Prepared by: Jonathan Keeling Date: 21-Sep-2017

Description: This change request includes several specific technical modifications to the variant calling pipeline and data loader for the Clinical Hotspot pipeline.

HPS-50: Change Variant calling pipeline wrapper to Bpipe from Perl. The legacy perl code of the old variant calling pipeline is difficult to maintain, not modular, and not adaptable to different situations. By converting the pipeline wrapper code to Bpipe, we can reduce the possibility of introducing errors when changes are made, and easily modify the pipeline if future needs require it.

HPS-51: Modify loader to deal with Torrent 5.4 Database Changes. The upgrade of the Torrent software to 5.4 resulted in modifications to the structure of the underlying Postgres database. These changes need to be accommodated in the loader script of the Hotspot pipeline.

HPS-52: Change variant calling pipeline to use Torrent Variant Caller (TVC) 5.4. The 5.4 release of the Torrent Suite comes with Torrent Variant Caller 5.4. The variant calling pipeline must now be modified to use TVC 5.4.

HPS-53: Change value of filter\_unusal\_predictions parameter for TVC in variant calling pipeline. Sequencing runs comparing TVC 5.0.3 and 5.4 revealed a flaw in the parameter settings used for the validated Hotspot variant calling pipeline which resulted in the miss of a variant in NRAS. Further analysis revealed that the setting on a particular parameter in the TVC caller was causing the variant to be missed in an otherwise clean looking BAM file. After consultation with the vendor, it was determined that the setting for the filter\_unusual\_predictions parameter will be set to 0.3 for all future runs which is the vendor recommended value.

Reason for change: Changes HPS-51 and HPS-52 are necessary because of the upgrade of Ion Torrent software to version 5.4. Change HPS-50 is being made in preparation for future maintenance and re-use of the pipeline for other panels. Change HPS-53 is the result of a root-cause analysis that was done in response to an error detected in the previous version of the validation Clinical Hotspot pipeline.

Software Changes: This request requires changes to the variant calling pipeline and the data loader.

Impact: The expected impact to the codebase of these changes is major however the risk is minor for the following reasons: The recoding of the variant calling pipeline has already been tested using Bpipe, TVC 5.4, and the parameter changes. Results indicate that these changes will either have no effect, or should actually improve the accuracy of the variant caller pipeline.

**Approval**

*Test Scripts have been reviewed and the change has been approved for release to production.*

Business owner/Designee: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_

Quality Assurance Review: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_

Clinical Lab Director/Designee: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_

Dir of Bioinformatics/Designee: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_

**Post Go-live**

Implemented by: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ Date: \_\_\_\_\_\_\_\_\_\_\_

Date Changes Implemented: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_