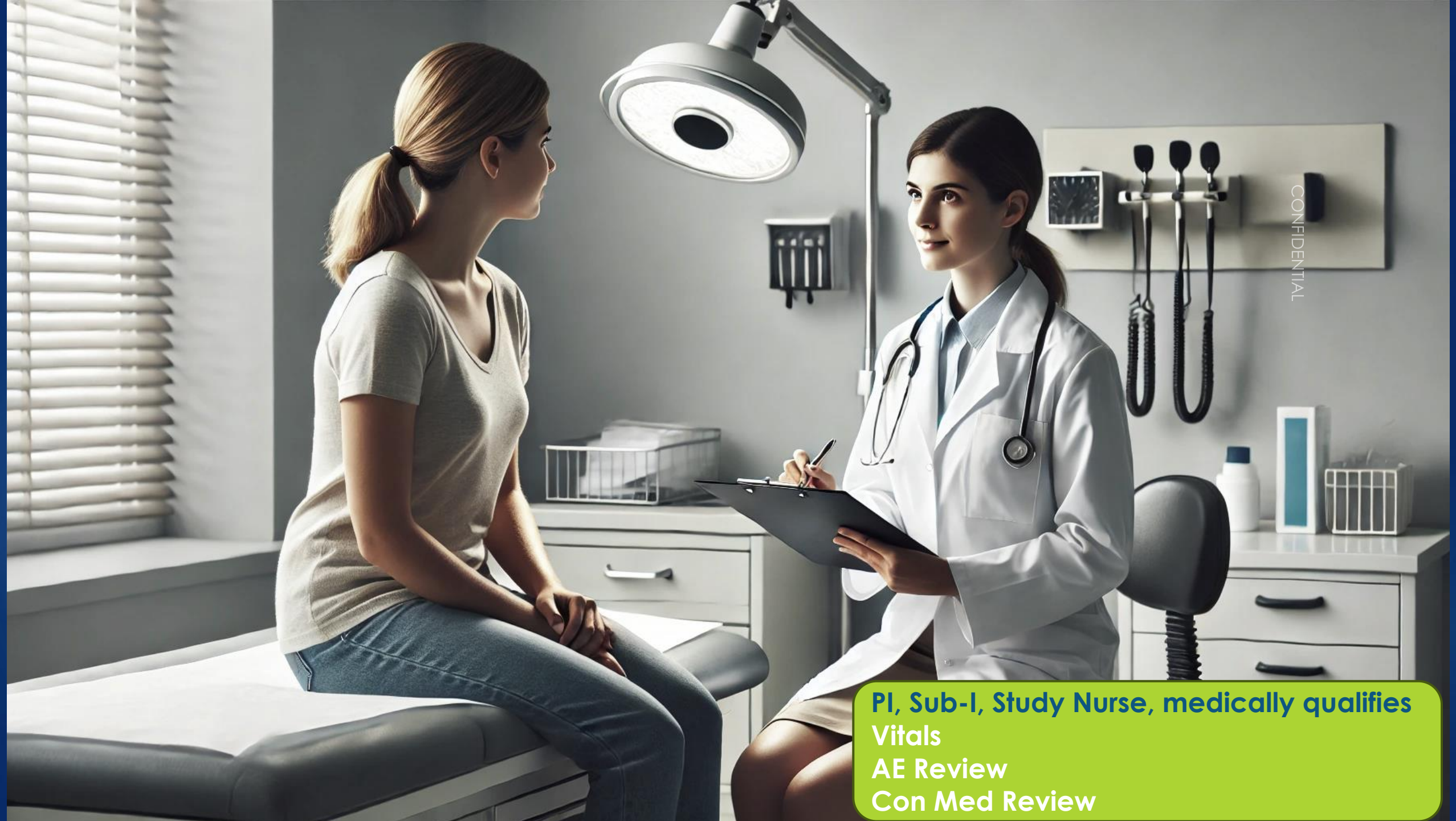
CONFIDENTIAL

DAY 0: PRE-DOSE

Helpful hint: Prepare the dosing room the day before. Ensure all devices are charged and in place.

CONFIDENTIAL

CONFIDENTIAL

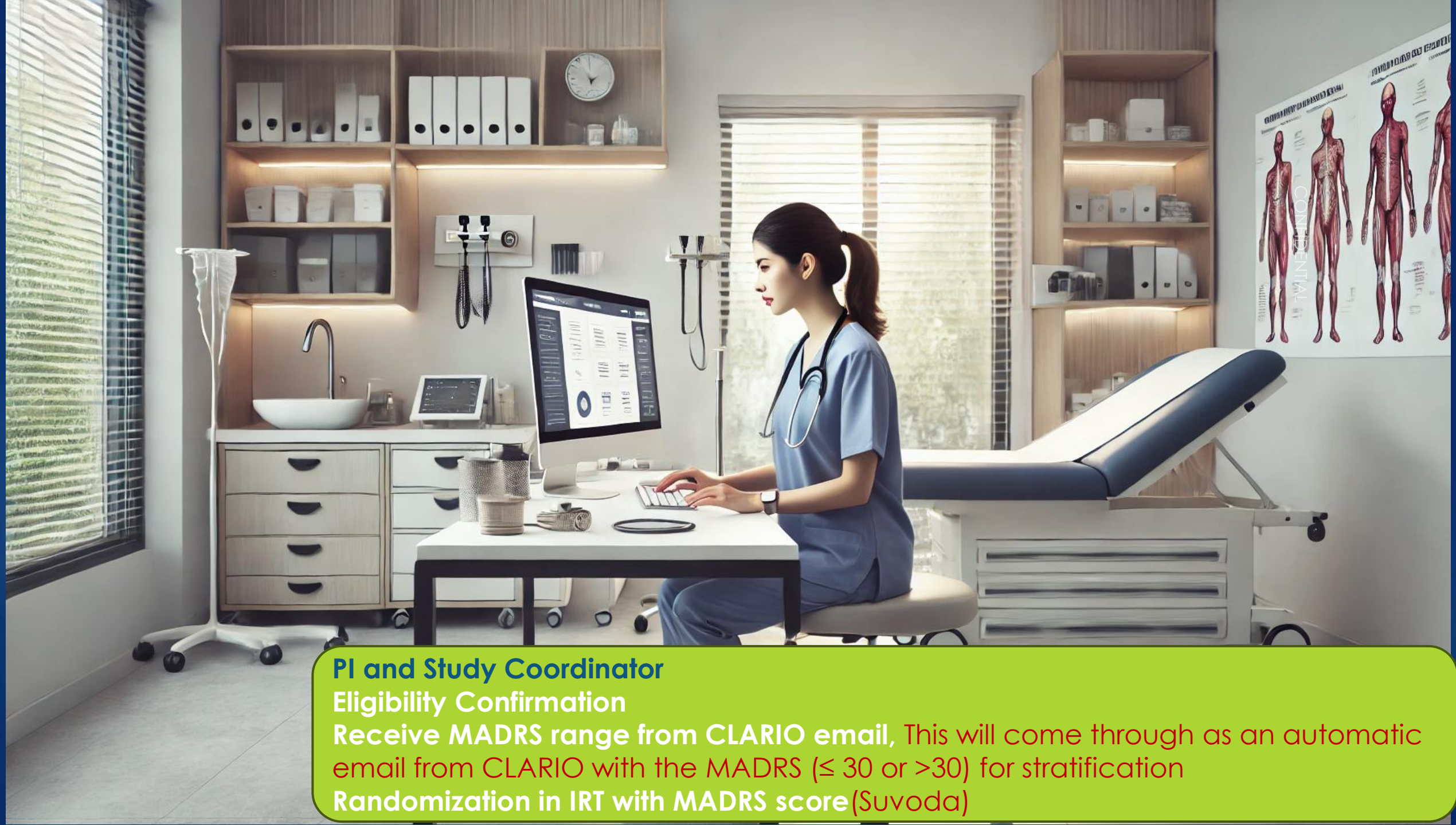

CONFIDENTIAL
PI, Sub-I, Study Nurse, medically qualifies
Vitals
AE Review
Con Med Review


CONFIDENTIAL
PI, Sub-I, Study Nurse, medically qualifies
Drug & Alcohol Screen
Urine pregnancy test
COVID test, if not completed at Visit 2


CONFIDENTIAL
PI, Sub-I, Study Nurse, medically qualifies
12-Lead ECG (CLARIO machine provided)

Blinded Independent Site Rater (efficacy rater)
PCRS: Placebo-Control Response Script
MADRS- audio recorded
HAM-A- audio recorded
On CLARIO (eCOA) Tablet
Note: Paper until go-live; provide MADRS score to SC

CONFIDENTIAL



PI and Study Coordinator

Eligibility Confirmation

Receive MADRS range from CLARIO email, This will come through as an automatic email from CLARIO with the MADRS (≤ 30 or >30) for stratification

Randomization in IRT with MADRS score(Suvoda)

CONFIDENTIAL

Unblinded Pharmacist
RE104 Preparation
Reference Pharmacy Manual

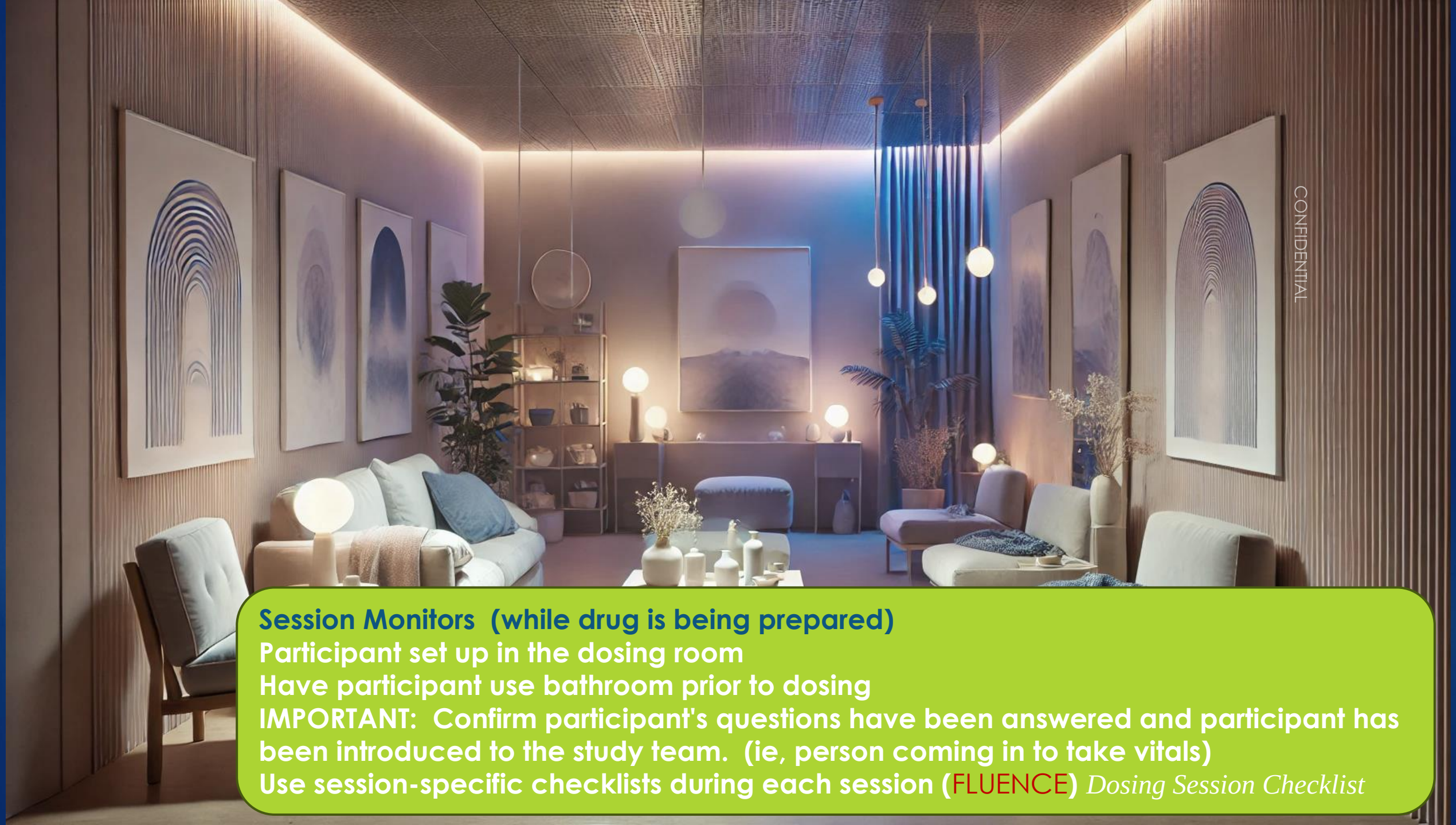
CONFIDENTIAL

Unblinded Pharmacist

RE104 Preparation, pull RE104 vial from the freezer

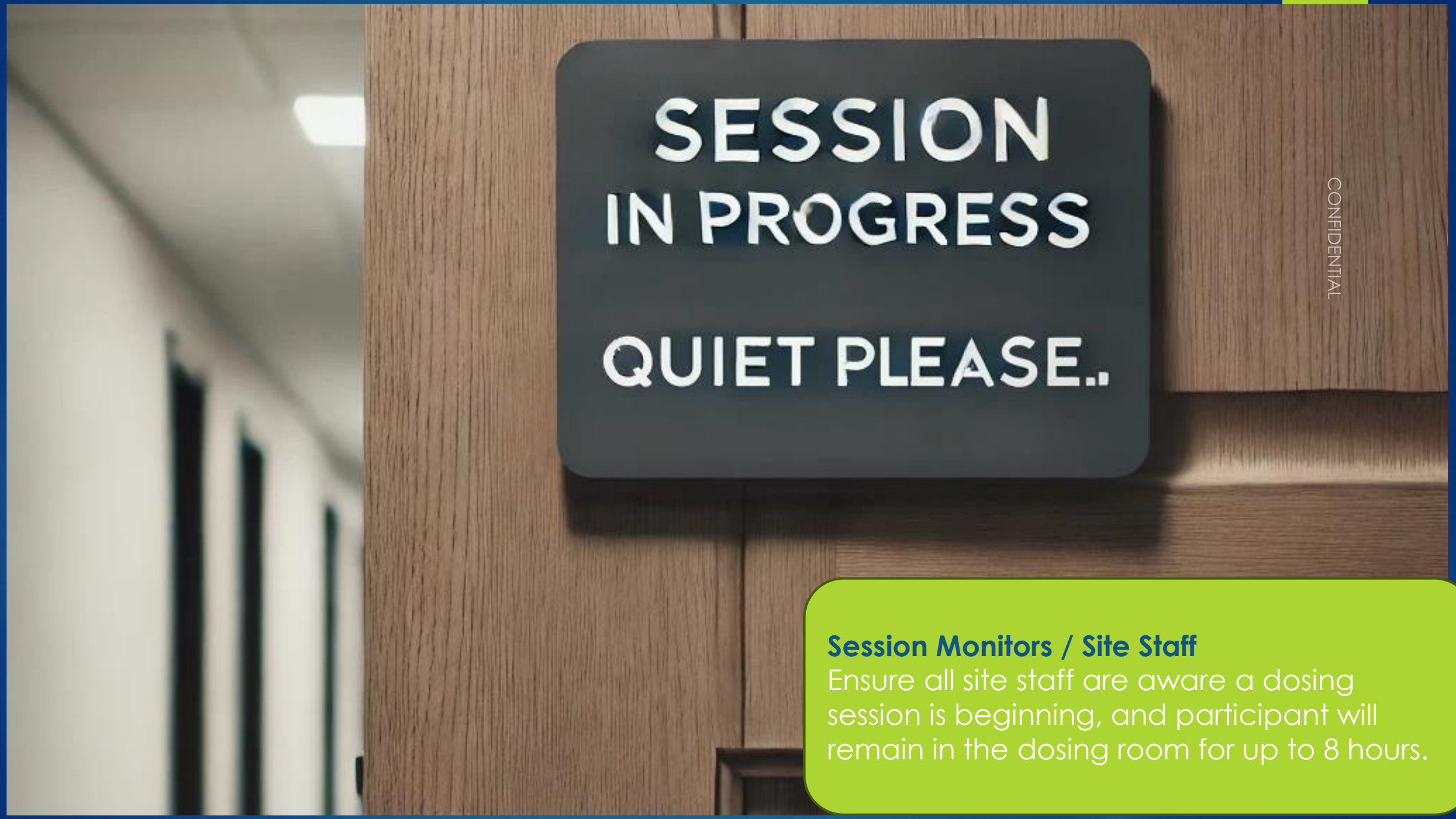
Vial to come to room temperature (30-60 minutes)


CONFIDENTIAL
Unblinded Pharmacist
RE104 Preparation, reconstitution; following Pharmacy Manual
1.1 mL diluent, swirl and invert
Use within 4 hours



CONFIDENTIAL

Session Monitors (while drug is being prepared)
Participant set up in the dosing room
Have participant use bathroom prior to dosing
IMPORTANT: Confirm participant's questions have been answered and participant has been introduced to the study team. (ie, person coming in to take vitals)
Use session-specific checklists during each session (FLUENCE) *Dosing Session Checklist*



CONFIDENTIAL

Session Monitors / Site Staff
Ensure all site staff are aware a dosing session is beginning, and participant will remain in the dosing room for up to 8 hours.

Session Monitors

Confirmation patient is ready for dosing session.

Ensure CLARIO (video) tablet is ready **for recording (Ideally set up the NIGHT BEFORE)**

Ensure music for dosing, mp3 player, speaker, headphones is ready (set up night before)

CONFIDENTIAL

Unblinded Pharmacist

Delivery of the prepared IP (& vial), using provided white boxes.

DAY 0: DOSING

CONFIDENTIAL

CONFIDENTIAL

Unblinded Pharmacist and Unblinded Staff
Enters dosing room

Session Monitors & Blinded Staff
Leaves dosing room

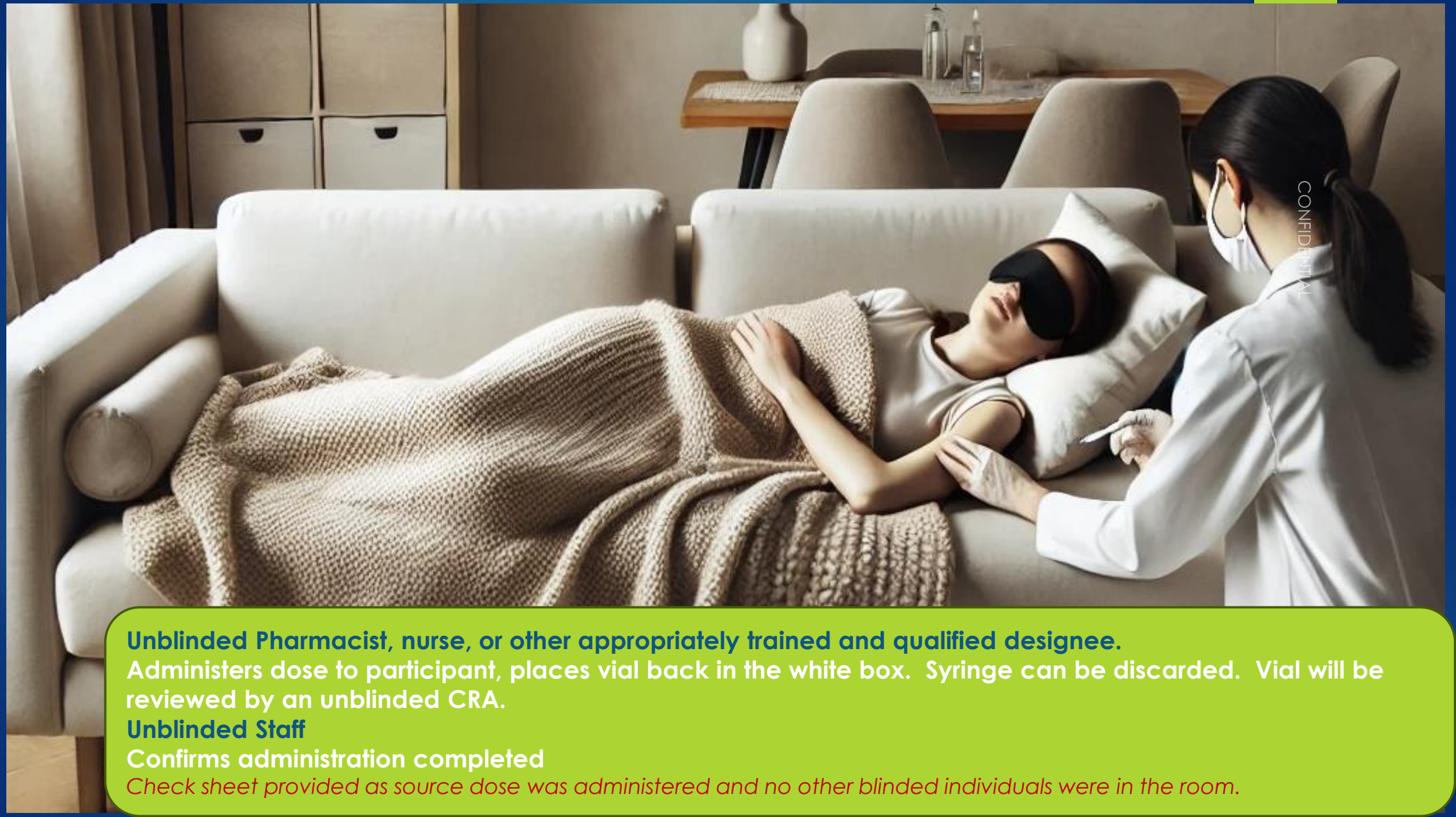
Participant
Lays down and places eye shades on,
headphones optional during dose administration.

Unblinded Pharmacist, nurse, or other appropriately trained and qualified designee.
Draw dose into syringe per randomization assignment

Unblinded Staff
Confirms amount drawn matches randomization assignment

VERY IMPORTANT the participant's eye shades are on. They cannot see the vial or syringe due to potential unblinding.

CONFIDENTIAL

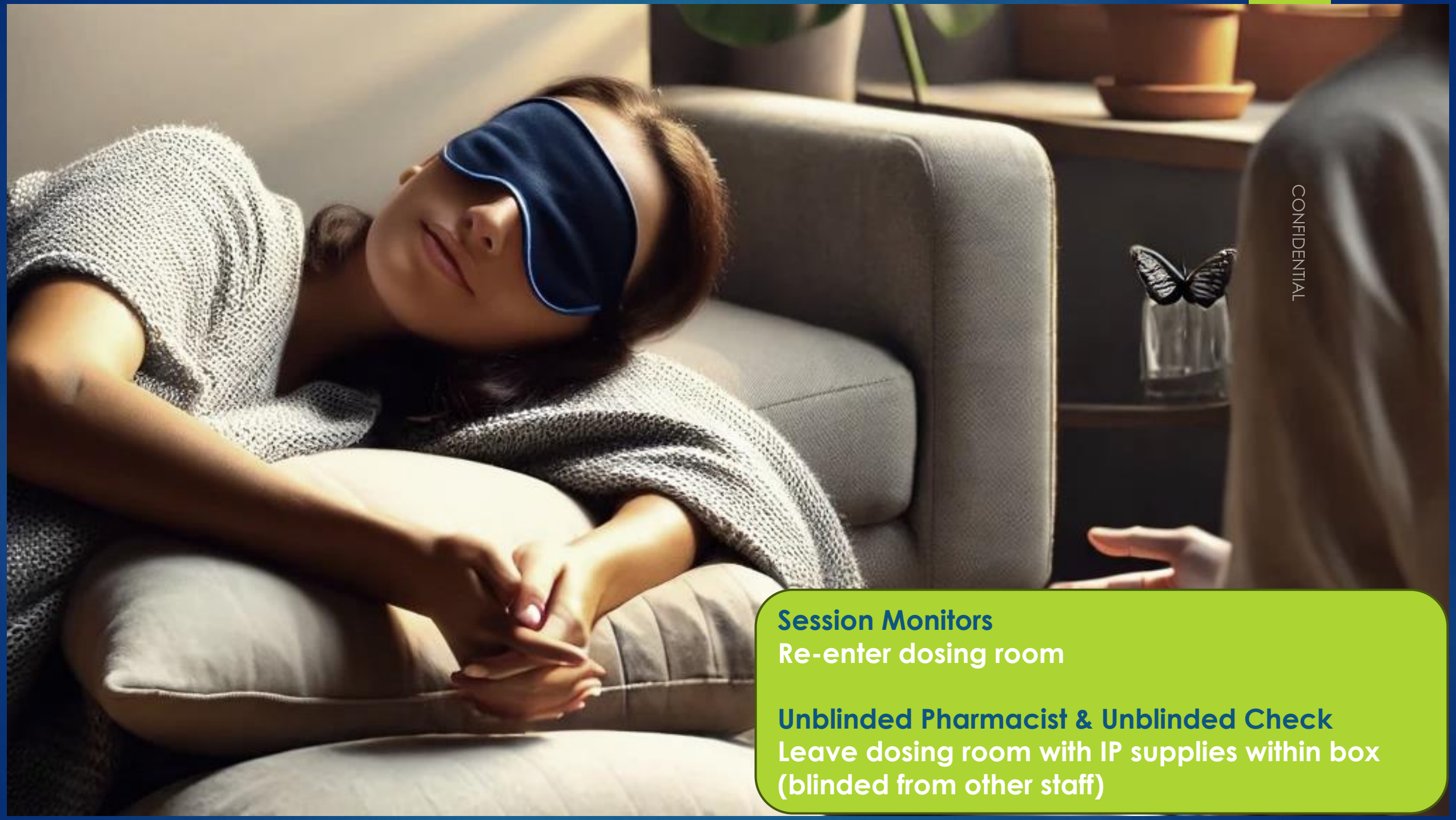


CONFIDENTIAL

Unblinded Pharmacist, nurse, or other appropriately trained and qualified designee.
Administers dose to participant, places vial back in the white box. Syringe can be discarded. Vial will be reviewed by an unblinded CRA.
Unblinded Staff
Confirms administration completed
Check sheet provided as source dose was administered and no other blinded individuals were in the room.

DAY 0: POST-DOSE

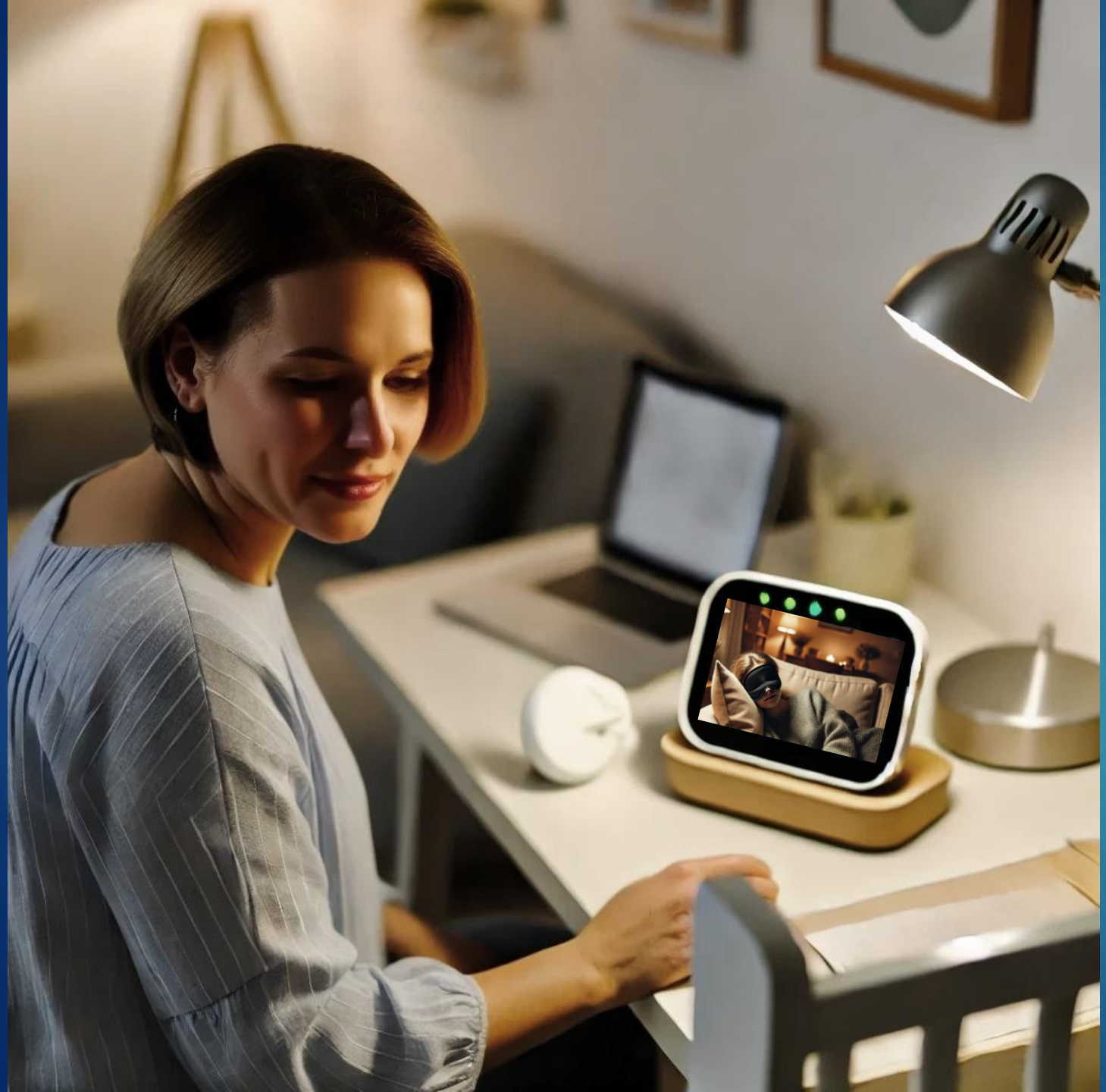
CONFIDENTIAL


CONFIDENTIAL
Session Monitors
Re-enter dosing room
Unblinded Pharmacist & Unblinded Check
Leave dosing room with IP supplies within box
(blinded from other staff)

CONFIDENTIAL

Participant
Place headphones

Session Monitors
Take session notes, including recording any AE, AESI, SAE
Please note, session monitors should always be available for the participant during the dosing session. Avoid use with electronics. Light book is acceptable.



Session Monitor

At least 1 Session Monitor will always be physically present with the patient until effects of dosing have resolved (through at least 5 hours post-dose);

if only 1 Session Monitor is physically present in the dosing room, the other must monitor the session on-site live via remote video monitoring.

Baby monitor can be provided if needed.

CONFIDENTIAL

CONFIDENTIAL

PI or designated Sub-I who qualifies

In addition, if the LSM is not a licensed physician, a licensed physician will be available or on call and be able to reach the treatment room within 15 minutes in the event of a medical emergency.

1 hour post dose

CONFIDENTIAL

Study nurse, or other appropriately trained and qualified designee.

Session monitor can collect vitals if medically qualified.

Collect vital signs; Vital signs will include temporal temperature, heart rate, and blood pressure in the supine position after 5 minutes of rest.

CONFIDENTIAL

CONFIDENTIAL

Patient & Session Monitors

Bathroom Protocol: If the participant needs to use the bathroom, they must be accompanied by the LSM or ASM. Interaction with anyone who is not study personnel should be avoided.

Doors should not be locked.

CONFIDENTIAL

3 hours post dose

CONFIDENTIAL

Study nurse, or other appropriately trained and qualified designee *(Session Monitor)*. Collect vital signs; Vital signs will include temporal temperature, heart rate, and blood pressure in the supine position after 5 minutes of rest.

4, 5, 6, and 7 hours post dose

CONFIDENTIAL

Study nurse, or other appropriately trained and qualified designee.

Discharge readiness assessments

The post-dose discharge readiness evaluation will be a clinical examination which will include an assessment of the patient's psychiatric and physical status and associated health parameters including vital signs and status of any treatment emergent AEs.

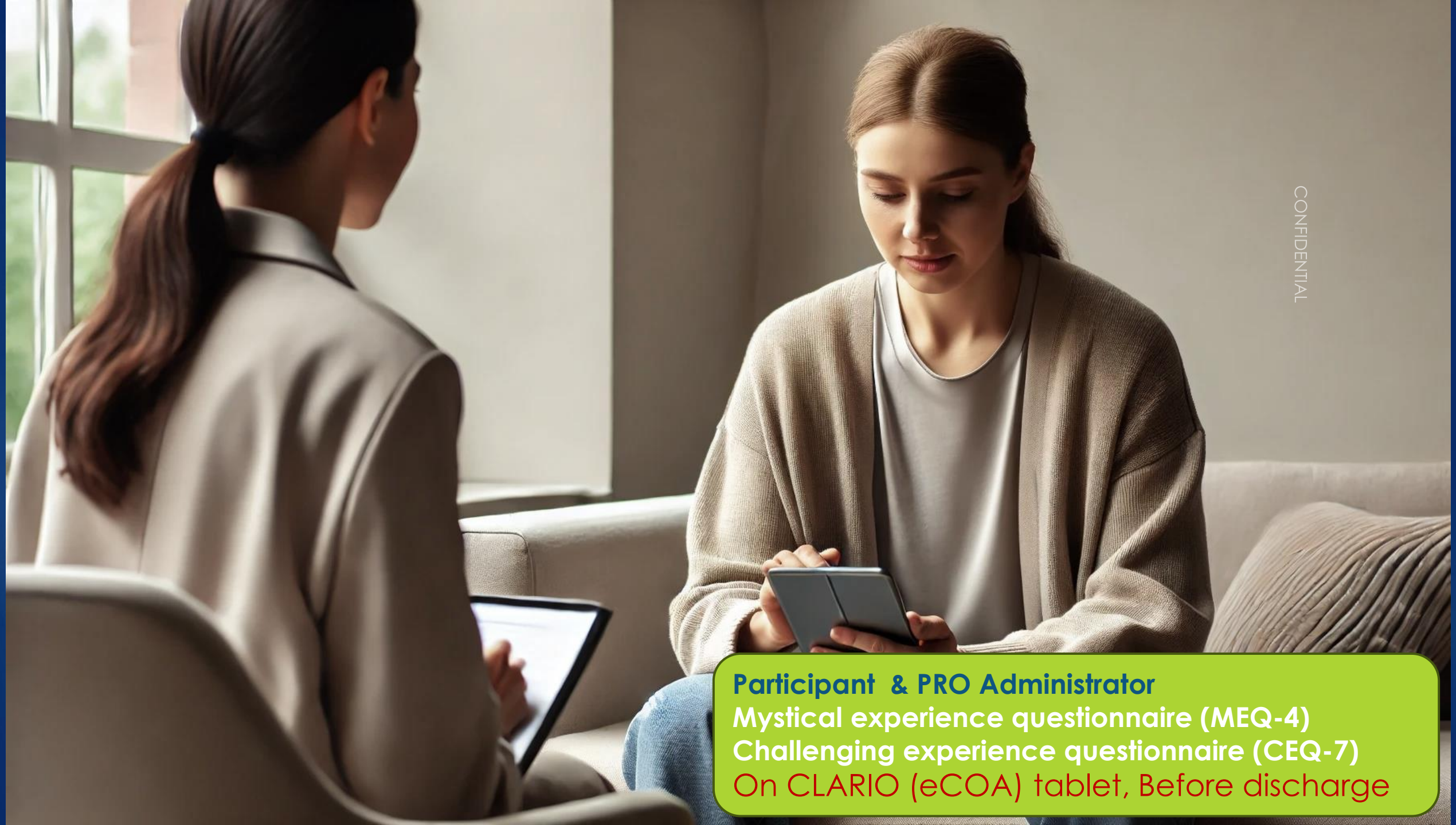
CONFIDENTIAL

CONFIDENTIAL

Session Monitor & PI or designee.
Review AE / AESI / or SAE

CONFIDENTIAL

8 hours post dose


CONFIDENTIAL
Participant & PRO Administrator
Mystical experience questionnaire (MEQ-4)
Challenging experience questionnaire (CEQ-7)
On CLARIO (eCOA) tablet, Before discharge

CONFIDENTIAL

Blinded Site Rater (Clinician Rater)
Columbia-Suicide Severity Rating Scale (C-SSRS)
Brief Psychiatric Rating Scale (BPRS+)
On CLARIO (eCOA) tablet, Before discharge

CONFIDENTIAL

CONFIDENTIAL

Study nurse, or other appropriately trained and qualified designee.
Discharge readiness assessments
Set up time for phone call check in, *Confirm it would be okay to speak with family member / caregiver if participant is sleeping.*
Remind the participant of their next appointment for an integration session and who will be conducting that session (the same LSM or a different LSM from the team).

CONFIDENTIAL

Participant family member, friend, caregiver

At the 8-hour post-dose timepoint and once deemed ready for discharge, patients will be allowed to go home and must be escorted by a trusted friend or family member, or caregiver.

Session Monitor and/ or medically qualified Investigator or designee.

Remote check-in will occur a few hours post discharge at the time agreed upon with the patient. Check in with the participant (and/or family member, etc. if applicable) to confirm that the participant is comfortable and stable.