B7451014 Newsletter

JADE
REGIMEN B7451014

April 2020 ■ Issue 14

In This Issue

A Message from the Study Team

Hello Study Investigators and Coordinators,

Around the globe, many countries are experiencing the effects of the COVID-19 pandemic. The B7451014 study team recognizes that this has presented challenges for some clinics participating in the study. Please reference the **COVID-19 Protocol Administrative Change Letter** dated 10Apr2019 distributed via email for guidance on conducting study visits and laboratory testing.

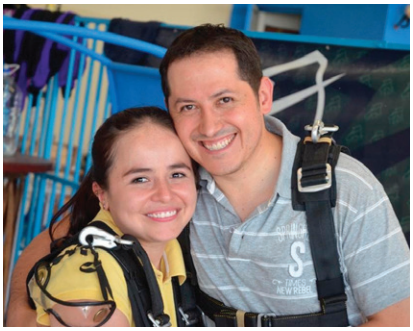
We are grateful for your continued commitment to the B7451014 study and we wish you and your families good health during this difficult time.

Please see further guidance regarding COVID-19 in the clinical section of this newsletter.

Study Team Spotlight:

Ricardo Benitez—Pfizer Site Relationship & Excellence Partner, Mexico

I am a Site Relationship and Excellence Partner and the main Pfizer point of contact for investigative sites. I am also accountable for safeguarding the quality and patient safety at the investigator site. In this role, I am responsible for site monitoring and oversight, as well as building and retaining relationships from site activation through the lifecycle of studies.



I am from Mexico city where I live. In my spare time, I enjoy swimming, reading, meditation & I share these activities with Naye, my girlfriend. We also enjoy walking in small villages or just watching a movie together.

At Pfizer, I am currently assigned to JADE studies in Mexico (B7451014, B7451015 and B7451036). The best part of working on these studies is that people from the sites are really friendly and always available to discuss any challenges.

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Site Spotlight:

Pesquisare Research Clinic in Brazil

Pesquisare is a Research Clinic in Brazil with more than 10 years of experience developing projects in several therapeutic areas. We have had the pleasure of acquiring knowledge and experience with the companies we work with. In turn, we are able to better serve our community.

The B7451014 study is a pioneer at our site for Atopic Dermatitis. We are happy to see how well the patients respond to this treatment and how they feel in terms of quality of life and above all, their self-esteem. Something we'd like to share about this study is a touching letter we received from a subject's mother who told us that her child took the first dose of the study drug at the clinic and went back home still feeling down because of the dermatitis condition. However, the next day, all of the child's itching and redness was gone. The family is so thankful and happy for these results.

We'd like to thank Pfizer for allowing us the opportunity of achieving knowledge and growth in the area of dermatology.

eCRF Completion Requirements for Flare Visits

The Data Management and Clinical Teams have noted numerous subjects with incorrect data entry for flare visits that then require correction. Please see below for instructions for correct data entry for subjects who meet flare criteria.

Please refer to 7.35.1 of the eCRF completion requirements:

If subject returns to the clinic for a **Planned visit and it is determined that they have met the 'Flare' criteria**:

- ***Only the DOV and Rescue visit forms need to have data entered for the planned visit.*** All other forms within the planned visit should have "Not Done" entered at the item level. This planned visit will then turn into the Day 1 Rescue Visit and all forms for Rescue Visit 1 should be completed

If subject returns to the clinic on an **unplanned visit and it is determined that they have met the 'Flare' criteria:**

- An UNPL visit should be created and the Rescue Visit form should be entered. This will activate the Day 1 Rescue Visit and update. The DOV may be the same as the UNPL Visit date which activated the Rescue Visit form.

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COVID and Safety Events

- During the COVID crisis, sites must continue to collect serious- and non-serious adverse event (S/AE) and medication data. When this data is collected outside of the investigational site, sites should request copies of the subject's medical records.
- Investigators must continue to perform safety reporting responsibilities as stated in the protocol.
- Investigators should maintain regular and documented contact per the protocol defined visit schedule, with participants who are unable to make on-site visits to ensure pertinent safety information is collected and recorded.
- Any confirmed or suspected COVID-19 infection should be reported as an Adverse Event following protocol requirements for AE reporting.
  - In order to accurately capture **COVID-19/coronavirus infections** in the database, site staff are to enter these adverse events as COVID-19 infection which will then code to Coronavirus infection and be easily identified.
    - × Do not enter COVID-19 positive
    - ✓ It is important to capture the infection part of the event term; if only COVID-19 is reported, a query will be issued to clarify if the verbatim term refers to an infection/positive test result.
- Currently established processes should be followed for reporting SAEs whenever possible. However, as a result of the COVID-19 global pandemic, it is recognized that some investigator sites that use fax machines for SAE reporting may not have access to the site and/or use of the fax machine. Please contact your CRA for assistance with alternative SAE submission, if needed.
- Refer to the **Protocol Administrative Change Letter (PACL) dated 10Apr2019** for further details on:
  - **the expectations of conducting remote site visits**
  - **determining drug accountability,**
  - **delivering study drug to the subject,**
  - **assessing flare, and**
  - **rolling over onto the 1015 study**

NOTE: Implementation of the PACL must comply with sites' local and national regulatory requirements. Please contact your ICON CTM (Clinical Trial Manager) regarding local or country requirements related to PACL review, approval and implementation.

B7451014 EASI DCR Process

Please be aware that the EASI DCR Process that is in place for the B7451015 study will not be used for B7451014.

If there are discrepancies with a subject's EASI calculation/score, please **do not** submit an ERT DCR (Data Correction Request) to create an unscheduled visit within the ERT system. An unplanned visit should never be opened for missing data that is not in the tablet. DCRs will not be approved and processed for this.

Please continue to use the same process that has been used in the past on the B7451014 study—submit a DCR to change/correct the **individual attributes** that ultimately change the subject's EASI calculation/score. Submitting a DCR to request to change the EASI score is not acceptable for B7451014. The DCR must include the changes to the individual attributes—these attributes will then be updated (via the DCR). A calculation will then occur to ultimately update/correct the EASI score.

Clinical Reminders

End of Treatment Essentials

At the **Week 52** and **Rescue Week 12** End of Treatment (EOT) visits, site staff are responsible for ensuring that all procedures outlined in the B7451014 protocol are completed. Some common items forgotten at these visits include:

- **Administer the last 1014 dose at the EOT visit.**
- **The last date entered on the dosing log should be the same day as the EOT visit under normal circumstances when no AE is involved** (remember to adjust the number of missed doses, if necessary).
- **Collect the Banked Biospecimens from all subjects unless prohibited by local regulations** (Prep B1.5 and Preb B2.5 collection tubes) Refer to protocol section 7.2 for more details.
- **Be certain that a pNRS value is captured on the B7451014 eDiary.**

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Clinical Reminders *Continued from page 3*

Speaking of pNRS...

Results from the database release on 19DEC19 have revealed that over 100 subjects did not record a pNRS score in either the B7451014 or B7451015 protocol at the B7451014 Week 12 visit. Your most focused attention is required to prevent this issue in subjects completing the Week 52 and Rescue Week 12 visits. Below is a reminder of the steps that must be followed to ensure capture of this critical data point.

1. Prior to the visit, remind subjects to bring the handheld device (e-Diary) to the site or have available during a remote visit.
2. The Pruritus NRS will only appear on the handheld once the tablet has transmitted the study visit. If the subject is on site for a visit, complete all clinical outcome assessments and have the subject complete all patient reported outcome assessments for the relevant visit on the site tablet and transmit data by using the refresh icon in the upper right-hand corner of the tablet. If COVID-19 requires conducting a remote visit, activate the site tablet and begin the visit to activate the visit on the subject's hand-held device. Refresh the tablet.
3. Ask the subject to also refresh the handheld (e-Diary).
4. Ask the subject to complete the dosing diary, PSAAD and P NRS **before the visit has ended**.

NOTE: It is critically important that the subject does not complete any B7451015 procedures until site personnel confirm that the subject completed the pNRS on the B7451014 eDiary.

Completing the Disposition Form

Please refer to the recently updated (v12) CRF Completion Requirements (section 7.40) for very specific examples of how to complete the disposition page.

Choosing NOT to roll over to 1015 is NOT considered withdrawing from the 1014 study.

Withdrawal by subject is not the same as withdrawal of consent: Withdrawal by Subject occurs when the subject decides to stop study participation but has NOT gone the additional step to refuse all further data collection. These subjects should NOT have a Withdrawal of Consent CRF form completed (see Section 7.41). **Withdrawal of Consent** occurs when the subject formally withdraws their consent both to participate in the study and for any further data collection. We cannot have data in the database following the date of Withdrawal of Consent. In this case, Status should be "Withdrawal by Subject" and Specify Status should be "Withdrawal of Consent", and the Withdrawal of Consent CRF must be completed.

Important FLARE Reminders

When a subject meets the criteria for flare, remember to...

- **Provide topical rescue treatment on the day of flare.** Not providing topical rescue treatment within a day of protocol-specified flare is a protocol deviation.
- **Provide only acceptable topical rescue treatments that are topical corticosteroids, topical calcineurin inhibitors, and crisaborole.**
- **Record only acceptable topical flare treatments on the Rescue Concomitant Medication Log.** The ONLY medicines allowed on the RESCUE Concomitant Medication log are acceptable topical flare treatments administered during the RESCUE PERIOD.
- **Subjects may start and stop the same or different topical rescue treatments as long as needed during the rescue period.**

Refer to the PACL dated 10Apr2020 for important guidance on COVID-19 impacts on study procedures and tests. If a participant in the Blinded Treatment phase is suspected of reaching protocol-defined atopic dermatitis flare, only a site visit will confirm a **true** flare event. There are, however, **2 options for Investigators when flare is suspected during a remote visit:**

1. The Investigator may withdraw study drug, permanently discontinue the subject from the study, and immediately proceed with standard of care treatment. This subject has no option to roll over onto the B7451015 study.
2. If study discontinuation is not in the best interest of the patient, and the Investigator considers returning to 200 mg QD PF-04965842 treatment is the best benefit/risk decision, the Investigator may immediately enter the subject into rescue therapy. To do this, enter all maximum

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values into the tablet for IGA, EASI, and BSA and the subject will then qualify for flare. Rescue study drug may be dispensed and shipped to the subject. On the AE log, document the AE term of ATOPIC DERMATITIS FLARE-COVID-19 with the event Category—ADVERSE EVENT. This will document a "flare in error" impacted by COVID-19. Upon completion of rescue therapy and meeting minimum criteria, this subject may roll over onto the B7451015 study. In all cases of suspected flare, please notify the sponsor via your ICON contact.

Refer to slides from the March Site forum located in Firecrest for correct documentation of flare as well as drug interruption and drug withdrawal due to adverse events.

Tuberculosis Retests

Following one year of total exposure to study drug since the last TB test, all subjects in regions which are above a low risk for Tuberculosis (i.e., >10/100,000 incidence) will undergo tuberculosis testing. This includes subjects from Argentina, Brazil, Bulgaria, Chile, China, Latvia, Mexico, Poland, Romania, Russia, Serbia, and Taiwan. In addition to TB testing as specified in this clinical protocol (Section 7.3.4), a chest X ray will be performed to aid in TB status determination for all adults, and recommended for adolescents according to local guidelines and standard of care and/or in countries with a high incidence rate of TB.

Patient Reported Outcome Assessments (PROs)

Remember to have subjects complete all PRO assessments on the tablet at every onsite visit. Many protocol deviations have been recorded for missed PROs. If the subject does not have time to complete the tablet PROs at the site visit, the subject may return to the site to complete these important efficacy tests. Most of the subject visits will remain open on the tablet for 48 hours. However, the Week 52 EOT and the Rescue EOT visits will remain on the tablet indefinitely with no expiration. This provides some flexibility to ensure the subject PROs are always completed

Key Vendor Information and Important Reminders

Please see the table below for where study supplies may be requested, depending on which country your site is located in. We have different import considerations for each country, so in order to get materials to your site as quickly and efficiently as possible, you may need to either order supplies online through the vendor portal or contact your monitor with your re-supply request.

Country	Covance Lab Kits	ERT ECG Supplies	Print Materials Re-Supply
Argentina	ICON monitor	ICON monitor/Parexel	ICON monitor/Parexel
Belgium	Lablink	ERT Studyworks	Cyberchrome portal
Brazil	ICON monitor	ICON monitor/Parexel	ICON monitor/Parexel
Bulgaria	Lablink	ERT Studyworks	Cyberchrome portal
Canada	Lablink	ERT Studyworks	Cyberchrome portal
Chile	ICON monitor	ERT Studyworks	Cyberchrome portal
China	Lablink	Monitor/Parexel	Monitor/Parexel
Germany	Lablink	ERT Studyworks	Cyberchrome portal
Israel	Lablink	ICON monitor/Parexel	Cyberchrome portal
Italy	Lablink	ERT Studyworks	Cyberchrome portal
Latvia	Lablink	ERT Studyworks	Cyberchrome portal
Mexico	ICON monitor	ERT Studyworks	Cyberchrome portal
Netherlands	Lablink	ERT Studyworks	Cyberchrome portal

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Key Vendor Information and Important Reminders *Continued from page 6*

Poland	Lablink	ERT Studyworks	Cyberchrome portal
Romania	Lablink	ERT Studyworks	Cyberchrome portal
Russia	Lablink	ICON monitor/Parexel	ICON monitor/Parexel
Serbia	Lablink	ICON monitor/Parexel	Cyberchrome portal
Slovakia	Lablink	ERT Studyworks	Cyberchrome portal
Spain	Lablink	ERT Studyworks	Cyberchrome portal
Taiwan	Lablink	ICON monitor/Parexel	Cyberchrome portal
United States	Lablink	ERT Studyworks	Cyberchrome portal

Covance Central Lab

Reminder! Please remember to frequently check the Covance XIP portal for messages from Covance, particularly during the COVID crisis. If there are any universal restrictions from couriers during this time, Covance may send your site a message through the portal with this information.

If your site is in **Argentina, Brazil, Chile** or **Mexico**, please do not place small orders for lab supplies online. Rather, work with your CRA to order kits for your site quarterly. If you require any bulk supplies, please let your monitor know ASAP. This will help us to work around the very long import timelines into these countries while reducing import costs and ensuring that you have enough kits on hand for your patients. Thank you for help with this process!

For all other sites, please consider the following when ordering lab supplies online through the Lablink portal:

- When ordering bulk supplies such as pregnancy tests, urine cups, wipes, etc., please do not order small quantities. Rather, order a larger amount that will last you several months.
- The shelf life of pregnancy tests is 18 months, so it is preferable that you place one order of these bulk items that will last you the remainder of the study.
- Lab kits have a shelf life of approximately 6 months

ERT ECG

Note! **If you are receiving a "leads off" message on your ECG machine while taking subject readings, this could be because your ECG electrodes have expired. Please check the expiry date on your electrodes before use.**

If your site is in **Argentina, Brazil, Russia, China**, or **Taiwan** and you need additional ECG electrodes or paper, please notify your CRA who can arrange for these materials to be sent to you from a local Parexel depot. Please DO NOT order electrodes through Study Works! We can get the materials to your site faster from a local depot than through ERT directly.

For sites in **Chile** and **Mexico**, we have arranged for larger shipments of electrodes and ECG paper to be delivered directly to your sites. Please contact your monitor if you need additional materials.

For all other sites in North America and EMEA please order your ECG electrodes and paper through Study Works. There are no import challenges in these countries and the supplies should arrive at your site fairly quickly.

As mentioned above for lab kits, it is preferable that you order larger quantities of ECG electrodes and paper well in advance of when you will need them for subject visits. Consider that one subject will need approximately 130 electrodes over the course of the study and please order a larger number to have on hand, rather than many small individual supply orders.

ERT eCOA (Site Tablets and Subject Handheld Devices)

Reminder! For any performance issues with ERT tablets or subject handheld devices, please immediately call the ERT helpdesk and open a customer care ticket. This should be your first step if an eCOA device is not performing as expected. In many cases, the ERT customer care team can help you immediately over the phone. If you cannot get the assistance you need from ERT, please escalate the issue to your CRA or a study team member.

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All site tablets (Yoga Books) must now be running software version 15.02

How to Update Your eCOA Tablet:

1. The user will be prompted to install an update to the existing application. Tap **Install** followed by **Done**
2. Confirm that the software version has been downloaded to the eCOA Tablet by checking the Study Version number located on the left sidebar of the Home page.

If the Tablet(s) at your site has not updated automatically to version 15.02, please follow the instructions below to perform this manually:

3. Please navigate to the AirWatch Agent on the home screen.
4. Once in the agent, select **manage apps** at which time the app upgrade will be displayed.
5. The user will be prompted to install an update to the existing application. Tap **Install** followed by **Done**.
6. Verify that the version number has updated.
7. Once the app is installed and verified, select the home button to return to lockdown.
8. Confirm that the software version has been downloaded to the eCOA Tablet by checking the Study Version number located on the bottom left sidebar of the Home page.

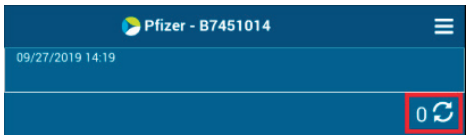
★You have received an email communication from the B7451014 study team that contains screen shots of this process. Please use the email as a visual reference.

ERT Handheld Devices

Latent Data on Handheld Devices

The Week 52 EOT and Rescue Week 12 EOT visits are very important! We need to ensure the pNRS data is captured at these visits. For subjects already completing study, this data may have been captured on the handheld during the final visit and may still be on the device. To check for this, please look at the handheld screen.

1. If you see a circle of arrows with a number in it, please click the arrows to transmit the data. If there is no number, there is no data on the device.



2. If you do not see a circle and instead see the QR Code, the phone is ready for the next subject and no data is on the device.

PLEASE CONTACT CUSTOMER CARE if you have any questions.

★The call center is open 24 hours a day, 7 days a week, 365 days a year. Global toll-free numbers are available at: https://www.ert.com/contact-customer-care/.

On Site Creative

Most sites will order additional print supplies online from the Cyberchrome portal. Please reference the CTSM ordering guide in the back of your Investigator Site File for ordering instructions for resupply of print materials.

However, for some countries, there are also print materials stored in a local Parexel depot. If your site is located in **Argentina, Brazil, China, Russia** or **Taiwan,** please contact your monitor and they will arrange for supplies to be sent to your site.

Printed Columbia Suicide Scales

With the upcoming Protocol Amendment 5 implementation, many sites will be completing C-SSRS assessments with their subjects at each study visit going forward. As regulatory approvals are granted for the protocol amendment, sites will be shipped print C-SSRS forms, along with new printed mini bound protocols for your reference. ***It is very important that you do not use these print assessments with subjects until the new informed consent documents have been signed.*** We have included a note with the print materials as a reminder of this. Thank you for your cooperation as we implement this new version of the study protocol!

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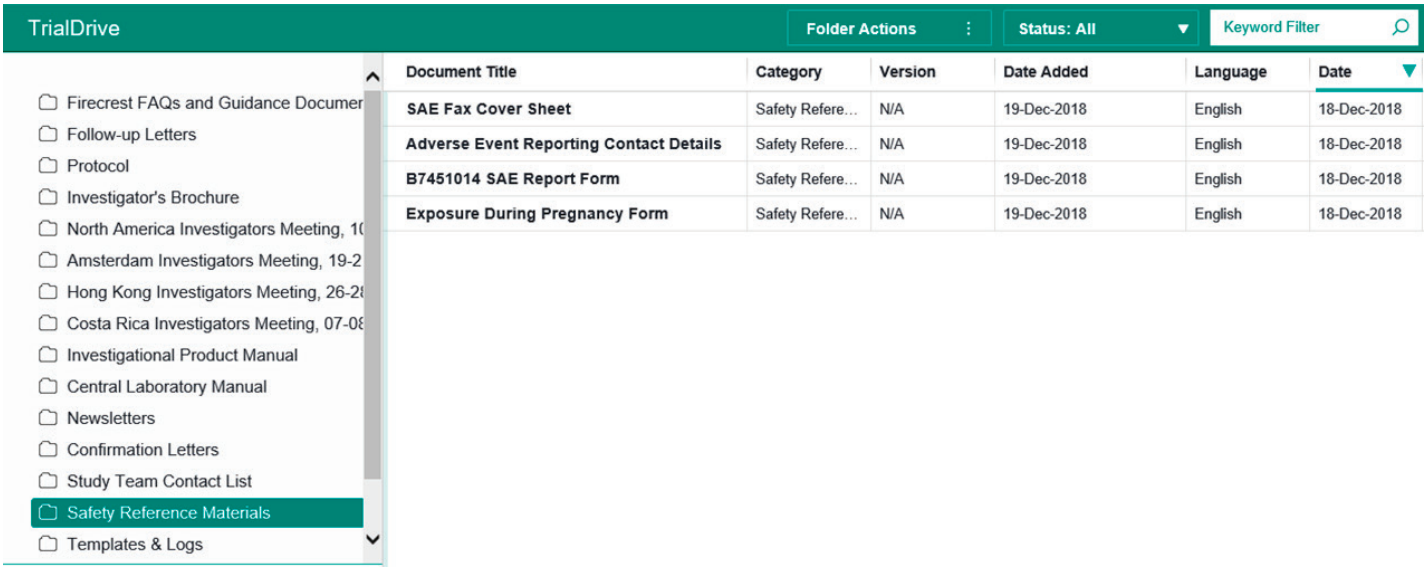
SAE Reporting Information

Be sure to report all SAEs within 24 hours of learning of them!

Serious adverse event reporting information, including contact details, can be found in Firecrest:



Study Contact Information

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Pfizer	Clinical Data Scientist	Global	Ketty Terri	ketti.k.terry@pfizer.com	+1 860 441 1582

Study Vendor Customer Care Contacts

Vendor	Telephone		Weblink/Email
Covance (Central Lab)	Argentina Belgium, Bulgaria Brazil Canada Chile China Germany, Israel, Italy Latvia Mexico Netherlands Poland Romania Russia Serbia Slovakia, Spain Taiwan USA	0800 288 5288 + 800 88 77 44 11 0800 890 0288 866 762 6209 800 225 288 800 820 85 92 + 800 88 77 44 11 800 031 43 01 800 288-2872 + 800 88 77 44 11 00 800 41 11 08008 9 52 14 810 800 201 71041 +41 58 822 7901 + 800 88 77 44 11 0800 165 1493 866 762 6209	http://www.covance.com/customers/investigators/investigator-study-team.html
ERT	USA: +1 908 595 2020 For country-specific contact numbers: http://www.ert.com/contact-customer-care/		customercare@ert.com
Firecrest	N/A		http://www.firecrestclinical.com/pfizer Pfizer@firecrestclinical.com
IMPALA	USA +1 877 433 2619		http://impala.pfizer.com