Hotspot Clinical Pipeline

**Technical Requirements Specification (TRS)**

**TRS-HPS-0001**

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# OVERVIEW

The Technical Requirements Specification details the system environment, hardware and integration requirements for the clinical pipeline developed in-house.

## Deployment Model

SEMA4-CT will be deploying the solution on premises. There is one instance of the Torrent Cluster deployed on one physical server with 20 processing nodes. There is one instance of the variant calling server deployed on one physical server. There are two instances of the dashboard server: TEST and PROD (production). TEST exists on a virtual server; PROD exists on a physical server.

SEMA4-CT will size the PROD environment to 10 concurrent users.

## High Availability

The Hotspot Clinical Pipeline is electronically backed up using the Bitbucket service (https://bitbucket.org). In the event of disaster, IT infrastructure will be restored according to the IT disaster recovery plan. The clinical pipeline can then be restored on the corresponding Linux server.

SEMA4-CT backups are performed according to SEMA4-CT backup procedure.

## Network and Security

If remote access is required from a third party, SEMA4-CT will provide VPN accounts for each user that requires it. The third party will provide the name(s) of each user requiring remote access and is responsible for notifying SEMA4-CT of any changes. VPN soft token is provided by Symantec.

SSH access will be provided by SEMA4-CT.

# Hardware

This section details the hardware to which the Hotspot Clinical Pipeline will be deployed as well as external devices that are required.

## Servers

NOTE: For high availability environments, servers that are clustered (or load balanced) should be identical in configuration.

|  |  |
| --- | --- |
| **Server Usage** | Torrent Cluster |
| **Server Environment** | Production |
| **Existing or New?** | Existing |
| **If new, expected date available.** | N/A |
| **Server Make** | Dell |
| **Server Model** |  |
| **Processors** |  |
| **Permanent Storage Type** |  |
| **Permanent Storage Capacity** |  |
| **RAM Capacity** |  |
| **Operating System** | Ubuntu 14.04.4 LTS |
| **Torrent Suite Version** | 5.4 |
| **Network Interface** | Gigabit Ethernet |

|  |  |
| --- | --- |
| **Server Usage** | Variant Calling Server |
| **Server Environment** | TEST & PROD |
| **Existing or New?** | Existing |
| **If new, expected date available.** | N/A |
| **Server Make** | Dell |
| **Server Model** | PowerEdge R930 |
| **Processors** | 16 x Intel Xeon E5-2690 @ 2.90 GHz |
| **Permanent Storage Type** | Hard Drive RAID |
| **Permanent Storage Capacity** | 790 GB |
| **RAM Capacity** | 132 GB |
| **Operating System** | Ubuntu 14.04.4 |
| **Network Interface** | Gigabit Ethernet |

|  |  |
| --- | --- |
| **Server Usage** | Dashboard Server |
| **Server Environment** | PROD |
| **Existing or New?** | Existing |
| **If new, expected date available.** | N/A |
| **Server Make** |  |
| **Server Model** |  |
| **Processors** |  |
| **Permanent Storage Type** |  |
| **Permanent Storage Capacity** |  |
| **RAM Capacity** |  |
| **Operating System** |  |
| **Database Version** |  |
| **Network Interface** | Gigabit Ethernet |

|  |  |
| --- | --- |
| **Server Usage** | Dashboard Server |
| **Server Environment** | TEST |
| **Existing or New?** | Existing |
| **If new, expected date available.** | N/A |
| **Server Make** | VMWare |
| **Server Model** |  |
| **Processors** |  |
| **Permanent Storage Type** | VMWare Datastore |
| **Permanent Storage Capacity** |  |
| **RAM Capacity** |  |
| **Operating System** |  |
| **Network Interface** |  |

## Clients

SEMA4-CT uses Windows 7 and OSX on all systems with the latest version of IE (IE 11) and Safari. SEMA4-CT also uses Chrome. NOTE: Chrome is the recommended browser for BRCA Clinical Dashboard.

## Interfaces

The Hotspot clinical dashboard interfaces with LIMS through a provided JSON SDK and with the Torrent Server through direct database queries.

### Sanger Submission

Sanger requests are generated in JSON format by the clinical dashboard. They include the gene, gene strand, variant position, variant reference allele, and variant alternate allele for each variant to confirm along with the sample ID and amplicon ID to use. The JSON is then submitted to the LIMS using the supplied JSON SDK. The JSON is generated in the following format:

{request

{PARENT\_SAMPLE\_LOT:sampleLot#}

{entityTypeName:SANGER SUBMISSION}

{CI\_CLIN\_VARIANT\_LIST:geneName(strandDirection),chr#\_variantPos\_refAllele\_altAllele}

}

### Sanger Results

Sanger results are received through a webform in the Clinical Dashboard. The user indicates the status of the confirmation with the following options:

1. Pending: sample has yet to be processed for confirmation of this variant
2. Processing: sample is currently undergoing the confirmation process
3. Detected: sample has undergone the confirmation process and has produced a positive result for that variant
4. Not Detected: sample has undergone the confirmation process and has produced a negative result for that variant
5. Sample Failure: sample has failed to generate a result that passed quality control
6. Control Failure: control sample has failed to generate a result that passed quality control or has produced an unexpected result
7. NTC Failure: no-template control sample has produced an unexpected result

A word document containing chromatogram images of the Sanger trace output is also required to be uploaded.

### qPCR Submission

qPCR requests are generated in JSON format by the clinical dashboard. The first JSON request is generated with the chromosome number, variant position, variant reference allele, and variant alternate allele for each variant to confirm. This request queries the LIMS to determine if a validated assay exists for that variant. The JSON is generated in the following format:

{request  
 {values  
 MTS\_ASSAY\_NAME  
 MTS\_GENE\_NAME:*geneName*  
 MTS\_VARIANT\_NAME: *chr#\_variantPos\_refAllele\_altAllele* }  
}

If a validated assay does exist a response is received with that information in the following format

{response  
 {QPCR\_REF\_ASSAY  
 entityId:*ID#* MTS\_ASSAY\_NAME:*assayName*  
 MTS\_GENE\_NAME:*geneName*  
 MTS\_VARIANT\_NAME: *chr#\_variantPos\_refAllele\_altAllele*  
 }  
}  
  
A second JSON request is then sent to LIMS identical to the first but with the MTS\_ASSAY\_NAME now filled in which starts the process.

### qPCR Results

qPCR results are received as an Excel XLS file that is output by the Mutation Detector v2.0 software. The result is uploaded to the Clinical Dashboard through a webform. An example format of the file is below:

Header Information  
  
Operator: *operator*  
Date: *date*  
Comments: *comments*  
  
Results Summary:  
Plate Sample Quantity Assay Detection Cutoff Detected? %Mutation  
  
#Valid Replicates(mu) Avg Ct(mu) Std Dev(mu) Ref Assay #Valid Replicates(rf)

Avg Ct(rf) St Dev(rf) dCt Calibration dCt dCt\_norm Flag

# APPROVAL

Signing this protocol indicates that the contents of this document have been reviewed and correspond to the approved validation/testing plan:

Signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Print Name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Role: Dir of Bioinformatics/Designee

# VERSION HISTORY:

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| --- | --- | --- | --- |
| **Date** | **Version** | **Description of Document Updates** | **Author** |
| 09/25/2017 | 1.0 | Initial Release | Jonathan Keeling |
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