

SMRT® Link Software Installation (v8.0)

Introduction

This document describes the procedure for installing **SMRT Link v8.0** on a customer system. This document is for use by Customer IT or SMRT Link Administrators.

SMRT Link is the web-based end-to-end workflow manager for the Sequel[®]/Sequel II System. It includes software applications for designing and monitoring sequencing runs, and analyzing and managing sequence data. SMRT Link provides a web interface that can control **multiple** Sequel/Sequel II Systems.

SMRT Link is the primary access point for applications used by researchers, laboratory technicians, instrument operators, and bioinformaticians for various interactions with applications related to the Sequel platform. The applications include:

- **Sample Setup**: Calculate binding and annealing reactions for preparing DNA samples for use on the Sequel/Sequel II System.
- Run Design: Design runs and create and/or import sample sheets which become available on the Sequel/ Sequel II System.
- Run QC: Monitor run progress, status and quality metrics.
- **Data Management**: Create Projects and Data Sets; manage access permissions for Projects and users; generate QC reports for Data Sets; view, import, export, or delete sequence, reference, and barcode files.
- **SMRT Analysis**: Perform multiple types of secondary analysis, including sequence alignment, variant detection, *de novo* assembly, structural variant calling, and RNA analysis.

Note: SMRT Link and the Sequel/Sequel II System are for research use only (RUO).

Overview

- 1. Install or upgrade the SMRT Link software. (See "Installation Summary" on page 5 and "Configuring LDAP" on page 11 for details.)
- 2. (**Optional**) Configure SMRT Link to use an SSL Certificate. (See "Step 1: Obtain a domain-specific certificate from the appropriate Certification Authority." on page 14 for details.)
- 3. (**Optional**) Add SMRT Link Users and Assign User Roles. (See "Adding SMRT Link Users and Assigning User Roles" on page 13 for details.)
- 4. (**Optional**) Change the admin and pbicsuser passwords. (See "Changing admin and pbicsuser Passwords" on page 10 for details.)
- 5. (Optional) Configure LDAP. (See "LDAP Integration" on page 11 for details.)

PacBio Compute Infrastructure Partners provide HPC solutions designed to support the Sequel II System.

Sequel II System Compute Requirements

Head Node			
Cores	32		
RAM	64 GB		
tmp_dir (Local Storage)	1 TB recommended, 500 GB minimum		
db_datadir (Local Storage)	250 GB		
Compute Nodes			
Cores (Total)	384 ^a		
Minimum RAM per Slot (1 slot = 1 core)	4 GB/8 GB de novo assembly large complex genomes		
tmp_dir (Local Storage) 100 GB			
Shared Data Storage ^b			
Sequence Data	40 TB		
(jobs_root) Analysis Data	Data 70 TB		
Network			
10 GBE recommended, 1 GBE required			

- a. For a standard CCS sequencing collection (415 GB sequencing data, 25 GB Unique Molecular Yield, 15 kb insert size, 30-hours movie), CCS Analysis takes 6.5 hours on this configuration. SMRT Link will work on less powerful compute configurations, however analysis time will be significantly longer.
- b. Storage is calculated for one Sequel II System, assuming 100 human genomes per year at 50-fold coverage, *de novo* assembly.

Data Examples

Human Assembly

• Genome size: 3.3 GB; Sequence data 400 GB; Analysis data 700 GB; Analysis time: 72 hours wall. This is 50-fold coverage human genome analyzed on the compute configuration listed above.

Rice Assembly

• Genome size: 0.43 GB; Sequence data 55 GB; Analysis data 90 GB; Analysis time: 20 hours wall. This is 50-fold coverage rice genome analyzed on the compute configuration listed above.

For Sequel Instrument requirements, see "Appendix C: Sequel System Compute Requirements" on page 21 for details.

Data storage

- The SMRT Link software **root** directory **must** be readable and writable by the SMRT Link install user and **must** have the same path across all compute nodes via NFS. PacBio recommends /opt/pacbio/smrtlink for the SMRT Link software root directory (referred to as \$SMRT_ROOT), and smrtanalysis for the SMRT Link install user (referred to as \$SMRT_USER).
- The SMRT Analysis **output** directory is used to store output from SMRT Analysis jobs. The software accesses this directory from a symbolic link at \$SMRT_ROOT/userdata/jobs_root, which can be modified manually or by using the installation script. The symbolic link destination should be on a shared file system (NFS); it **must** be writable by the \$SMRT_USER, and it **must** be accessible along the same path on **all** compute nodes. This is usually symbolically linked to a large storage volume.

- The SMRT Analysis database directory is used to store database files and backups. The software accesses this directory from a symbolic link at \$SMRT_ROOT/userdata/db_datadir, and it can be modified manually or by using the installation script. This symbolic link destination should be a local directory (not NFS) and be writable by \$SMRT_USER. This directory should exist only on the SMRT Link install host.
- The SMRT Analysis **temporary** directory is used for fast I/O operations during run time. The software accesses this directory from a symbolic link at \$SMRT_ROOT/userdata/tmp_dir, and it can be modified manually or using the installation script. This symbolic link destination should be a **local** directory (not NFS), it must be writable by \$SMRT_USER, and it must exist (or be creatable) as an independent directory on **all** compute nodes. The temporary directory exists on **both** the head node, and the compute nodes.

Software Prerequisites: Server Operating Systems

- SMRT Link server software is supported on English-language CentOS 6.x; 7.x and Ubuntu 16.04; 18.04 64-bit Linux® distributions. (This also applies to SMRT Link compute nodes.)
- SMRT Link is **not** guaranteed to work on Linux versions that are no longer supported by the Operating Systems' vendors.
- SMRT Link server software **cannot** be installed on macOS® or Windows® systems.

Software/Hardware Prerequisites: Client Systems

To use SMRT Link on a client operating system:

- SMRT Link **requires** the Google[®] Chrome web browser, version 74 or later.
- SMRT Link requires a minimum screen resolution of 1600 by 900 pixels.

Network Configuration

- Please refer to the IT Site Prep Guide provided with your instrument purchase for more details.
- For network connectivity considerations, see the network diagram in the **Computer Requirements** section of the **IT Site Prep Guide**.

SMRT Link Server Environment Assumptions

- The SMRT Link server should run on a dedicated 64-bit Linux host with libc 2.12.1 or greater.
- Installing as the same non-root user (\$SMRT USER) that will be used to run the system.
- The \$SMRT_USER has full permissions in the file system in the \$SMRT_ROOT directory and in all linked directories for jobs_root, db_datadir and tmp_dir. (Common problems include NFS setup problems, ACLs, and so on.)
- When running in distributed mode, all other nodes have the same path for \$SMRT_ROOT and for all linked directories.
- During the installation, no other daemons/services are bound to the same ports.
- PacBio highly recommends that the system clock be synchronized to a public NTP time server.
- The \$SMRT_USER service account must have both the nofile and nproc limits set to a minimum of 8192. (See the ulimit(1) and limits.conf(5) Linux man pages for more information.)

General Security Notes

- PacBio recommends that you install the SMRT Link server on networks that are only accessible to trusted users, and discourages installing SMRT Link on public networks.
- Do not install SMRT Link using root as the user.

SMRT Link v8.0 Security Notes

SMRT Link v8.0 restricts access to the web services API to clients running on localhost (like the WSO2 server that handles authentication and permissions) or remotely using SSL encryption and password-based authentication.

Ports and firewalls: The instrument **must** be able to access the SMRT Link server on port 8243. This port is also used by the Sequel Instrument Control Software (ICS), so it needs to be available to **any** Sequel Systems as well.

- If your network is already configured to leave this port open, **no additional changes** are required to use v8.0.
- The instrument must be have access to port 8243 of the SMRT Link server.

Installation/Upgrade Checklist

Following is a list of items you should have ready **before** starting a new installation or upgrading an existing installation. **Note**: Paths that include spaces are **not** supported.

- Full path to the installation root directory, used for the main installation root.
- Job Management System settings.
- Full path to a directory on the shared file system the jobs root directory.
- Full path to a directory on the local file system on each node the tmp dir directory.
- Full path to a directory on the local file system on the install node the db_datadir directory.
- (Optional) LDAP Settings. See "Configuring LDAP" on page 11 for details.
- (Optional) SSL Certificate for WS02. See "SMRT® Link and SSL Certificate Procedures" on page 14 for details.

Installation Summary

Following are the steps for installing SMRT Link v8.0 on a **new** system. (See "Appendix A: SMRT Link Workflow Terminology" on page 19 for details.) To upgrade SMRT Link to v8.0 from a **previous version**, follow the upgrade steps on Page 7. SMRT Link v8.0 can be used with 4 versions of ICS:

- v6.x.x (Sequel System)
- v7.x.x (Sequel II System)
- v8.0.0.78867 (Sequel II System)
- v8.0.0.84541 (Sequel System)

Step	Installation Summary - SMRT Link v8.0		
1	Download SMRT Link software: Download and extract the SMRT Link software installer from http://www.pacb.com/support/software-downloads.		
2	Definitions and variables: For clarity, this document uses these conventions to refer to site-specific information:		
	 \$SMRT_ROOT: The SMRT Link Install Root Directory, such as /opt/pacbio/smrtlink. \$SMRT_USER: The SMRT Link Install User, such as smrtanalysis. smrtlinkhost.mydomain.com: The fully-qualified domain name of the SMRT Link Install Host. smrtlinkhost: The short host name of the SMRT Link Install Host. 		
	For \$SMRT_ROOT, define a convenience variable in the shell so the commands below may be run verbatim. To do so, use something like: SMRT_ROOT=/opt/pacbio/smrtlink		
	The fully qualified version of the SMRT Link Install Host may always be used in place of the short host name. But in some cases, particularly when working with WSO2, the fully qualified domain name is required.		
3	Log onto the SMRT Link Install Host (such as the hostname or IP address) as the SMRT Link Install User (such as \$SMRT_USER.)		
4	Install SMRT Link by invoking the SMRT Link Installer: smrtlink_8.0.0.80529.runrootdir \$SMRT_ROOT Note: The \$SMRT_ROOT directory must not exist when the installer is invoked, as the installer will try to create it, and will abort the installation if an existing \$SMRT_ROOT location is found. If a previous installation was canceled or otherwise failed, the installer can be invoked without extraction. Rerun using theno-extract option:		
	smrtlink_8.0.0.80529.runrootdir \$SMRT_ROOTno-extract		
	See "Appendix A: SMRT Link Workflow Terminology" on page 19 for additional information.		
5	Start SMRT Link services: \$SMRT_ROOT/admin/bin/services-start		
6	Run the Site Acceptance Test from the command line: \$SMRT_ROOT/admin/bin/run-sat-services Successful completion of run-sat-services, which produces a Site Acceptance Test (SAT) analysis job in the SMRT Analysis module of the SMRT Link GUI, indicates that the HPC configuration is functioning correctly.		
7	(Optional) Clear the Browser Cache:		
	This is a good troubleshooting step if needed.		
	1. Open the Chrome Browser and choose More Tools > Clear browsing data , choose All Time from the Time Range droplist, then check Cached images and files . Click Clear data .		
	2. Restart the browser.		

Ston	Installation Summany CMDT Link v0 0
Step	Installation Summary - SMRT Link v8.0
8	 Run the Site Acceptance Test from the browser: 1. Using the Chrome browser, open SMRT Link at http://smrtlinkhost:9090. The port number should match the GUI port defined during installation; the default is 9090. The URL will redirect to a secure URL at hard-coded port 8243. If port 9090 is blocked, go directly to the redirect URL at https://smrtlinkhost.mydomain.com:8243/sl/home. Check with your IT group if port 8243 is blocked; access to port 8243 on the SMRT Link Install Host is required to access the browser UI and for communication with the instrument.
	Bypass the Chrome browser's privacy error check:
	Without an SSL certificate installed, Chrome will issue a "Privacy Error" and state that "Your connection is not private". Bypass by clicking on the Advanced link on the bottom left of the page. Then click on the Proceed to smrtlinkhost.mydomain.com (unsafe) link. To avoid the "Privacy Error" in the future, follow the instructions for installing the SSL Certificate in Step 10 below.
	3. Log in to SMRT Link by entering the default Administrator credentials: admin/admin.
	 Submit SMRT Link notification selections: Select options for notifying PacBio of successful installations and for sending ongoing SMRT Link analysis usage information. Click Save.
	5. Go to the SMRT Analysis page:
	On the SMRT Link home page (https://smrtlinkhost.mydomain.com:8243/s1/), click SMRT Analysis.
	6. Create a new analysis: Click + Create New Analysis.
	7. Select analysis settings and start the analysis:
	a) Enter SMRT Link 8.0.0 SAT Test (or any descriptive name) in the Analysis Name field.
	b) Select Sequel Data as the Data Type.
	c) In the Data Sets table, check the box next to PacBio Tiny SAT Dataset Example.
	d) Click Next.
	e) Select Site Acceptance Test (SAT) from the Analysis Application drop down list, at the top left. The Reference field will be auto-populated with lambdaNEB.
	f) Click Start in the top right corner to start the analysis.
	8. Wait for the analysis to complete successfully. On the Analysis Results - SMRT Link 8.0.0 SAT Test page (Example: https://smrtlinkhost.mydomain.com:8243/sl/#/analysis/job/15):
	 The Analysis Overview page is updated periodically, and will clearly indicate success or failure.
	Successful completion of the Site Acceptance Test (SAT) indicates that SMRT Link analysis is working correctly. It shows that the analysis was configured and started via the browser GUI, through the SMRT Link Services, and dispatched jobs to the HPC cluster (if distributed mode was configured during installation).
9	(Optional) Configure LDAP:
	See "Configuring LDAP" on page 11 for details.
10	(Optional) Configure SMRT Link to use a Signed SSL Certificate:
	See "SMRT [®] Link and SSL Certificate Procedures" on page 14 for details.
11	(Optional) Change the pbicsuser and admin passwords:
	We recommend that you change the admin and pbicsuser account passwords. See "Changing admin and pbicsuser Passwords" on page 10 for details.

Upgrading SMRT® Link

Supported Upgrade Path

- SMRT Link upgrades to v8.0 are supported from any v6.x.x or v7.x.x release.
- You cannot upgrade to SMRT Link from SMRT Analysis v2.3.0 or earlier. Additionally, analysis job
 directories and run history from SMRT Analysis v2.3.0 or earlier are not compatible with SMRT Link and
 cannot be imported.

SMRT Link v8.0 can be used with 4 versions of ICS:

- v6.x.x (Sequel System)
- v7.x.x (Sequel II System)
- v8.0.0.78867 (Sequel II System)
- v8.0.0.84541 (Sequel System)

Step	Upgrading SMRT Link			
1	Download SMRT Link software: Download and extract the SMRT Link software installer from http://www.pacb.com/support/software-downloads.			
2	Definitions and variables: For clarity, this document uses these conventions to refer to site-specific information:			
	• \$SMRT_ROOT: The SMRT Link Install Root Directory, such as /opt/pacbio/smrtlink.			
	• \$SMRT_USER: The SMRT Link Install User, such as smrtanalysis.			
	• smrtlinkhost.mydomain.com: The fully-qualified domain name of the SMRT Link Install Host.			
	smrtlinkhost: The short host name of the SMRT Link Install Host.			
	For \$SMRT_ROOT, define a convenience variable in the shell so the commands below may be run verbatim. To do so, use something like:			
	SMRT_ROOT=/opt/pacbio/smrtlink			
	The fully qualified version of the SMRT Link Install Host may always be used in place of the short host name. But in some cases, particularly when working with WSO2, the fully qualified domain name is required.			
3	Log onto the SMRT Link Install Host (such as the hostname or IP address) as the SMRT Link Install User (such as \$SMRT_USER.)			
4	Stop the SMRT Link services:			
	\$SMRT_ROOT/admin/bin/services-stop			
	Note: Ensure that no active SMRT Link analysis jobs are running before stopping services.			
5	Upgrade SMRT Link by invoking the SMRT Link installer:			
	smrtlink_8.0.0.80529.runrootdir \$SMRT_ROOTupgrade			
	Note: The \$SMRT_ROOT directory must be an existing SMRT Link installation. Several validation steps will occur to ensure that a valid \$SMRT_ROOT is being updated.			
	If a previous upgrade was canceled or otherwise failed, the installer can be invoked without extraction. Rerun using theno-extract option:			
	smrtlink_8.0.0.80529.runrootdir \$SMRT_ROOTupgradeno-extract			
	See "Appendix A: SMRT Link Workflow Terminology" on page 19 for additional information.			
6	Start the SMRT Link services:			
	\$SMRT_ROOT/admin/bin/services-start			

Step	Upgrading SMRT Link		
7	Run the Site Acceptance Test from the command line:		
	\$SMRT_ROOT/admin/bin/run-sat-services		
	Successful completion of run-sat-services, which produces a Site Acceptance Test (SAT) analysis job in the SMRT Analysis module of the SMRT Link GUI, indicates that the HPC configuration is functioning correctly.		
8	(Optional) Clear the Browser Cache:		
	This is a good troubleshooting step if needed.		
	1. Open the Chrome Browser and choose More Tools > Clear browsing data , choose All Time from the Time Range droplist, then check Cached images and files . Click Clear data .		
	2. Restart the browser.		
9	Run the Site Acceptance Test from the browser:		
	1. Using the Chrome browser, open SMRT Link at http://smrtlinkhost:9090.		
	- The port number should match the GUI port defined during installation; the default is 9090. The URL will redirect to a secure URL at hard-coded port 8243. If port 9090 is blocked, go directly to the redirect URL at https://smrtlinkhost.mydomain.com:8243/sl/home.		
	 Check with your IT group if port 8243 is blocked; access to port 8243 on the SMRT Link Install Host is required to access the browser UI and for communication with the instrument. 		
	2. Bypass the Chrome browser's privacy error check:		
	Without an SSL certificate installed, Chrome will issue a "Privacy Error" and state that "Your connection is not private". Bypass by clicking on the Advanced link on the bottom left of the page. Then click on the Proceed to smrtlinkhost.mydomain.com (unsafe) link.		
	3. Log in to SMRT Link by entering the Administrator credentials: admin/admin. (admin is the built-in password, which may have been changed previously.)		
	4. Submit SMRT Link notification selections: Select options for notifying PacBio of successful installations and for sending ongoing SMRT Link analysis usage information. Click Save .		
	5. Go to the SMRT Analysis page:		
	On the SMRT Link home page (https://smrtlinkhost.mydomain.com:8243/s1/), click SMRT Analysis.		
	6. Create a new analysis: Click + Create New Analysis.		
	7. Select analysis settings and start the analysis:		
	a) Enter SMRT Link 8.0.0 SAT Test (or any descriptive name) in the Analysis Name field.		
	b) Select Sequel Data as the Data Type.		
	c) In the Data Sets table, check the box next to PacBio Tiny SAT Dataset Example.		
	d) Click Next.		
	e) Select Site Acceptance Test (SAT) from the Analysis Application drop down list, at the top left. The Reference field will be auto-populated with lambdaNEB.		
	f) Click Start in the top right corner to start the analysis.		
	8. Wait for the analysis to complete successfully. On the Analysis Results - SMRT Link 8.0.0 SAT Test page (Example: https://smrtlinkhost.mydomain.com:8243/sl/#/analysis/job/15):		
	 The Analysis Overview page is updated periodically, and will clearly indicate success or failure. 		
	Successful completion of the Site Acceptance Test (SAT) indicates that SMRT Link analysis is working correctly. It shows that the analysis was configured and started via the browser GUI, through the SMRT Link Services, and dispatched jobs to the HPC cluster (if distributed mode was configured during installation).		
10	(Optional) Change the pbicsuser and admin passwords:		
	We recommend that you change the admin and phicsuser account passwords. See "Changing admin and phicsuser Passwords" on page 10 for details.		

Updating the SMRT Link Chemistry Bundle Using the SMRT Link GUI

SMRT Link Chemistry Bundle updates allow updating of SMRT Link features **without** having to reinstall the SMRT Link software. The update also updates **Sequel**[®] **Instrument Control Software (ICS).**

Note: Only SMRT Link users with the **Admin** role can perform this update. In addition, update services **must** be enabled.

- 1. In SMRT Link, choose **About SMRT Link** from the Gear menu. (A red circle indicates that a Chemistry Bundle Update is available.)
- 2. Click the **Update** button.
- 3. If there are any problems, clear the browser cache: Choose **More Tools > Clear browsing data**, choose **All Time** from the **Time Range** droplist, then check **Cached images and files**. Click **Clear data**. Refreshing the browser tab or clearing the browser cache may be necessary for the Chemistry Bundle update to take effect.

Updating the SMRT Link Chemistry Bundle On the Instrument

- 1. On the instrument, choose **Admin** from the Main menu. (A red circle indicates that a Chemistry Bundle Update is available.)
- 2. Click the **Updates** tab, then click **Install**. The instrument software then restarts, which will take around 10 minutes.
- 3. Click the **question mark** to check the version number to validate the Chemistry Bundle update.

Installing only SMRT Tools

To install **only** command-line SMRT Tools, use the <code>--smrttools-only</code> option with the installation command, whether for a new installation or an upgrade. (This installs the **same** command-line tools as a full installation.) Examples:

```
smrtlink-*.run --rootdir smrtlink --smrttools-only
smrtlink-*.run --rootdir smrtlink --smrttools-only --upgrade
```

Note: Using <code>--smrttools-only</code> will **only** unpack the command-line applications, and will **not** run through the configuration prompts or provide the web services of a full SMRT Link installation. If command-line-only use with JMS integration is desired, please follow Steps 1 through 4 of the SMRT Link installation process. **Warning**: The Sequel instruments **cannot** communicate with a <code>--smrttools-only</code> installation.

Updating the SMRT Link Chemistry Bundle for smrttools-only Installations

Use this procedure only if you have installed the SMRT Link package using the --smrttools-only switch.

Download the Chemistry Bundle from the PacBio website, then unpack the files and place them in a user-defined directory. The value of the \$SMRT_CHEMISTRY_BUNDLE_DIR environment variable then defines where the software finds the updated files. Following are the suggested best practices for installing the Chemistry Bundle:

- 1. Download the Chemistry Bundle from http://www.pacb.com/support/software-downloads.
- 2. (Optional) Define \$SMRT_ROOT for convenience: SMRT_ROOT=/opt/pacbio/smrtlink
- Make directories, unpack, and link:

```
mkdir -p $SMRT_ROOT/userdata/chemistry/chemistry-pb-6.0.0.xxxxx
tar -C $ SMRT_ROOT/userdata/chemistry/chemistry-pb-6.0.0.xxxxx -xf /path/to/chemistry-pb-5.1.0.xxxxx.tar.gz
ln -s ./chemistry-pb-6.0.0.xxxxx $SMRT ROOT/userdata/chemistry/chemistry-pb-active
```

4. Set/export \$SMRT CHEMISTRY BUNDLE DIR and validate:

```
export SMRT CHEMISTRY BUNDLE DIR=$SMRT ROOT/userdata/chemistry/chemistry-pb-active
```

5. Set the variable in the user environment to make it permanent. Example: Use ~/.bashrc.

Changing admin and pbicsuser Passwords

The SMRT Link admin account has full access to SMRT Link, and is used to create users and grant users access.

SMRT Link comes with a default Instrument Control Software (ICS) user account (pbicsuser) which is used by the Sequel/Sequel II Systems to communicate with SMRT Link Web Services over a secure, encrypted connection. The pbicsuser account is **required** for instruments to communicate with SMRT Link. (Note that the pbicsuser credentials can **only** be used to access SMRT Link resources – it is **not** an account on the Linux system.)

The passwords for the admin and pbicsuser accounts are set to default values that are the same for all SMRT Link installations. Because the passwords can be used to access SMRT Link accounts and information, the passwords should be changed and only given to **trusted** users who require access.

To change the admin and pbicsuser passwords, use the following procedure:

```
$SMRT_ROOT/admin/bin/services-stop

$SMRT_ROOT/admin/bin/set-wso2-creds -u admin -p NEW-PASSWORD

$SMRT_ROOT/admin/bin/set-wso2-creds -u pbicsuser -p NEW-PASSWORD
```

To verify the admin and phicsuser passwords, use the following procedure:

```
$SMRT_ROOT/admin/bin/services-start

$SMRT_ROOT/smrtcmds/bin/pbservice status --host localhost --user admin --ask-pass

$SMRT_ROOT/smrtcmds/bin/pbservice status --host localhost --user pbicsuser --ask-pass
```

Printing pbservice status information and exiting with an exit status of 0 indicates success.

You must **also** change the pbicsuser account password in the Instrument Control Software (ICS) to match the new password. To do so: Select **Menu > Admin > SMRT Link** on the instrument touch screen to change the password.

Changing Your Usage Tracking Settings

When first logging in to the SMRT Link GUI after a successful installation or upgrade, users are prompted to notify PacBio of the upgrade/installation, and asked to enable the sending of SMRT Link analysis usage information to PacBio. Once set, these settings may **only** be viewed and modified from the command line using the accept-user-agreement tool.

WARNING: To use the accept-user-agreement tool, services must be running:

```
$SMRT ROOT/admin/bin/services-start
```

To set new settings, use the following command, specifying true or false for the options accordingly. For example:

```
$SMRT ROOT/admin/bin/accept-user-agreement --install-metrics true --job-metrics true
```

PacBio will be notified of a successful installation or upgrade immediately if the install metrics setting is true.

To view the current settings, run the command without any arguments:

```
$SMRT ROOT/admin/bin/accept-user-agreement
```

Note: If accept-user-agreement is run without arguments and the settings have not been previously set (either in the GUI or on the command line), **both** the install and job metrics settings will automatically be set to true and PacBio will be immediately notified of the installation or upgrade.

LDAP Integration

SMRT Link supports integration with LDAP for user login authentication. **Without** LDAP integration with SMRT Link, only **one** user (with the login admin/admin) is enabled.

If you are interested in configuring SMRT Link integration with your organization's LDAP, PacBio recommends that you consult your LDAP administrator to help determine the correct LDAP settings.

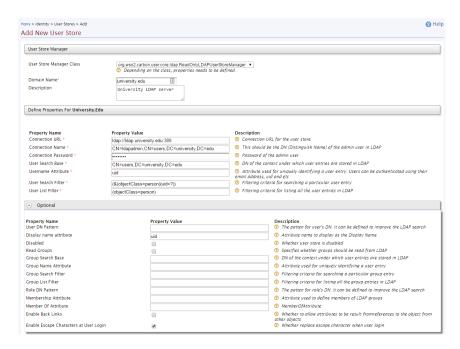
Note: Existing LDAP configurations are **automatically** migrated during upgrade.

Configuring LDAP

- LDAP is configured after SMRT Link v8.0 is installed, using the WSO2 API Manager software, as shown below.
- SMRT Link must **first** synchronize with your organization's LDAP objects before any directory accounts can be enabled and given a role to facilitate SMRT Link access.
- 1. Enter the following in your browser: https://<hostname>:9443/carbon/ where <hostname> is the host where SMRT Link is installed.
- 2. Login using admin/admin.
- 3. Click User Stores > Add.



4. Edit the fields as necessary for your site.



The following fields are **required**. (**Note**: Values provided in the example above are listed below for clarity. Actual values should be provided by your LDAP administrator):

- User Store Manager Class: org.wso2.carbon.user.core.ldap.ReadOnlyLDAPUserStoreManager
- Domain Name: university.edu
- Connection URL: ldap://ldap.university:389
- Connection Name: CN=ldapadmin, CN=users, DC=university, DC=edu (This is the bind DN, which is used to authenticate to the LDAP environment.)
- Connection Password: <password>
- User Search Base: CN=users, DC=university, DC=edu
- Username Attribute: uid
- User Search Filter: (& (objectClass=person) (uid=?))
- User List Filter: (objectClass=person)
- Display name attribute: uid

For more information on LDAP, consult the following web pages:

https://en.wikipedia.org/wiki/Lightweight_Directory_Access_Protocol https://en.wikipedia.org/wiki/LDAP_Data_Interchange_Format https://msdn.microsoft.com/en-us/library/ms677605%28v=vs.85%29.aspx

Problems with the LDAP server may be debugged by looking at the log file located here:

\$SMRT ROOT/userdata/log/smrtlink-analysisservices-gui/wso2/wso2-apigw-errors.log

SMRT® Link User Roles

SMRT Link supports three user roles: **Admin**, **Lab Tech**, and **Bioinformatician**. Roles define which SMRT Link modules a user can access. The following table lists the privileges associated with the three user roles:

Tasks/Privileges	Admin	Lab Tech	Bioinformatician
Add/Delete SMRT Link Users	Υ	N	N
Assign roles to SMRT Link users	Υ	N	N
Update SMRT Link software	Υ	N	N
Access Sample Setup Module	Υ	Υ	N
Access Run Design Module	Υ	Υ	N
Access Run QC Module	Υ	Υ	Υ
Access Data Management Module	Υ	Υ	Υ
Access SMRT Analysis Module	Υ	Υ	Υ

PacBio recommends the following role assignments:

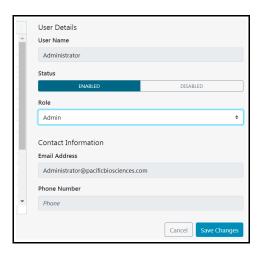
- Assign at least one user per site the Admin role. That individual is responsible for enabling and disabling SMRT Link users, as well as specifying their roles. The Admin can also access all SMRT Link modules, as well as every file in the system. (SMRT Link supports multiple users with the Admin role per site.)
- Assign users who work in the lab preparing samples and performing runs the Lab Tech role. Lab Tech can also access all SMRT Link modules.
- Assign users who work only on data analysis the Bioinformatician role. Bioinformatician can only access
 the Run QC, Data Management and SMRT Analysis modules; this is the lowest access level.

Adding SMRT Link Users and Assigning User Roles

- You must first configure LDAP before you can manage users and assign SMRT Link roles to users.
- After LDAP is configured, if you do not assign a SMRT Link role to a user, that user will not be able to login to SMRT Link.
- 1. Access SMRT Link: Enter http://<hostname>:9090, where <hostname> is the host where SMRT Link is installed.
- 2. Choose Configure from the Gear menu and click User Management.
- 3. There are 2 ways to find users:
 - To display all SMRT Link users: Click Display all Enabled Users.
 - To find a specific user: Enter a user name, or partial name and click Search By Name.



- 4. Click the desired user. If the Status is **Enabled**, the user has access to SMRT Link; **Disabled** means the user **cannot** access SMRT Link.
 - To add a SMRT Link user: Click the Enabled button, then assign a role. (See Step 5.)
 - To disable a SMRT Link user: Click the Disabled button.
- 5. Click the **Role** field and select one of the three roles. (A **blank** role means that this user **cannot** access SMRT Link.)
- 6. Click **Save**. The user now has access to SMRT Link, based on the role just assigned.



SMRT® Link and SSL Certificate Procedures

SMRT Link v8.0 uses SSL (Secure Sockets Layer) to enable access via HTTPS (HTTP over SSL), so that your SMRT Link logins and data are encrypted during transport to and from SMRT Link. SMRT Link includes an Identity Server, which can be configured to integrate with your LDAP/AD servers and enable user authentication using your organizations' user name and password. To ensure a secure connection between the SMRT Link server and your browser, the SSL Certificate can be installed **after** completing SMRT Link installation.

It is important to note that PacBio will **not** provide a Signed SSL Certificate. However, once your site has obtained a Signed SSL Certificate, PacBio's tools can be used to install it and configure SMRT Link to use it. (**Note**: PacBio recommends that you consult your IT administrator about obtaining an SSL Certificate.) You will need a certificate issued by a Certificate Authority (CA, sometimes referred to as a "certification authority"). PacBio has tested SMRT Link with certificates from the following certificate vendors: VeriSign, Thawte and DigiCert.

If your site does **not** provide an SSL Certificate, SMRT Link v8.0 will use a PacBio self-signed SSL Certificate. If you use the self-signed SSL Certificate, **each** user will need to accept the browser warnings related to access in insecure environment. You can also have your IT administrator configure desktops to **always trust** the provided self-signed Certificate. Note that SMRT Link is installed within your organization's secure network, behind your organization's firewall.

See "Using SMRT Link with a PacBio Self-Signed SSL Certificate" on page 17 for details on how to handle the security warnings when accessing SMRT Link.

Use the following procedures **only** if your site provides an SSL Certificate. These procedures are **not** applicable if you are using PacBio's Self-Signed SSL Certificate.

Note: If you have **already** setup an SSL Certificate in SMRT Link v4.0.0 or later, those settings will be carried over **automatically** when upgrading to SMRT Link v8.0.

Prerequisites

The keytool program is supplied with the SMRT Link installation.

- **Step 1**: Obtain a domain-specific certificate from the appropriate Certification Authority.
- **Step 2**: Download the new certificate in .p12 or .p7b format from the DigiCert website hostname domain com.p12.
- **Step 3**: Combine the certificate and the keystore files:

```
$ keytool -import -trustcacerts -alias server -file ${KEYNAME}.p7b -keystore ${KEYNAME}.jks
Enter keystore password:
Certificate reply was installed in keystore
```

Step 4: Generate an intermediate file in .pem format:

```
$ keytool -export -alias server -keystore ${KEYNAME}.jks -file ${KEYNAME}.pem
Enter keystore password:
Certificate stored in file <hostname nanofluidics com.pem>
```

Step 5: Generate the WSO2 truststore client-truststore.jks file using the .pem file:

```
$ keytool -import -alias server -file ${KEYNAME}.pem -keystore client-truststore.jks -storepass
$KEYPW

<Miscelaneous keytool output>
Trust this certificate? [no]: y
Certificate was added to keystore
```

Step 6: Stop the services by entering \${SMRT ROOT}/admin/bin/services-stop.

Step 7: Install the new .jks files and update the configuration files:

```
${SMRT ROOT}/admin/bin/install ssl cert.sh ${FQDN} ${KEYSTORE} ${TRUSTSTORE} ${KEYPW}
```

This script will install a signed SSL certificate to SMRT Link, removing the browser warnings that occur when using the default certificate. To run this script, you will need two files in Java Key Store (.jks) format:

- One containing the SSL keys and certificate.
- A separate client-truststore.jks required by the authentication manager.

Usage: install ssl cert.sh \$FQDN \$KEYSTORE \$TRUSTSTORE \$KEYPW where:

- \$FQDN is the fully-qualified domain name appropriate to the signed SSL Certificate, such as smrtlink.university.edu.
- \$keystore is the path to the keystore file generated from the SSL Certificate (.jks extension); this will be copied to the SMRT Link installation.
- \$TRUSTSTORE is the path to client-truststore.jks.
- \$KEYPW is the password used for generating keys.

The FQDN must match the <code>dnsname</code> specified in the installer The shorthand (such as "smrtlinkhost") will not work because the certificate is for a domain name, not an unqualified host name. When running the SMRT Link installer, do this by passing the arguments <code>--dnsname</code> <code>\$FQDN</code>.

Also note that if you are using LDAP authentication, you may need to reenter the password for the LDAP connection in the WSO2 administrative interface once SMRT Link has been started again, for example: https://smrtlink.pacb.com:9443/carbon.

This is because the password is stored encrypted with the SSL certificate key, which has now changed.

Step 8: Start SMRT Link services by entering \$SMRT ROOT/admin/bin/services-start.

Step 9: Final Check:

Go to http://hostname:9090 and login as admin/admin (if LDAP is not enabled). Note that SSL is not used on the UI port (i.e. 9090) because this only serves static content; the actual login credentials are sent to port 8243 which only uses SSL.

You will be redirected to https://hostname.domain.com:8243/sl/#/welcome, and should see a padlock sign in front of the URL which indicates that the site is secure.

Viewing a Java Keystore File

The keystore files for SSL certificates are binary files. Use the following command to verify if the same password was used in the SSL certificate generation and install process. If the same password was **not** used in the certificate installation process, this command will give an error. To list the contents of a Java keystore file, use the keytool -list command, as shown below:

```
Usage: keytool -list -v -keystore keystore.jks
```

```
Example: keytool -list -v -keystore smrtlink-test nanofluidics com.jks
```

```
Enter keystore password:
Keystore type: JKS
Keystore provider: SUN
Your keystore contains 1 entry
Alias name: server
Creation date: Feb 13, 2017
Entry type: PrivateKeyEntry
Certificate chain length: 3
Certificate[1]:
Owner: CN=smrtlink-release-test.nanofluidics.com, O="Pacific Biosciences of California, Inc.",
L=Menlo Park, ST=CA, C=US
Issuer: CN=DigiCert SHA2 Secure Server CA, O=DigiCert Inc, C=US
```

Errors/logs related to certificate installation can be found here:

\$SMRT_ROOT/current/bundles/smrtlink-analysisservices-gui/current/private/pacbio/smrtlink-analysisservices-gui/

Installing an Existing Certificate

If you **already** have a complete .jks file (suitable for Apache Tomcat, for example), including the signed certificate, you just need to change the alias of the keystore/certificate to server using the keytool command (-keyclone or -changealias subcommands).

Set the password to whatever you will supply to the install script in SMRT Link. Then, follow the instructions in "Adding the public key to client-truststore.jks" in https://docs.wso2.com/display/IS500/Creating+New+Keystores again with the same changes.

If you already have the SSL key in a .jks file and have obtained a certificate for this key in either PKCS #7 (.p7b) or PKCS #12 (.p12) Certificate format, run this command to combine them:

```
$ keytool -import -trustcacerts -alias server -file star.university.edu.p7b -keystore
star.university.edu.jks
```

Then follow the instructions above to generate the client-truststore.jks file, and run the install script.

Recovering from the SSL Certificate Installation

It may sometime be necessary to uninstall the user-provided SSL certificate and restore the default certificate. The following steps will revert changes made by \$SMRT ROOT/admin/bin/install ssl cert.sh:

Stop SMRT Link services:

\$SMRT ROOT/admin/bin/services-stop

- 2. Check that all SMRT Link processes have terminated by running ps -ef | grep smrtlink. Remaining processes should be terminated with kill <PID> or kill -9 <PID>.
- Restore backup settings:

```
cd ${SMRT_ROOT}/current/bundles/smrtlink-analysisservices-gui/current/private/pacbio/smrtlink-analysisservices-gui/wso2am-2.0.0/repository
mv conf conf.new
mv conf.orig conf
mv resources/security/client-truststore.jks.orig resources/security/client-truststore.jks
```

4. Start SMRT Link services:

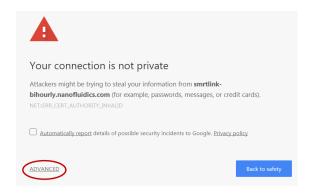
\${SMRT ROOT}/admin/bin/services-start

Using SMRT Link with a PacBio Self-Signed SSL Certificate

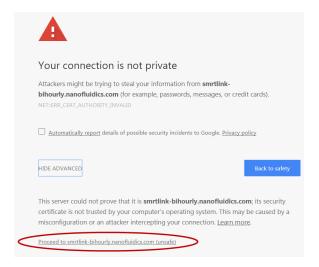
SMRT Link v8.0 ships with a PacBio self-signed SSL Certificate. If your site does **not** have a Signed SSL Certificate **and** you use the self-signed SSL Certificate, **each** user will need to accept the browser warnings related to access in insecure environment. You can also have your IT administrator configure desktops to **always trust** the provided self-signed Certificate. Note that SMRT Link is installed within your organization's secure network, behind your organization's firewall.

Security messages display when users try to login to SMRT Link for the **first time** using the Chrome browser. These messages may also display **other times** when accessing SMRT Link. **Each** SMRT Link user in your organization should address these browser warnings following the procedure below.

1. The first time you start SMRT Link after installation, you see the following text. Click the **Advanced** link.



2. Click the **Proceed...** link. (You may need to scroll down.)



3. Close the window by clicking the **Close** box in the corner.



4. The **Login** dialog displays, where you enter the User Name and Password. The next time you access SMRT Link, the Login dialog displays **directly**.

Importing Data into SMRT® Link

If you have a Sequel/Sequel II System installed and it is linked to the SMRT Link software during the instrument installation, your data will be **automatically** imported in SMRT Link.

You can manually import the following types of files directly, using the SMRT Link GUI:

- Sequel Data: XML file (.subreadset.xml) or ZIP file containing information about Sequel sequence data, such as paths to the BAM files.
- CCS Data: XML file (.subreadset.xml) or ZIP file containing information about CCS sequence data.
- Barcodes: FASTA (.fa or .fasta), XML (.barcodeset.xml), or ZIP files containing barcodes.
- References: FASTA (.fa or .fasta), XML (.referenceSet.xml), or ZIP files containing a reference sequence for use in starting analyses.

You can also import data in SMRT Link using the pbservice command-line utility, as shown below.

• The host and port for the Analysis Services are optional and default to localhost: 9090. You can change these settings using the --host and --port arguments.

Importing	Commands			
BAM Data Sets	Import individual SubreadSet XML files:			
Generated by the Sequel/Sequel II System	<pre>\$> pbservice import-datasethost \$HOSTport \$PORT /path/to/ subreads.subreadset.xml</pre>			
	Import a directory of SubreadSet XML files:			
	<pre>\$> pbservice import-datasethost \$HOSTport \$PORT /path/to/tree/ containing/subreadssets.xml/</pre>			
A FASTA Reference	Creating a ReferenceSet XML file from a FASTA file:			
	<pre>fasta-to-reference hg38.fasta /opt/smrtlink/references hg38organism Homo_sapiens > fasta2ref.log 2>&1</pre>			

Sending Log Files to Technical Support

Troubleshooting information can be sent to PacBio Technical Support multiple ways. If there is a connection to the PacBio Event Server, do the following:

- From the SMRT Link menu: About > Troubleshooting Information > Send.
- From a SMRT Link "Failed" analysis Results page: Click Send Log Files.

If there is a connection to the PacBio Event Server, run the following command to generate the information and automatically send it to PacBio Technical Support:

```
$SMRT ROOT/admin/bin/tsreport-install --bundle --update
```

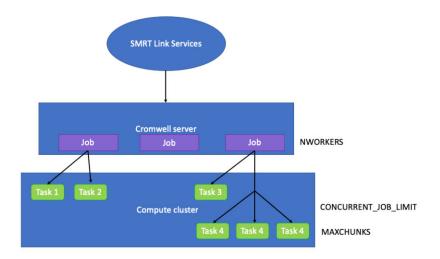
If there is **no** connection to the PacBio Event Server, run the following command to generate a .tgz file and email the file to support@pacb.com to file a case:

```
$SMRT ROOT/admin/bin/tsreport-install --bundle
```

The .tgz file can be found here: \$SMRT ROOT/userdata/tsreport/data/ts-install.tgz.

Appendix A: SMRT Link Workflow Terminology

Management of all SMRT Link activity is handled by the SMRT Link Services. In SMRT Link v8.0, the pbsmrtpipe workflow engine was replaced by Cromwell, an open-source engine developed by the Broad Institute (https://cromwell.readthedocs.io/en/stable/). A continually-running Cromwell server is launched at the same time as SMRT Link services, which executes all jobs directly without spawning new processes. Several user-configurable settings control the use of compute resources by Cromwell. A representation of the SMRT Link Services hierarchy is shown below.



NWORKERS: A SMRT Link Services setting that specifies the maximum number of simultaneous analysis jobs that may be run.

CONCURRENT_JOB_LIMIT: A Cromwell configuration setting that limits the total number of job submissions to a specific backend, across all running workflows.

MAXCHUNKS: A Cromwell workflow that limits the maximum number of pieces a large Data Set may be broken into for parallelized analysis.

NPROC (Not shown in diagram): A Cromwell workflow setting that limits the maximum number of slots that any single JMS cluster submission may request.

Appendix B: Distributed Computing Setup

PacBio supports the following Job Management Systems (JMS): **Sun Grid Engine (SGE)**, **PBS**, **LSF**, and **SLURM**. You may attempt to manually configure for alternate job management systems, but these are **not** guaranteed to work.

A Job Management System may be used to dispatch jobs to a distributed compute environment. If **no** Job Management System is specified, the system will run in non-distributed Mode, and **all** compute jobs will be run locally on the install host.

Available Job Management Systems are detected from the PATH environment variable, but may also be selected manually.

For more information on customizing all of the Job Management Systems, see the comments in the file \$SMRT_ROOT/userdata/user_jmsenv/user.jmsenv.ish. Note that changes to this file will apply to every job submitted to the cluster.

Appendix C: Sequel System Compute Requirements

	Head Node			
	Cores	32		
	RAM	64 GB		
	tmp_dir (Local Storage)	1 TB recommended, 500 GB minimum		
	db_datadir (Local Storage)	250 GB		
Shared Data Storage				
	Sequence Data	40 TB		
	(Jobs_root) Analysis Data 70 TB			
Network				
	10 GBE recommended, 1 GBE required			
	Comput	e Nodes		
	Targeted Applications HPC ^a	Targeted Applications PLUS HPC ^b	Whole Genome Applications HPC ^c	
Cores (Total)	18	96	384	
Minimum RAM per Slot (1 slot = 1 core)	4 GB	4 GB	4 GB/8 GB de novo assembly large complex genomes	
tmp_dir (Local Storage)	100 GB			

- a. Targeted Sequencing applications (LAA, Resequencing), assembly of bacterial genomes, targeted Iso-Seq application. Storage is calculated based on moderate usage of Sequel[®] System per year.
- b. Targeted Sequencing applications as noted above, plus occasional large-genome *de novo* assemblies, whole- transcriptome Iso-Seq. Storage is calculated based on moderate usage of Sequel System per year.
- c. For a standard CCS sequencing collection (300 GB sequencing data, 11 kb insert size, 30-hours movie), CCS Analysis takes 27 hours on this configuration. SMRT Link will work on less powerful compute configurations, however analysis time will be significantly longer.

Data Examples

Human Assembly CLR Data

• Genome size: 3.3 GB; Sequence data 400 GB; Analysis data 700 GB; Analysis time: 72 hours wall. This is 50-fold coverage human genome analyzed on the compute configuration listed above.

Rice Assembly CLR Data

• Genome size: 0.43 GB; Sequence data 55 GB; Analysis data 90 GB; Analysis time: 20 hours wall. This is 50-fold coverage rice genome analyzed on the compute configuration listed above.

For Research Use Only. Not for use in diagnostic procedures. © Copyright 2016 - 2020, Pacific Biosciences of California, Inc. All rights reserved. Information in this document is subject to change without notice. Pacific Biosciences assumes no responsibility for any errors or omissions in this document. Certain notices, terms, conditions and/or use restrictions may pertain to your use of Pacific Biosciences products and/or third party products. Please refer to the applicable Pacific Biosciences Terms and Conditions of Sale and to the applicable license terms at https://www.pacb.com/legal-and-trademarks/terms-and-conditions-of-sale/.

Pacific Biosciences, the Pacific Biosciences logo, PacBio, SMRT, SMRTbell, Iso-Seq and Sequel are trademarks of Pacific Biosciences. BluePippin and SageELF are trademarks of Sage Science, Inc. NGS-go and NGSengine are trademarks of GenDx. FEMTO Pulse and Fragment Analyzer are trademarks of Agilent Technologies Inc. All other trademarks are the sole property of their respective owners. See https://github.com/broadinstitute/cromwell/blob/develop/LICENSE.txt for Cromwell redistribution information.

P/N 100-749-900 Version 22 (January 2020)