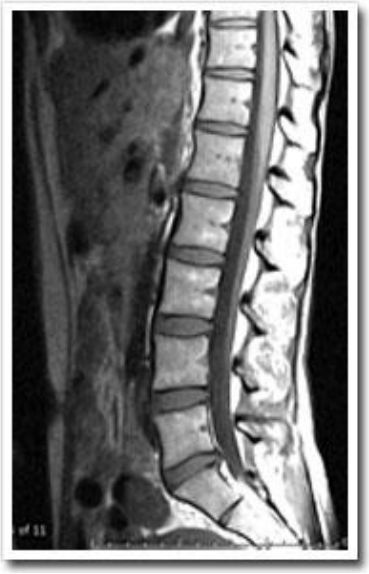

INVESTIGATOR SITE OPERATIONS MANUAL

NOVARTIS - CAIN457K2340 (SURPASS)

Project:	Novartis – CAIN457K2340 (SURPASS)
Document File Name:	236483 Investigator Site Operations Manual
Document Revision:	4.0
Version Date:	26 Nov 2018
Author's Name	Omkar Kayal

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REVISION HISTORY

Date	Author	Version	Description of Revision
26 Oct 2017	Omkar Kayal	1.0	Initial Release of Document
14 Mar 2018	Omkar Kayal	2.0	Added Section 2.2 Re-screening Subjects Updated section 2.6 PAREXEL Contact Information Updated section 3.2 Site Survey Completion Updated section 3.3 Test Transfer Acquisition Updated section 4.3 Image Data Transfer via Perceptive eTransfer (Preferred)
25 Jul 2018	Omkar Kayal	3.0	Updated 2.1 Study Background – Imaging Schedule table Updated section 4.3 Image Data Transfer via Perceptive eTransfer (Preferred)
26 Nov 2018	Omkar Kayal	4.0	Updated section 2 Study Background – Imaging Schedule table

Table of Contents

1 Abbreviations and Acronyms

CAN	Case Acceptance Notification
CD	Compact Disc
CIL	Core Imaging Laboratory
CQN	Case Query Notification
DICOM	Digital Imaging and Communications in Medicine
eTransfer	electronic Transfer
IAG	Image Acquisition Guidelines
IRA	Imaging Research Associate
IT	Information Technology
QC	Quality Control
SOM	Site Operations Manual

2 Introduction

2.1 Study Background

A phase IIIb, randomized, partially-blinded, active-controlled, multicenter study of secukinumab to demonstrate reduction of radiographic progression versus GP2017 (adalimumab biosimilar) at 104 weeks and to assess the long term safety, tolerability, and efficacy up to 2 years in patients with active ankylosing spondylitis, please reference the Study Protocol.

This Investigator Site Operations Manual provides instructions for the imaging component of the NOVARTIS CAIN457K2340 (SURPASS) study. This document is specifically related to the management of imaging data acquisition, including shipment, tracking, and quality control.

All imaging scans will be acquired in a standardized manner, following pre-established Image Acquisition Guidelines (IAG) developed by PAREXEL Informatics and approved by NOVARTIS. Images will be submitted to PAREXEL for processing and independent analysis. Imaging data for all subjects will be acquired according to the imaging schedule outlined in the protocol, as well as listed in the table below:

CAIN457K2340 Imaging Schedule

Imaging Data	Screening Period	Treatment Period			
	Screening Visit 1 (Week -10 to -4)	Baseline (Day 1)	Week 16	Week 52	Week 104[6]
X-Ray cervical and thoraco-lumbar spine [2]	X[1,3]	X[1,3]		X	X
X-Ray sacroiliac joints (AP view)[2]	X[3,4]				X
MRI[5] Spine and SI joints		X	X	X	X

[1]Spinal x-rays (cervical and thoraco-lumbar) to be collected during the screening period to confirm eligibility for subjects with CRP < 5 mg/L. If additional lateral thoracic spine x-ray is available, it may also be submitted for syndesmophyte eligibility review. Subjects with CRP ≥ 5mg/L and confirmed study eligibility should obtain the spinal x-rays at baseline.
[2]SIJ and spinal x-ray image acquisition must follow the vendor's Image Acquisition Guidelines. The SIJ x-ray will be centrally read for eligibility
[3]Re-screening subjects may utilize previous x-rays if taken within the past 3 months according to the imaging criteria
[4]Subjects may utilize previous obtained SIJ x-rays if taken within the past 3 months according to the imaging criteria
[5]MRI only performed in a sub-population of subjects at selected sites. All subjects at the selected MRI site should be considered for the MRI assessment
[6]For all subjects who discontinue from the study, the investigator should ensure that the subject completes the end of treatment visit (Week 104 assessments) 4 weeks after last study treatment of secukinumab or 2 weeks after last study treatment of GP2017. Every attempt should be made to obtain the scheduled x-ray and MRI images at the final visit, unless the last x-ray and/or MRI were taken within 12 weeks before discontinuation.

Note – All X-Ray Images obtained at Screening will be the Baseline Images for the Efficacy Reads

It is REQUIRED that your X-Ray & MRI facility be qualified by PAREXEL. All Imaging (Including the Screening image) must be performed per Image Acquisition Guidelines. Re-scan will be required in the event the Image Acquisition Guidelines are not followed.

Please Notify PAREXEL Immediately of any Equipment Changes/Upgrades

All X-Ray Screening images are required to be submitted to PAREXEL within 24 hours (1 business day) of acquisition
The X-Ray and MRI Baseline and Post-Baseline images should be submitted within 48 hours (2 Business days) of acquisition

Images received at PAREXEL **MUST NOT CONTAIN** any markings, assessments, or confidential subject information.

You must remove from the images the names of the subject and any other information that can be used to identify the subject and only study specific subject number must be used

Cases will be prepared for independent review for eligibility, interim analyses, database lock(s), or study completion.

PAREXEL is responsible to perform the independent confirmation of Imaging Specific inclusion/exclusion criteria as per protocol for the Screening X-RAY. However the Independent Reviewer findings done during the efficacy reviews are independent assessments and will not be communicated to the sites until final Clinical Study Report. All decisions related to subject care are made at the site by the Primary Investigator(s) including whether the subject should continue on the study. Independent Reviewer(s) will remain blinded to the other assessments made at the investigator sites.

2.2 Re-screening Subjects

Site can utilize previous X-Rays if taken within the past 3 month's according to the imaging criteria. Sites have to notify PAREXEL about the re-screening subject number and its original subject number via email or during eTransfer upload when resubmitting the same scan under re-screening subject number.

If notified via email about re-screening subject details, PAREXEL can use the same X-ray images that were submitted earlier for original subject and can generate the eligibility read results for re-screening subject based on original subject results and share with sites. No additional screening visit submission required in this case.

If submitting same set of images over eTransfer portal, sites have to specific the original subject number when re-screening subject scans are being uploaded for PAREXEL to generate the eligibility read results for re-screening subject based on original subject results and share with sites.

PAREXEL will not perform additional eligibility reads for re-screening subjects if the original subject reads were already completed for the eligibility portion of the study and sites are using same X-ray images for re-screening subject.

2.3 Purpose of this Manual

The purpose of this manual is to provide:

- Contact information for additional assistance
- Description of operating procedures for investigator sites
- Sample forms and Image Tracking Log templates

2.4 Start Up Package Components

PAREXEL Informatics will provide the investigator site with the necessary materials listed below to perform the functions associated with this Investigator Site Operations Manual.

- The **Image Acquisition Guidelines (IAG)** is generated by PAREXEL in an effort to standardize all imaging associated with the clinical trial across multiple investigator sites, subjects, and timepoints. The standardized guidelines are distributed to each investigator site participating in this study. Please note that in the IAG, there are separate procedures for acquiring each involved region and varying scanner types across X-RAY & MRI modality. Please also ensure that you keep the IAGs in the study binder.
- The **Imaging Study Tracking Log** is used by the investigator site to document only the courier shipment status of all images related to the clinical trial. The log is updated with information regarding image acquisition, shipment dates, and corresponding shipment tracking numbers. PAREXEL will send a copy of this log in the eSite to sites that are using courier submission.
- The **Media Labels** are completed with subject/visit information and placed on each individual film or media (CD, DVD), making sure not to obscure anatomy, being sent to PAREXEL. Please place the label on the actual media and not the media case.
- The **Case Acceptance Notification (CAN)** is sent from PAREXEL to the investigator site when acceptable imaging data is received. Please see a sample of this form in section 6.1 of this manual.
- The **Case Query Notification** (**CQN**) is sent from PAREXEL to the investigator site upon receipt of unacceptable imaging data or if any additional clarification will be needed for the respective images. The form will describe the query and indicate the action(s) required to be taken towards submission of acceptable imaging data. Please see a sample of this form in section 6.2 of this manual.
- The **Site Acceptance Form** is sent from PAREXEL to the investigator site when all qualification requirements have been met. This notification informs the site that they have been approved for the imaging portion of the study. The form may also contain recommendations and/or feedback regarding future transfer data.
- The **Request Support Form** is sent from the investigator site to PAREXEL for the purpose of requesting supplies and for asking questions related to technical or operational aspects of the imaging portion of the clinical trial (Direct e-mail or telephone contact may be used as an alternative). Please see a sample of this form in section 6.3 of this manual.

The preferred option of image submission to PAREXEL is eTransfer. Courier will only be accepted in exceptional cases. If your site is using courier, PAREXEL will deliver a hard copy site kit including shipping materials (see section 3.5 for more information). It will also contain:

- The **Archive Media Labels** which will need to be completed with the subject and visit information and placed on each individual film or archive media (e.g., CD), making sure not to obscure anatomy. Please place the label on the actual media and not the media case.
- **Additional Site Supplies:** Digital media (e.g. CD), bubble mailers, masking pencils, media labels, and airway bills.

2.5 Responsibilities

The **Core Imaging Laboratory (CIL)** is the centralized facility at PAREXEL Informatics for all processes associated with image data collection and review by Independent Reviewers. PAREXEL is responsible for the receipt, tracking, processing, Quality Control (QC), and archiving of the image data. Data generated by the reviewer(s) are maintained at the CIL and will be transferred to NOVARTIS (or designee) at a specified time.

The **investigator sites** are responsible for enrolling subjects and obtaining imaging per the Image Acquisition Guidelines and study protocol. The investigator site is also responsible for managing image scheduling and for preparing and forwarding image data to the CIL within 24 hours of acquisition for screening and 48 hours for the follow-up visits. Any changes in staff must be communicated to PAREXEL in a timely manner so that access to applicable applications/ portals (e.g., eTransfer portal) is appropriately updated.

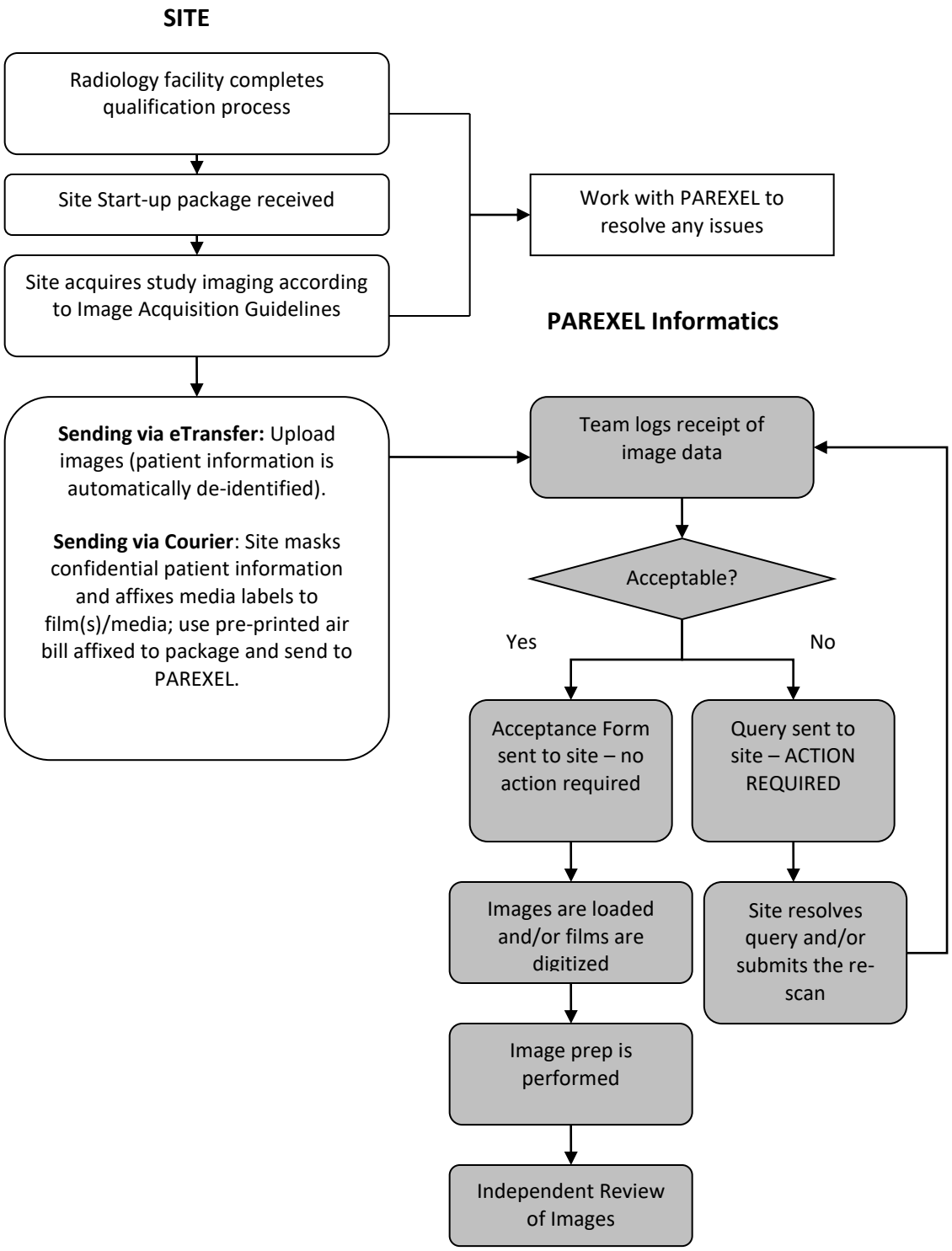
2.6 PAREXEL Contact Information

Project Team 236483 PAREXEL Informatics 2nd Federal Street Billerica, MA 01821 USA 236483-Imaging@PAREXEL.com Phone : +1 833-543-1079 PAREXEL will try to respond back to you within 24 hours or sooner.
Perceptive eTransfer – Technical Support +1 (888) 315-0790 toll free or +1(321)309-2710 (Global Toll Free Number) Support@dicomgrid.com (Available 24/7)
Omkar Kayal Project Manager Phone :- +91-40-4437-9835 Omkar.Kayal@PAREXEL.com

Note: Please use the project specific email address: 236483-Imaging@PAREXEL.com .

Contacts will change during the study. PAREXEL will send along updated spreadsheets periodically to keep sites informed of new contact information. Please place these updates in the study binder to keep current with communication needs

2.7 **Study Flowchart**



3 Site Standardization Procedures

This section details the site standardization procedures for the investigator sites participating in this clinical trial. Please notify the radiology staff in advance of a site initiation process and ensure that the Site Survey and the Image Acquisition Guidelines are reviewed prior to acquiring the test transfer scan or subject imaging. Please note that the test transfer must be submitted and approved by PAREXEL before the site's Site initiation visit (SIV).

Novartis and PAREXEL have agreed that the Test Transfer submission step prior to Imaging Qualification is **Not required if your site is already working with PAREXEL on similar indication with similar imaging requirement**. However In order to ensure that the Image quality requirements are met, we want sites to acquire the images for the first subject only, at the first attempt, and send this to PAREXEL for Quality Check. Please don't scan other subjects until you receive the approval/acceptance notification from PAREXEL for the first subject. Once first subject images are approved, the site can resume enrolling/scanning the other subjects as normal.

This step is very important and must be followed once you start acquiring the First subject Images

3.1 Roles and Responsibilities

R = Responsible for doing the task/document/deliverable
A = Accountable for the task/document/deliverable being completed
C = Consulted for input and/or in performing/completing the task/document/deliverable
I = Informed that the task/document/deliverable has been completed

Task/Document/Deliverable	Principal Investigator*	Study Coordinator	Radiologist/ radiology technician	CRA	PAREXEL
Site Survey completion	C	R	R	A	C
IAG Review	C	R	R	A	C
Site Operational Review	C	R	R	A	C
Study Supply Ordering	I	R	R	C	I
Study Supply Distribution	I	I	I	I	R
Direct Contact from/with sites	I	R	R	A	R
Issue Escalation	R	-	-	R	R

***Per GCP, the Principal Investigator is ultimately responsible for all site activities and tasks.**

3.2 Site Survey Completion

Performed by: Study Coordinator or Designee, Radiology Technician, CRA
References: Site Survey, Image Acquisition Guidelines (IAG)
Scope: This procedure describes the steps necessary to identify the site contact details as well as the hardware and software used. Please refer to the Site Survey for the specific information needed.

Prior to the start of the site qualification process, Novartis will provide PAREXEL with an investigator site list which will include all necessary site contact information. The CRA will partner with the site and PAREXEL to ensure that the correct communication channels are established.

Note: The primary contact of the site for PAREXEL should be either the Study Coordinator or the Radiology Technician.

1. PAREXEL will contact the investigator site providing instructions for completion of the required steps for standardization of image acquisition. PAREXEL will provide the Site Survey for completion and the IAG for reference.
2. The primary site contact or CRA will send the completed Site Survey to PAREXEL.
3. PAREXEL will review the Site Survey and check for completeness. Query or Acceptance feedback will be provided to the site by PAREXEL.

   Note: A Case Query Notification requires further action from the site; query responses should be provided to the PAREXEL study team within 5 business days or sooner when required.

4. Once the Site Survey has been accepted, and the site is considered trained as site has reviewed the Image Acquisition Guidelines and Site Operations Manual, PAREXEL will request that a test transfer be completed as described in Section 3.3.

3.3 Test Transfer Acquisition

Performed by: Study Coordinator, Radiology Technician
References: Image Acquisition Guidelines (IAG)
Scope: This procedure describes the steps necessary to acquire test transfer images and to provide PAREXEL with the necessary scan information. Please refer to the IAG for the specific parameters to be used for image acquisition.

1. Upon completion and submission of the site survey and site is considered trained as site has reviewed the Image Acquisition Guidelines and Site Operations Manual, PAREXEL will request a test transfer from the investigator site. If the test transfer is to be submitted to PAREXEL via courier, then supplies may be requested by the site. Upon site's or CRA request, PAREXEL will provide a prepaid airway bill, shipping supplies, and the necessary media for the imaging submission to be completed and sent to PAREXEL.
2. The radiologist or respective technician will acquire the test transfer images according to the IAG, unless the site is working with PAREXEL on similar indication with similar imaging requirement. The Radiology Technician will save the images to the site preferred media (CD, film, DVD) and maintain a copy of the exam at the facility. A test transfer image should be performed using a phantom. (Phantom is any dense object that is scanned to evaluate the performance of a scanner avoiding potential risk to a living subject. Phantom for test scanning will not be provided by PAREXEL.) If eTransfer is not being used, the technician must de-identify (blind) any information that can be used to identify the subject details contained in the DICOM Header.

Note: If you need to de-identify electronic data and your IT department is unable to help, you may wish to consider whether DicomEditor is appropriate. For more information about this free software, please visit: http://mircwiki.rsna.org/index.php?title=DicomEditor. DicomEditor is not a PAREXEL product. We do not endorse it, do not make any representations about its performance, and do not supply any training or support for the software. Please ensure you test DicomEditor prior to using it for study images so that you are sure there are no issues with it.

3. The study coordinator must verify that any information which can be used to identify the subject has been completely masked.
4. If the images are being saved to hardcopy films (Not applicable for MRI), please print two original copies, one will remain at the site and the other is sent to PAREXEL.

3.4 Test Transfer Preparation, Tracking and Transfer

Please refer to sections 4.2 - 4.7

3.5 Site Standardization Completion

Once the Site Survey and the Test Transfer have been accepted, PAREXEL will send an eStart-up Kit to the site in 1 business day. PAREXEL will inform the site of the completion of the site standardization process in a Site Acceptance Notification via email.

The kit, which contains all study related documents, will be sent via email to all sites who will be submitting the images electronically to PAREXEL. For those sites that will be using courier as the primary method to submit images, the kit will be sent via a courier and will include the shipping materials.

4 Image Processing Procedures

This section details the image acquisition, collection, and data transfer procedures for the investigator sites participating in this clinical trial. Please notify the radiology staff in advance of a study subject's visit and include the Image Acquisition Guidelines with the image requisition.

4.1 Image Acquisition

Performed by:	Study Coordinator, Radiology Technician
Scope:	This procedure describes the steps necessary to acquire study images and to provide PAREXEL with the necessary subject and visit information. Please refer to the Image Acquisition Guidelines for the specific parameters to be used for image acquisition.

1. The radiology or respective technician will acquire the images according to the IAG. The radiology technician will save uncompressed, DICOM format images to the site preferred media (CD, film, DVD) and maintain a copy of the exam at the facility. If eTransfer is not being used, the technician must de-identify (blind) the subject name and any other information that can be used to identify the subject contained in the DICOM Header.

   Note: If you need to de-identify electronic data and your IT department is unable to help, you may wish to consider whether DicomEditor is appropriate. For more information about this free software, please visit: http://mircwiki.rsna.org/index.php?title=DicomEditor. DicomEditor is not a PAREXEL product. We do not endorse it, do not make any representations about its performance, and do not supply any training or support for the software. If you haven't done so already, we suggest you try DicomEditor prior to using it for study images so that you are sure there are no issues with it.

2. The study coordinator must verify that the name of the subject and any other information that can be used to identify the subject have been completely masked and only study specific subject number is used
3. Confidential subject information is defined as individually identifiable information including but not limited to:
   - name (full name or first name and last initial or first initial and last name)
   - social security number
   - home address
   - phone number
   - medical record number
4. If the images are being saved to hard copy films (Not Applicable for MRI), please always print two original copies, one remains at the site and the other is sent to PAREXEL.

4.2 Preparation and Tracking of Images

Performed by: Study Coordinator or Designee

Scope: This procedure describes the methods used to prepare and track images for transfer from the investigator site to PAREXEL. All Screening images are required to be submitted to PAREXEL within 24 hours of acquisition (1 business day). The follow-up images should be submitted within 48 hours of acquisition (2 Business days).

The study coordinator receives the imaging data from the Radiology Department and verifies:

- Images stored on digital media are in **uncompressed DICOM format**
- No lesion markers or measurements are present
- Confidential subject information is de-identified.

1. The Study Coordinator will contact the site's Radiology Department if any problems are noted.
2. The Study Coordinator will complete and affix media labels directly onto the media, CD / DVD.
3. If hard copy films are to be sent, each film must have a media label attached in a manner that does not obstruct anatomy.
4. Submitting imaging data containing confidential subject information is not permitted.
5. The Study Coordinator is responsible for maintaining subject confidentiality by ensuring the imaging technicians de-identify confidential subject information on all exams being submitted on digital media.
6. Hardcopy films may be masked using the specialized masking pencils. Please contact PAREXEL to request masking pencils if needed.

4.3 Image Data Transfer via Perceptive eTransfer *(Preferred)*

Performed by: Study Coordinator or designee

Scope: This procedure describes the steps used to send images from the investigator site to PAREXEL via eTransfer.

This web-based electronic transfer solution allows investigator sites to transfer de-identified study images to PAREXEL Informatics through an internet browser. The eTransfer website is HIPAA and 21CFR Part 11 compliant.

There are only two requirements to use eTransfer:

1. A computer with internet access
2. JAVA plug-in (already installed on most computers)

Recommended internet browser: Google Chrome (no JAVA plug-in required).
Other compatible internet browsers: Internet Explorer (7, 8, 9 or 10), Safari, or Firefox (all require JAVA for upload).

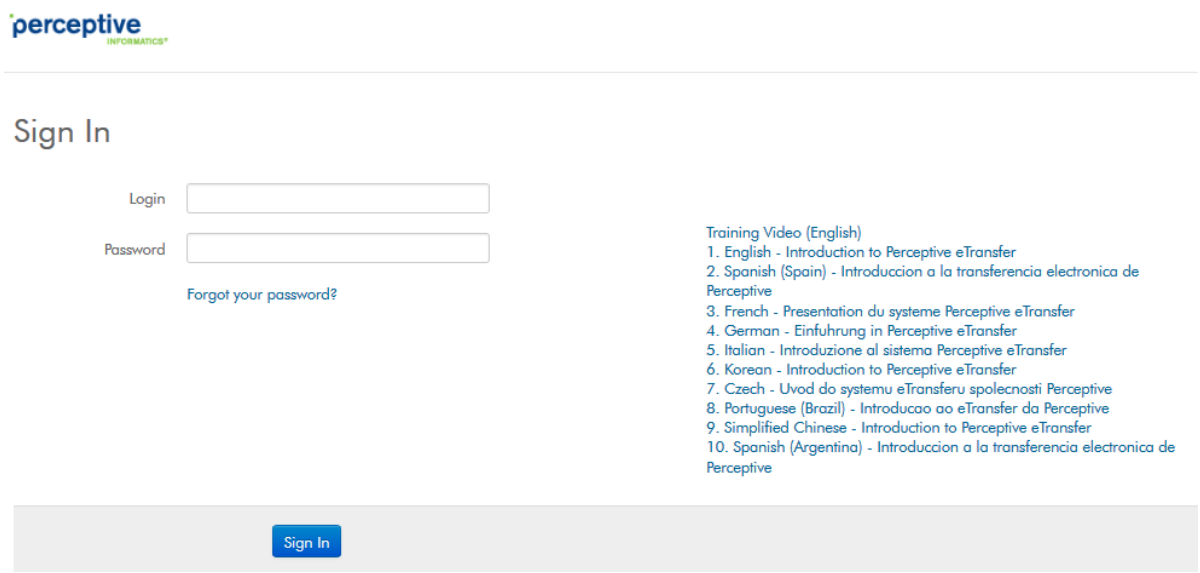
If JAVA is not installed, the Perceptive eTransfer system will guide the user through the java installation process. If installing the Java plug-in is blocked, the user will contact the Information Technology Administrator at the site.

User Access

1. The PAREXEL study team will create an account using the email address provided by the Novartis or site as the user login ID. The site user will then receive an email notification containing the account credentials and login instructions.
2. Additional user accounts can be requested by emailing the PAREXEL team at 236483-Imaging@PAREXEL.com
3. Navigate to the system login page and select the training link to view a 10 minute training clip.

4. Log into the system and the home page appears:

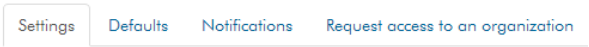
https://Perceptive.dicomgrid.com/



5. If login is not successful, please check the credentials again and/or contact the PAREXEL team.

User Settings

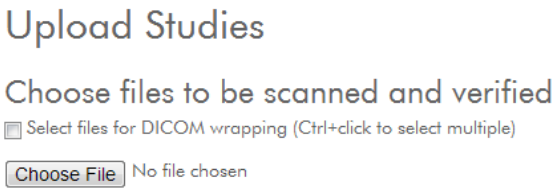
1. The user's name appears in the top right menu of the homepage. Select this to edit:
   - First and/or last name
   - Reset the password
   - Set email notifications



2. To edit notification preferences, the user will select the "Notifications" tab. To receive email notifications, select "On Upload".

Uploading Images

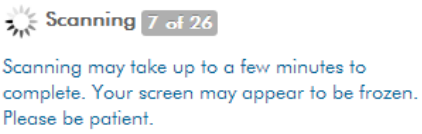
1. Select the trial/site from the dropdown list. Returning users will see the list of all previously transmitted images for the trial at the site.
2. To upload images, the user will select the trial, then the site from the "Studies" dropdown list, and finally select "Upload Studies".



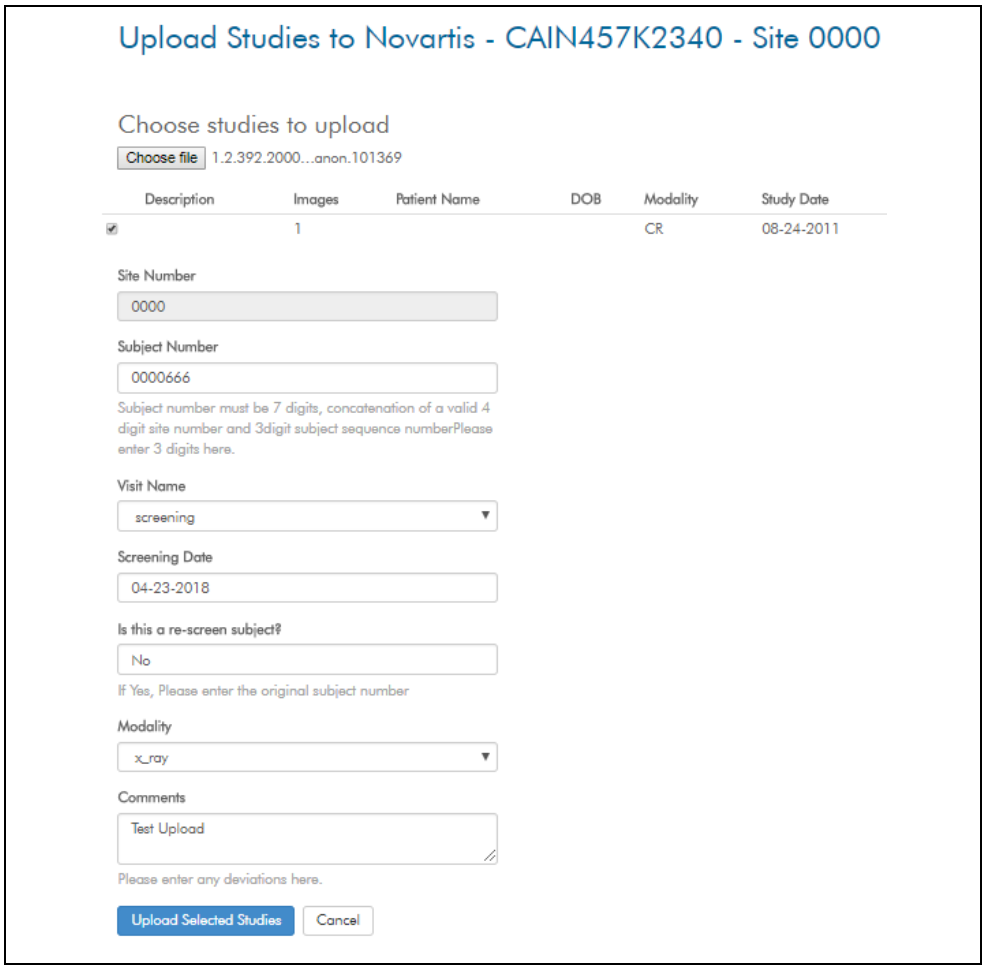
NOTE: If uploading a non-DICOM file (i.e. JPEG, AVI, DXA/IQC files), the user must check the "Select files for DICOM wrapping."

3. Select " Choose File" and a browsing window will appear. The user will select the folder where the study images are stored and select "Open".

4. The "Scanning" symbol will appear when a folder has been selected.



5. The user will complete the trial/subject required information.



6. You must provide "Screening Date "only during screening image submission and "Re-Screening Subject" number is optional.
7. The user will select "Upload Selected Studies". As the images upload, a status bar will appear. Do not navigate away from the webpage while the upload is in progress. Open another eTransfer webpage to upload another scan concurrently. Upon successful upload, the following message will be displayed:

8. If the image upload notification feature is on, the user will receive an email within minutes of a successful upload from Perceptive eTransfer.

Viewing Images in the Image Viewer

1. Once uploaded, images can be viewed through the browser using the "View study in viewer" button: NOTE: the viewer is only available if using Google Chrome or Mozilla Firefox.
2. The user can use the scroll to the bottom of the viewer to go through all images.

For technical support, contact the DicomGrid support team by phone at 1-888-315-0790 (available 24/7) or by email at support@dicomgrid.com and specific Protocol Number [CAIN457K2340 or PAREXEL Project Number [236483).

4.4 Image Transfer via Courier

Performed by:	Study Coordinator or Designee
References:	Imaging Study Tracking Log, Airbill
Scope:	This procedure describes the steps used to send images from the investigator site to PAREXEL.

1. The Study Coordinator will use the pre-printed airbills that are provided by PAREXEL for this study.

   Note: Additional airbills must be requested directly from PAREXEL
2. Complete the pre-printed airbills that are provided by PAREXEL for this study. Please request new labels from PAREXEL when required using the Request Support Form.

   Sites outside of U.S. will need to complete a commercial invoice.

Note: Pre-printed stickers do not require any further completion and non-preprinted airbills will not be accepted by the courier. If you are in need of UPS airbills, e-mail PAREXEL at 236483-Imaging@PAREXEL.com to obtain an electronic airbill to ship images and request additional pre-printed labels.

3. The Study Coordinator will place the hard copy films or digital media in the package for shipment.
4. If hardcopy films are being sent, these will be placed in the padded envelopes that can be provided by PAREXEL. Taping around the edges of the envelope will help to secure the images. Shipping boxes can also be obtained free of charge from the appropriate courier.
5. The date of shipment and airbill tracking number will be recorded on the Imaging Study Tracking Log.

   ***Note*:** Please ship imaging data to PAREXEL within 24 hours for Screening and 48 hours of acquisition for follow-up visits (do not wait for a subject to be randomized or wait to collect images for multiple timepoints).

   The sites will be required to complete **Imaging Study Tracking Log** to document only the courier shipment status of all images related to the clinical trial. The log is updated with information regarding image acquisition, shipment dates, and corresponding shipment tracking numbers and stored locally and is not required to be sent back to PAREXEL.

4.5 Case Acceptance

Performed by: Study Coordinator or Designee
References: Case Acceptance Notification
Scope: This procedure outlines the actions required by the Study Coordinator upon receipt of a Case Acceptance Notification (CAN). The form will be sent from PAREXEL in a timely manner upon receipt of acceptable image data.

1. PAREXEL will perform a quality assurance check on the imaging data received.
2. A CAN is sent from PAREXEL to the investigator site upon receipt of image data informing the site that the imaging for the timepoint is complete and of acceptable quality.
3. This form may also contain feedback or recommendations for subsequent visits.
4. The CAN also serves as documented resolution to a Query.
5. File the CAN in the study's binder. No further action is required.

4.6 Query Process

Performed by: Study Coordinator or Designee
Scope: This procedure outlines the actions required by the Study Coordinator upon receipt of a Case Query Notification (CQN) from PAREXEL. A CQN will be sent from PAREXEL in a timely manner. The study coordinator may complete and return the CQN via fax or email or may choose to respond via phone or login to the MyQueries portal to resolve the query.

1. A CQN is sent from PAREXEL to the investigator site upon receipt of unacceptable image data. The query text will describe the issue and indicate the action(s) required to resolve the issue(s).
2. The study coordinator is required to respond within 5 business days of CQN receipt or sooner if required. **Note: For the Screening Visit Related Queries must be responded within 1 (One) business day.**
3. If a written response on the CQN is being sent to PAREXEL, the study coordinator is required to maintain a copy of the query response in the study's binder.
4. Do not include any confidential subject information in the CQN response. Only the subject number should be used to identify a subject.
5. The study coordinator or Designee may respond to the query by simply replying to the email, responding to the query form, or updating the response on MyQueries portal. If the site opts to use the query form, it should be printed out, the response should be written on the form, and the form should be scanned and emailed (236483-Imaging@PAREXEL.com) back to PAREXEL.
6. If resolution of the query cannot be completed, the site is required to notify PAREXEL. This notification must include a definitive date for when the response to the query will be provided.

   Note: Increased frequency when approaching study milestones as requested by Novartis.
7. If the site is unable to successfully resolve the query, PAREXEL may request the assistance of the monitor and notify Novartis of the issue.
8. PAREXEL GQT (Global Query Team) also may reach-out to the study Coordinators/Monitors via phone and address the open queries.

Potential issues include:

•ISSUE: Unacceptable image quality

Action: Provide better quality images or document no other images are available in the comments field of the Query Form.

•ISSUE: Image Acquisition Guidelines were not followed

Action: Provide additional images if available or document no other images are available in the comments field of the Query Form.

•ISSUE: Missing anatomy

Action: Provide additional images or document no other images are available in the comments field of the Query Form.

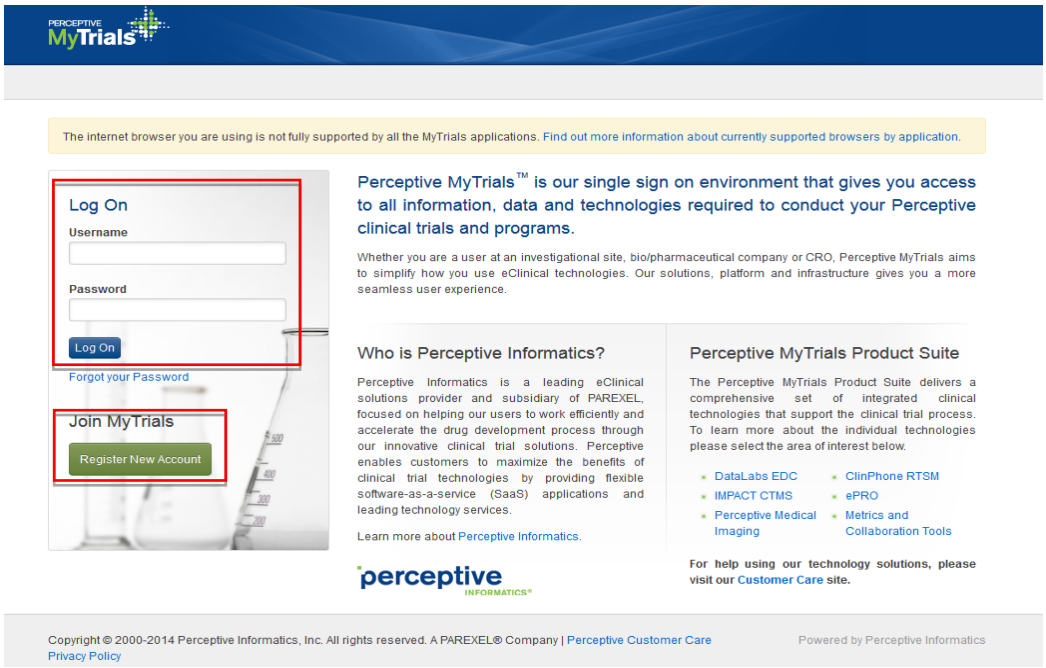
4.7 MyQueries Portal

Performed by: Study Coordinator or Designee

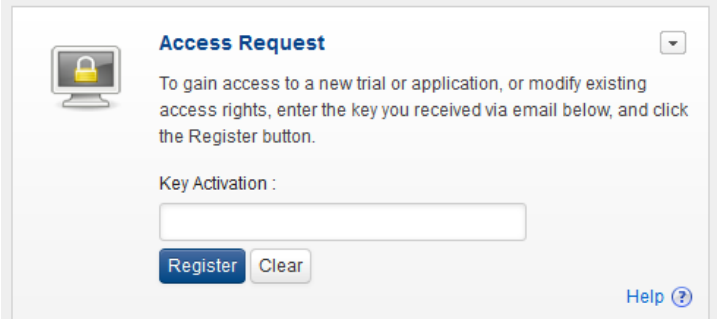
Scope: This procedure describes the process for responding to queries sent from PAREXEL via MyQueries

MyQueries is a web-based service for investigator sites to receive, view, track, and respond to queries from any computer with web access.

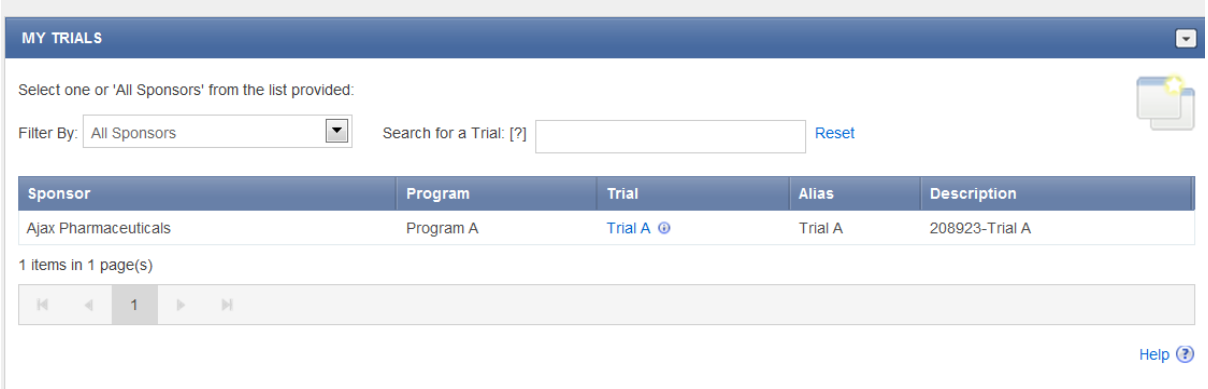
1. Study Coordinators will be granted access to MyTrials by default. Please contact the PAREXEL team and request an account for MyTrials if additional users will need access.
2. An email will be sent from Perceptive Customer Care with the following email address: do-not-reply@perceptive.com with an activation code.
3. Login to MyTrials @ WWW.MYTRIALS.COM.
   - If you already have an account, log on with your User Name and Password.
   - If you are using MyTrials for the first time, select "register new account" in the "Join MyTrials" box.



4. After logging into the system or creating a new account, enter the activation key(s) that you have received via email. **Please note you may receive more than one key**

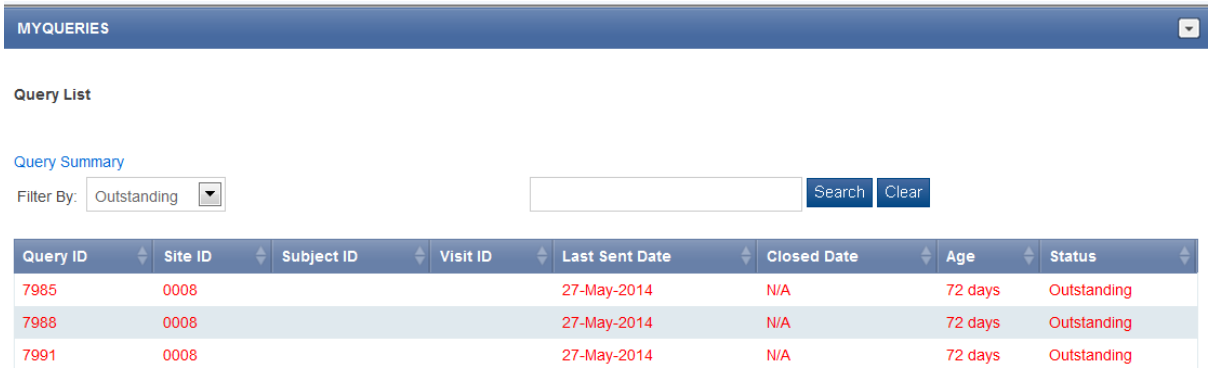


5. All trials that you have access to will appear upon login. Select the desired project.



6. Listed under the MyQueries tab are the new and outstanding queries for the project.

7. Click the links to view the queries.



Query List (Queries can be filtered by any column header)

- **Subject ID** - If the query is regarding a site issue, this field may be blank.
- **Query ID** - A query with a number after the query ID (e.g., 1234-3) represents the number of times the query was resent.
- **Site ID** - If the query is regarding a site issue, the subject field may be blank.
- **Visit ID** - The visit description. If a query is not associated to a visit, this field may be blank.
- **Last Sent Date** - The date the query was sent or resent from the PAREXEL. The Last Sent Date is updated with every response from the team but may not be the latest date in the query history.
- **Age** - The number of days since the query was created.

Status

- **New** - Queries that have not been opened/viewed by the site user. Queries can be new to one user and outstanding to another.
- **Outstanding** - Queries that have not been closed by PAREXEL (only PAREXEL can change the status to 'closed'). Outstanding queries may be filtered by "overdue" and "responded".
    - **Overdue** – A query that has not been responded to within 10 business days. The status remains "outstanding" and will be displayed in red text.
    - **Responded** – A query that a site responded to (the status remains "outstanding").
- **Closed** - Queries that have been closed by the PAREXEL team.

Search for Queries

- A user can search for queries, including specific text from the query comments section.
- All fields in the query record are included in the search. The search text must be in English.

View Query Details

Select a query from the Query List to view details or to respond. The following information is displayed:

- **Query Comments** - The most recent communication is displayed in this section.
- **Query History** - Click "Show" to see the query history. All communications between PAREXEL and site / monitor users are included.
- **Query Response** - If the selected query is outstanding and the user has the appropriate permissions, the user will be able to send a query response to PAREXEL. The response must be in English. Enter the response into the query response field and select "send".
- To navigate between queries in the list, click Next or Previous at the bottom of the Query Detail Page.

4.8 Requesting Support

Performed by:	Study Coordinator or Designee
References:	PAREXEL Informatics Contact Information, Request Support Form
Scope:	This procedure describes the steps taken to request support from PAREXEL for the imaging portion of the CAIN457K2340 clinical trial.

1. For all inquiries and other requests regarding the imaging portion of the clinical study, please contact PAREXEL. Refer to the Contact list (Section 2.6).
2. Upon completion/resolution of the request, PAREXEL will communicate a response via phone or email.

   Note: Please use the Request Support Form template when making requests.

5 Confirmation of Imaging Specific inclusion/exclusion criteria:

PAREXEL is responsible to perform the independent confirmation of inclusion/exclusion criteria as per protocol. Novartis acknowledges that the Central read confirmation is based only on the image data made available to PAREXEL, does not constitute medical advice, and may not be used for patient care. All responsibility for patient care and the final decision whether a patient should be enrolled in the study rests with the principal investigator and not with PAREXEL or its independent readers.

In the case a patient is screened for enrollment in the study, all images have to be sent to PAREXEL within 24 hours of acquisition. All queries issued by PAREXEL related to a patient in screening need to be answered by the site within 24 hours. Once all associated queries are closed, PAREXEL will independently assess the screening exams within 5 business days.

Upon completion of the Central read, PAREXEL will send results directly to the sites and related distribution list. Eligibility results will be sent via email with central read result (pdf) attachment.

Study contacts with the following roles will receive the Central read results from PAREXEL:

- Principal Investigator
- Study Coordinator
- Site Monitor
- Clinical Study Manager (If Applicable)
- Novartis Study Leads

In case the site investigator desires clarification regarding the basis of the central read confirmation, the investigator will initiate the contact through Study Monitor.

Note: If the Screening X-RAY SIJ exam has been assessed as Positive the Screening X-Ray SPINE exams will not be presented for the independent review assessment at PAREXEL and no results will be shared for such subjects.

Central Read Results – X-Ray – SIJ

PAREXEL
YOUR JOURNEY. OUR MISSION.™

Novartis CAIN457K2340
Central mNY Read Results

PAREXEL has completed the expedited central read that was requested for your Novartis CAIN457K2340 subject. Please find the results below and file with the subject's source documents. Please do not hesitate to contact your study monitor with any questions or concerns.

Site ID	<Site ID>
Subject ID	<Subject number from Tracking>
Timepoint Read	Screening
Earliest Scan Date	DD/MMM/YYYY
Unilateral sacroiliitis grade 3-4 on x-ray	Yes (Positive) or No (Negative) or NA (Unable to Evaluate)
Bilateral sacroiliitis grade 2-4 on x-ray	Yes (Positive) or No (Negative) or NA (Unable to Evaluate)
SIJ mNY Radiograph Eligibility Result	Yes (Positive) or No (Negative) or NA (Unable to Evaluate)
Date of Report Generation	DD/MMM/YYYY

PAREXEL is responsible to perform the independent confirmation of Imaging Specific inclusion/exclusion criteria as per protocol. Novartis acknowledges that this assessment is based only on the image data made available to PAREXEL, does not constitute medical advice, and may not be used for patient care. All responsibility for patient care and the final decision whether a patient should be enrolled in the study rests with the principal investigator and not with PAREXEL or its independent readers. Novartis shall ensure that any site receiving information about inclusion/exclusion criteria confirmation has agreed to an acknowledgement that is substantially similar to the acknowledgement in the preceding sentences.

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Central Read Results – X-Ray SPINE

PAREXEL
YOUR JOURNEY. OUR MISSION.™

Novartis CAIN457K2340
Central Read Results

PAREXEL has completed the expedited central read that was requested for your Novartis CAIN457K2340 subject. Please find the results below and file with the subject's source documents. Please do not hesitate to contact your study monitor with any questions or concerns.

Site ID	<Site ID>
Subject ID	<Subject number from Tracking>
Timepoint Read	Screening
Earliest Scan Date	DD/MMM/YYYY
Presence of at least one syndesmophyte	Yes or No or N/A (Unable to Evaluate)
Total Spinal Ankylosis	Yes or No or N/A (Unable to Evaluate)
Date of Report Generation	DD/MMM/YYYY

PAREXEL is responsible to perform the independent confirmation of Imaging Specific inclusion/exclusion criteria as per protocol. Novartis acknowledges that this assessment is based only on the image data made available to PAREXEL, does not constitute medical advice, and may not be used for patient care. All responsibility for patient care and the final decision whether a patient should be enrolled in the study rests with the principal investigator and not with PAREXEL or its independent readers. Novartis shall ensure that any site receiving information about inclusion/exclusion criteria confirmation has agreed to an acknowledgement that is substantially similar to the acknowledgement in the preceding sentences.

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6 Sample Forms

6.1 Case Acceptance Notification

This form is sent from PAREXEL to the investigator site upon receipt of acceptable imaging data at PAREXEL.

PAREXEL.

2 Federal Street
Billerica, MA 01821, USA
236483-Imaging@PAREXEL.com

Acceptance Communication – CAIN457K2340

To	"To" Contacts	Fax	Email	Sample SC: ABC@investigator.com
CC	"CC" Contacts	Fax:	Email:	Sample CRA: CRA@xyz.com
From:	"From" Contacts		Email:	236483-Imaging@PAREXEL.com

Date: 11-Sep-2017

Info

Project:	Sponsor: Novartis	TIMS: 236483	Protocol: CAIN457K2340
Investigator	Dr. Investigator		
Site:	Site ID: XXXX	Site Name:	Investigator Site
Subject:	Subject ID: XXXXXXX		DOB:
Visit:	Screening		

CIL COMMENTS:

The PAREXEL Core Imaging Laboratory has received acceptable images and forms of following patient:

Image

Image Modality	Exam Date	Image Series
X-Ray	02-Sep-2017	SIJ (AP View)

Thank you for submitting the **Visit: Screening** for **Subject: XXXXXXX**.
These images have been accepted. No further action is required. Thank you.

Thank you for your participation!

The information in this communication is intended only for the use of the individual(s) named abnove. If you are not the intended recipient, or an employee or agent of the recipient who is ressponsible for delivering this comunication, any dissemination, distribution or photocopiying or other use of this communication or the information in this information is sticty prohibited. If you received this in error, please call PAREXEL Informatics at 1-978-313-3900, so that we may arrange for the return of the original communication.

Thank you.

2 Federal Street, Billerica, MA 01821, USA || 236483-Imaging@PAREXEL.com

6.2 Case Query Notification

This form is sent from PAREXEL to the investigator site when unacceptable imaging data is submitted to PAREXEL. The form will describe the issue of concern such as missing data or deviations from the Image Acquisition Guidelines. The form will also indicate the action required.

PAREXEL.

2 Federal Street
Billerica, MA 01821, USA
236483-Imaging@PAREXEL.com

Query Communication – Novartis CAIN457K2340

To	"To" Contacts	Fax	Email	Sample SC: ABC@investigator.com
CC	"CC" Contacts	Fax:	Email:	Sample CRA: CRA@xyz.com
From:	"From" Contacts		Email:	236483-Imaging@PAREXEL.com

Date:	11-Sep-2017	Query#:	10010

Info

Project:	Sponsor: Novartis	TIMS: 236483	Protocol: CAIN457K2340
Investigator	Dr. Investigator		
Site:	Site ID: XXXXX	Site Name:	Investigator Site
Subject:	Subject ID: XXXXX		DOB:
Visit:	Baseline		
Query:	Required Scan Missing		
Issue:	Missing Screening		

CIL COMMENTS:
Dear Site / Investigator

Please submit the Screening visit image for Subject No. XXXXXXX.
All study related images must be submitted to PAREXEL within 24 hours of acquisitions.
Thank You!

Site COMMENTS:

Thank you.

2 Federal Street, Billerica, MA 01821, USA | 236483-Imaging@PAREXEL.com

6.3 Request Support Form

This form is sent from the investigator site to PAREXEL for the purpose of requesting supplies or for technical or operational support for the imaging portion of the clinical trial.

Request Support Form
Novartis CAIN457K2340

ATTENTION: **Project 236483 Team**
236483-Imaging@PAREXEL.com
PAREXEL Informatics

REQUESTER: _____
PI NAME/SITE #: _____
PHONE #: _____
DATE: ___/_____/_____
DD/MMM/YYYY

Nature of Request (Check One):	☐ **Technical**	☐ **Operational**	☐ **Supplies Needed**

SUPPLIES (Please Indicate Quantity):

- ☐ Archive media labels #_____(Sheets)
- ☐ Optical Disks #_____
- ☐ Blank CDs #_____
- ☐ Pre-printed courier airbills #_____
- ☐ Small Padded envelopes for shipping #_____
- ☐ Padded envelopes for X-ray Films #_____
- ☐ Other _____ #_____

Shipping Address (if different than site address):

_____
_____
_____

Operational/Technical Questions:

6.4 Imaging Study Tracking Log

The Imaging Study Tracking Log is used to document the shipping status of study data.

NOVARTIS

PAREXEL
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PROTOCOL – CAIN457K2340
236843 - STUDY TRACKING LOG

Imaging Study Tracking Log

To be completed by the person responsible for transferring the scan to PAREXEL Informatics. To be filled in the study specific files.

Site ID: _____

Subject Number	Timepoint	X-Ray/MRI	Number of films/CD	Exam Date dd/mmm/yyyy	Date Shipped to PAREXEL dd/mon/yyyy	Airbill Number	Sent by (initials)
Make additional copies of this form if necessary							

6.5 Media Labels

The media labels are completed with applicable subject and visit information. The label is placed on each individual film or media (CD, DVD, film) being sent to PAREXEL. When affixed, the label must not obstruct any anatomy on the films.

Novartis – CAIN457K2340
PAREXEL Informatics - 236483

Site#: _____ Subject #: _____

Visit: SCREENING BSL WK16 WK52 WK104/Discontinuation (Circle One)

Scan Date : ___ ___ / ___ ___ ___ / ___ ___ Modality : X-Ray / MRI (Circle One)
DD MMM YY

Comments:_____

Signature Approval Page

This document has completed a review and is understood and accepted by the following:

Sawata Hiroshi

Digitally signed by Sawata Hiroshi
DN: dc=com, dc=novartis, ou=people, ou=GD, serialNumber=606541, cn=Sawata Hiroshi
Reason: I am approving this document
Date: 2018.11.26 15:50:44 +01'00'

Hiroshi Sawata
Global Trial Director
Novartis Pharma AG

Date

Signatures of the appropriate PAREXEL team members are captured electronically and appended to the last page of this document.

PAREXEL International Electronic Signature Page

This page is the manifestation of the electronic signature(s) used in compliance with PAREXEL International's electronic signature policies and procedures and in compliance with applicable regulations.

UserName: Kayal, Omkar (kayalo)
Title: Project Manager, MEDICAL IMAGING
Date: Tuesday, 27 November 2018, 10:54 AM GMT Standard Time
Meaning: Document contents approved.
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