User Requirement Specifications

for the tender (AZ-2017-0155)

„Implementation of a LIMS system and 3 years license“

at

TRON

Translationale Onkologie an der
Universitätsmedizin der JGU Mainz gGmbH

subsequently mentioned as „purchaser“

Tenderer = Contractor (AN)

Inhalt

1 Subject and aim of the tender

The purchaser is searching for the implementation of a Laboratory Information Management System (LIMS) for secure and traceable sample related data management and long term storage.

The currently used project based data management system is based on a cascade of several Excel spreadsheets used for tracking of all above mentioned steps. Due to increasing throughput and moving to more clinically relevant applications of Next Generation Sequencing in TRON´s Genomics laboratory, an electonic sample tracking has to be implemented.

Briefly, the contractors system has to fulfil the following criteria:

- 21 CRF Part 11 compliance
- Uninterrupted sample tracking from sample in to data out
- Full compatibility to NGS workflows
- Preconfigured workflows for common NGS protocols and QC steps
- Complete implementation, direct, bidirectional interface to the existing Illumina NGS instruments and
- Monitoring of NGS run qualities
- Acquisition, interpretation and approval of QC data
- Creation of configurable sample reports
- User management
- Audit trail
- Reagent management
- SOP compliance
- Electronic signatures

2 Performance description

2.1 Overall description

The LIMS will primarily be used in the purchaser´s Genomics laboratory controlling and tracing all steps of the Next Generation Sequencing workflow including sample reception, generation of unique identifiers, extraction of nucleic acids, NGS library preparations, quality controls, normalization and pooling of samples, sequencing using the purchaser´s NGS instruments (Illumina MiSeq, HiSeq2500 and Illumina NovaSeq), sequencing run monitoring, connection to the purchaser´s bioinformatics group and statistical evaluation of all steps regarding efficiency, capacities and error rates.

2.2 21 CRF Part 11 compliance

The LIMS needs to meet all criteria for 21 CFR Part 11 compliance.

- ➔ The system needs to be able to undergo computer system validation (CSV). The contractor needs to provide assistance in the validation process.
- ➔ The LIMS needs to track information and provide reporting especially on the NGS instrument performance to proove that all lab instrumentation in working within it´s specifications.

2.3 Uninterrupted sample tracking from sample in to data out

The LIMS needs to provide solutions for data sequrity and patient privacy

- ➔ Automatic backups to ensure data security
- ➔ Effective scanning of files for viruses
- ➔ Encrypted data transfer
- ➔ Enforcements of data entries
- ➔ Automatic parsing of result files
- ➔ Providing sample histories

2.4 Compatibility to NGS workflows

Supporting of planning for efficient sample processing in the Genomics laboratory

- ➔ Planning of lab operations
- ➔ Grouping of samples for process steps
- ➔ Workflow for sample acquisition, nucleic acid extraction, library preps, QCs, NGS run monitoring and data analysis
- ➔ Applications Programming Interface (API) for custom bioinformatics solutions and instrument or existing LIMS integration

2.5 Preconfigured workflows for common NGS protocols

The System should easily integrate with NGS methods

- ➔ Reduced implementation time through preconfigured workflows for common NGS, RT-PCR and QC methods
- ➔ NGS workflows for Whole Genome Sequencing, Whole Exome Sequencing, RNA Seq, Amplicon Sequencing and custom sequencing solutions
- ➔ Preconfigured QC data parsing from Agilent Bioanalyzer, AATI Fragment Analyzer and Fluorescence Platereaders
- ➔ Automated parsing of result files into the LIMS
- ➔ Automated assignment of QC Pass/Fail according to predefined thresholds

2.6 Complete implementation, direct, bidirectional interface to the existing Illumina NGS instruments

Intergration of the purchaser´s existing NGS instrumentation:

MiSeq:

- ➔ Automated tracking of sequencing run steps
- ➔ Matching of runs between the sequencer and LIMS using reagent IDs
- ➔ Run tracking per instrument
- ➔ Tracking of RTA run directory location
- ➔ Automatic generation or capture of the „Run info XML" and „Run parameters XML" files

- ➔ Creatiion of the sample sheet for use with MiSeq Reporter to support the following workflows: resequencing, assembly, generate FASTQ, library QC, metagenomics, PCR amplicon, custom amplicon and enrichment.
- ➔ Upon run completion, RTA primary analysis metrics need to be automatically captured:
  Raw Yield (Gb), % Bases >Q30, Cluster Density (K/mm^2), Clusters Raw, Clusters PF, %PF, Intensity Cycle 1, % Intensity Cycle 20, % Phasing, % Prephasing, % Aligned, % Error Rate

HiSeq2500:

- ➔ Automated tracking of sequencing run steps
- ➔ Matching of runs between the sequencer and LIMS using reagent IDs
- ➔ Run tracking per instrument
- ➔ Monitoring oft he run status (cycle number) for multiple instruments
- ➔ Tracking of RTA run directory location
- ➔ Automatic generation or capture of the „Run info XML" and „Run parameters XML" files

NovaSeq6000:

- ➔ Automated validation of container barcodes
- ➔ Automated calculation of sample molarity and pool volumes
- ➔ Automated generation of a sample sheet
- ➔ Automated generation of a run recipe file (*.json file)
- ➔ Automated upload oft he run recipe file tot he instrument
- ➔ Automated tracking of sequencing run and parsing of run statistics

2.7 Monitoring of NGS run qualities

The LIMS needs to acquire sequencing run quality data from the existing Illumina sequencers in real time and inform the user about the run quality.

- ➔ Real time parsing of run quality data from NGS instruments
- ➔ Interpretation of common run qualtiy parameter like Q-Scores, number of clusters, number of clusters passing filter, error rate, alignment rates, Phasing, Prephasing and intensities

2.8 Acquisition, interpretation and approval of QC data

The system should easily integrate with QC instruments.

- ➔ Preconfigured or configurable QC data parsing from Agilent Bioanalyzer, AATI Fragment Analyzer, Nanodrop and Fluorescence Platereaders
- ➔ Automated parsing of result files into the LIMS
- ➔ Automated assignment of QC Pass/Fail according to predefined thresholds

2.9 Creation of configurable sample reports

The system needs to provide freely configurable reports on samples, sample groups, projects, instruments and lab operators.

- ➔ Pre-configured and configurable reports
- ➔ Sample information on processing and QC results
- ➔ Reports on capacities, turnaround times of the lab
- ➔ Reporting on sequencing runs
- ➔ Reporting on OOS results
- ➔ Reporting on changes and deviations

2.10 User management

The LIMS hast o provide a user management to create, modify and archive users ans well as permissions.

- ➔ Configurable role-based user access and permissions
- ➔ 4-Eye-Principle for critical process steps
- ➔ Role-based restriction of user rights

2.11 Audit trail

The system needs to provide an audit trail for every sample, data point and user.

- ➔ Tracking of every action on any sample with time stamp and user information.
- ➔ All reagent lots used for processing of the sample
- ➔ Tracking of used lab instrumentation

- ➔ Tracking of changes, deviations and CAPAs
- ➔ Visualization of sample histories
- ➔ Event Log for user actions
- ➔ Detail Log for changes resulting from the actions recorded in the Event Log including both the updated values and the previous values.

2.12 Reagent management

Uninterrupted tracking of used reagents for sample processing

- ➔ Reagent lot tracking (name, lot number, expiry dates, flags)
- ➔ Checking for expiry dates
- ➔ Role-based control of available reagent lots
- ➔ Tracking of reagent stock levels

2.13 SOP compliance

Compliance with already existing SOPs for tracking of training status, changes, devitations, CAPAs, instrument qualification status, etc.

- ➔ Reagent and controls tracking
- ➔ Alerts of OOS reults
- ➔ Possibility to raise alerts and wait for supervisor approval
- ➔ Checking for user training status
- ➔ Checking for instrument maintenance and qualification status
- ➔ Upload of paper-based documentations

2.14 Electronic signatures

Actions taken in the LIMS need to be signed by the responsible user electronically.

- ➔ Enables review and approval of samples
- ➔ Role-based signature rights
- ➔ At certain workflow steps, samples cannot enter the next step without an electronic signature (process control)

3 Implementation phases

The delivery and implementation of the system should take place in 2017 and consist of the following steps. All necessary preparation and installation steps should be executed in 2017. Full implementation should be finshed in Q2 2018.

- ➔ Planning workshop and providing detailed timelines for installation, implemantation, training and go-live.

- ➔ Installation of the LIMS onsite including installation and operational qualification of the software package including all preconfigured features and workflows.

- ➔ Implementation of customized solutions
  - → Interface to Labware LIMS, which is used in the Biosampling unit
  - → Interface to QC instruments (Agilent Bioanalyzer, AATI Fragment Analyzer, Nanodrop)
  - → Interface to existing Illumina NGS instruments (MiSeq, HiSeq2500, NovaSeq6000)
  - → Interface to different units (Biosampling, Bioinformatics)
  - → Implementation of customized NGS workflows

- ➔ Training of all users

4 Licences

TRON is looking for a 3-year subscription for different users from different units of the company. The purchaser aims for 15 independent liscences with concurrent user functionality.

5 Support und Warranty

The warranty should at least last for 12 months and should optionally offered for 36 months.

The support level should include:

- ➔ 24/7 email support: resonse time <24h
- ➔ Phone support: Monday through Friday, 09:00 – 17:00 (GMT)
- Rund-um-die-Uhr-Zugriff auf die Hersteller Support Website
- Automatische Störungsmeldung per Mail oder Web an den Hersteller

6 Concept

The contractor should offer the following items based on this URS document. If any additional items have tob e offered to meet the above mentioned criteria the contractor needs to expand the list.

POS	**Description**	Units
1	Preconfigured LIMS System licence p.a.	3
2	Illumina MiSeq, HiSeq2500 and NovaSeq6000 integration p.a.	3
3	User Subscription Licens p.a. (15 users, 3 years)	45
4	On Site user Training for 15 users	1
5	Consulting service for customized implementations	1