December 2015

HL7 LIMS Interface Specification

For use with GeneRead™ Link software

Sample to Insight

QIAGEN

Contents

Introduction

This document describes the HL7 interface between LIMS and GeneRead Link. This document is intended for use by LIMS Interface programmers and QIAGEN Field Service Specialists to support the configuration of an HL7 interface between LIMS and GeneRead Link. GeneRead Link is software that is intended to provide bi-directional connectivity with a Laboratory Information Management System (LIMS) and specific QIAGEN® instruments used in the next-generation sequencing (NGS) GeneReader™ workflow for solid tumor. GeneRead Link receives work lists from a LIMS system and transfers the test results to the LIMS.

Definitions of Terms and Acronyms

FPC: Full Process Control

HL7: Health level 7

IHE: Integrating the Healthcare Enterprise. An initiative by healthcare professionals and industry to improve the way computer systems in healthcare share information.

LIMS: Laboratory Information Management System. A software-based laboratory and information management system that provides a set of key features that support a modern laboratory's operations.

MLLP: Minimal Lower Layer Protocol

NGS: Next-generation sequencing

TCP/IP: Transport Control Protocol/Internet Protocol

Version	Publication date
1.0	December 2015

Overview

Reference to standard

The GeneRead Link LIMS interface is based on version 2.5.1 of the Health Level Seven (HL7) Standard for electronic data exchange in all healthcare environments. It follows the *IHE Laboratory Technical Framework* for "Laboratory Testing Workflow". The GeneRead Link interface implements only a small subset of the HL7 Standard, namely the OML message for ordering of tests, the ORL message for acknowledging orders, and the OUL message for results transmission. The contents of both of these messages as used by this interface are described in detail in the following sections.

Transport layer

The message transfer is based on the TCP/IP protocol. The Minimal Lower Layer Protocol (MLLP) as defined by the HL7 standard is used to separate the messages:

Header	Payload	Trailer
0x0B	HL7 message	0x1C 0x0D

For the transmission of test orders from LIMS to GeneRead Link, GeneRead Link shall act as server and the LIMS shall act as client. For the transmission of results from GeneRead Link to LIMS, the LIMS shall act as server and GeneRead Link shall act as client. This means that two TCP/IP connections are required, as shown in Figure 1 below.

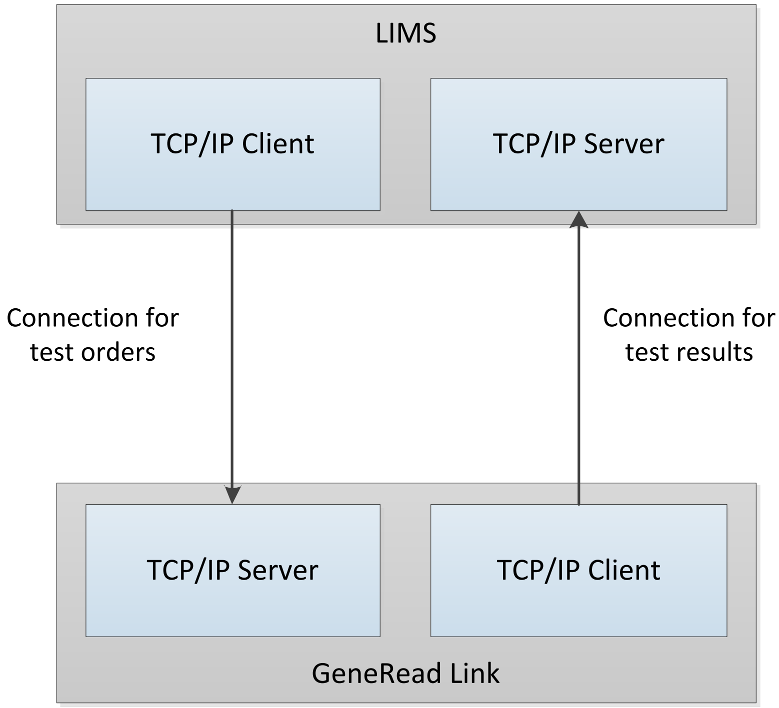

Figure 1. Required TCP/IP connections.

Message structure

The following sections explain details about the messages that are used for test ordering and results transmission.

The following abbreviations are used in the tables describing the message structure:

Abbreviation	Description
M	Mandatory For messages from LIMS to GeneRead Link, this means that the component must be included in the message. For messages from GeneRead Link to LIMS, this means that the component will always be present.
O	Optional For messages from LIMS to GeneRead Link, this means that the component is not required by GeneRead Link, but will be evaluated if present. For messages from GeneRead Link to LIMS, this means that the component will only be present under certain circumstances.
N	Not supported For messages from LIMS to GeneRead Link, this means that the component will be ignored by GeneRead Link if present. For messages from GeneRead Link to LIMS, this means that the component will never be used.

Interface Specification

Request

The LIMS can use the following message formats to order tests within GeneRead Link:

Supported LIMS order message types

HL7 version	Message type	Message structure
2.5.1	OML^O33	MSH SPM { ORC OBR }

Note: "{}" denotes repeating segments; "[]" denotes optional segments.

Each message header segment MSH has exactly one specimen segment SPM. Each specimen segment may hold one or many order segments ORC.

Table 1. MSH for OML messages

Seq.	M/O/N	Element name	Content
1	M	Field separator	Shall be defined by the LIMS in accordance with the HL7 standard.
2	M	Encoding characters	Shall be defined by the LIMS in accordance with the HL7 standard.
3	O	Sending application	Can be used to identify the sending system.
4	O	Sending facility	Can be used to identify the sending system.
5	M	Receiving application	Shall be set to Middleware. Messages with a different or no receiving application will be ignored.
6	N	*Receiving facility*	*Not used.*
7	M	Date/time of message	Timestamp of when the message was created by the sending system. Format: YYYYMMDDHHMMSS.
8	N	*Security*	*Not used*
9	M	Message type	Only OML^O33 is supported. All others will be rejected.
10	M	Message control ID	Unique identifier for each message.
11	M	Processing ID	Only P is supported. All others will be rejected.
12	M	Version ID	Only 2.5.1 is supported. All others will be rejected.
13–18	N	*Misc.*	*Not used*
19	M	Character set	Only UTF-8, ISO-8859-1 and US-ASCII are supported. All others will be rejected.

Table 2. SPM for OML messages

Seq.	M/O/N	Element name	Content
1	*N*	*Set ID*	*Not used*
2	M	Specimen ID	This field contains a unique identifier for the sample as referenced by the Placer application. Due to restrictions of specimen ID of connected instruments, the following rules must be followed: ● Length: 1–20 characters. ● No spaces or special characters allowed. ● The values "unindexed" and "internal_control_" are strings reserved by GeneReader and may not be used as a specimen ID. ● No distinction between small and capital letters. Specimen ID "Sample01" will be considered the same as "sample01".
3	*N*	*Specimen parent IDs*	*Not used*
4	M	Specimen Type	Shall specify the specimen type.
5–29	*N*	*Misc.*	*Not used*

Table 3. ORC for OML messages

Seq.	M/O/N	Element name	Content
1	M	Order control	Only NW (New order) is supported, all others will be rejected.
2	M	Placer order number	Order id assigned by the Placer application. Must be the same if multiple ORC segments are sent within one SPM segment. Otherwise, must be unique. Maximum 25 characters allowed.
3	O	Filler order number	Will not be evaluated by GeneRead Link.
4–8	*N*	*Misc.*	*Not used*
9	O	Date/time of transaction	Date / time of the order. Format: YYYYMMDDHHMMSS. If not provided, the system date/time of the filler system is used.
10–25	*N*	*Misc.*	*Not used*

Table 4. OBR for OML messages

Seq.	M/O/N	Element name	Content
1–3	*N*	*Misc.*	*Not used*
4	M	Universal Service Identifier	Identifier of required test
5–47	*N*	*Misc.*	*Not used*

The combination of Placer Order Number (OCR-2) and Specimen ID (SPM-2) must be unique for orders sent in different message elements (MSH).

For Specimen Type “DNA”, only a single test can be requested.

The combination of Universal Service Identifier and Specimen Type must be a known GeneRead Link test configuration.

Acknowledge to LIMS test request

GeneRead Link will acknowledge each OML^O33 message by sending a corresponding ORL^O34 message. The acknowledgement confirms reception of the message and provides error messages (for error or rejection) for message format errors and validation errors.

The ORL^O34 message will comply with the following structure: MSH MSA.

The tables below specify the details of each message component.

Table 5. MSA for ORL messages

Seq.	M/O/N	Element name	Content
1	M	Acknowledgement code	AA, AR or AE (see below).
2	M	Message control ID	Message control ID of the OML message that is being acknowledged.
3	M	Text message	If AA, “Message will be processed”. Otherwise, an error or warning message.
4–6	*N*	*Misc.*	*Not used*

The Acknowledgment code is:

- AA for an accepted message.
- AR if the message was rejected. This can happen if:
  - The HL7 version is not “2.5.1”
  - The encoding is not correct
  - The message type is not OML^O33
  - Any validation error that occurred during processing
- AE if the message cannot be parsed by the HL7 parser.

Table 6 below displays the list of text messages used in the acknowledgement message:

Table 6. Acknowledgement messages

MSH-1 acknowledge code	**MSH-3 text m**essage [template]	**Message ex**ample
AA	Message will be processed	Message will be processed
AR	"[message type]" is not asupported Message Type. Expected "OML_O33".	"OML_O35" is not a supported Message Type. Expected "OML_O33".
AR	"[processing id]" is not a supported Processing ID. Expected "P".	"T" is not a supported Processing ID. Expected "P".
AR	Test order with order id "[order id]" and source "[order source]" already exists.	Test order with order id "O1" and source "LIMS" already exists.
AR	Unable to process request for specimen "[sample id]" of type "[sample type]". Duplicate Universal Service Identifier "[test]".	Unable to process request for specimen "S1" of type "FFPE". Duplicate Universal Service Identifier "101X".
AR	Unable to process request for specimen "[sample id]" of type "[sample type]". Placer Order Number "[order id]" should match "[expected order id]".	Unable to process request for specimen "S1" of type "FFPE". Placer Order Number "O2" should match "O1".
AR	Could not parse message.	Could not parse message.
AR	Unsupported charset. Expected one of "[UTF-8, ISO-8859-1, USASCII]".	Unsupported charset. Expected one of "[UTF-8, ISO-8859-1, USASCII]".
AR	"[order control]" is not a supported Order Control. Only "NW" is supported.	"RC" is not a supported Order Control. Only "NW" is supported.
AR	Multiple tests found for name "[test]" and sample type "[sample type]".	Multiple tests found for name "666X" and sample type "FFPE".
AR	Unable to find the test with name "[test]" and sample type "[sample type]".	Unable to find the test with name "666X" and sample type "FFPE".
AR	"[version]" is not a supported version. Expected "2.5.1".	"2.5" is not a supported version. Expected "2.5.1".
AR	Parallel tests on "[sample type]" are not supported.	Parallel tests on "DNA" are not supported.
AR	"[internal control *]" cannot be used as sample ID.	"internal control 123" cannot be used as sample ID.
AR	"[unindexed]" cannot be used as sample ID.	"unindexed" cannot be used as sample ID.
AE	An error occurred. Message could not be processed.	An error occurred. Message could not be processed.

Results

GeneRead Link will only report results to LIMS for those samples in which the test was ordered by LIMS. Results for manually ordered tests will not be reported to LIMS. This means in particular that results for FPC will not be reported to LIMS.

GeneRead Link will use the following message types to report results to LIMS:

Table 7. Supported LIMS Result Message Types

HL7 version	Message type	Message structure
2.5.1	OUL^R22	MSH SPM OBR OCR [{[OBX] [{NTE}]}]

Note: "{}" denotes repeating segments; "[]" denotes optional segments.

Note: The OBX component will be repeated to report different result files. In this case, the NTE segments are repeated after each OBX.

The tables below specify the details for each message component.

Table 8. MSH for OUL^R22 messages

Seq.	M/O/N	Element name	Content
1	M	Field separator	Always |
2	M	Encoding characters	Always ^~\&
3	M	Sending application	Always Middleware
4	*N*	*Sending facility*	*Not used*
5	M	Receiving application	Always LIMS
6	*N*	*Receiving facility*	*Not used*
7	M	Date/time of message	Timestamp of when the message was created by the sending system. Format: YYYYMMDDHHMMSS.
8	*N*	*Security*	*Not used*
9	M	Message type	OUL^R22
10	M	Message control ID	Unique identifier for each message
11	M	Processing ID	Always P
12	M	Version ID	2.5.1
13–14	*N*	*Misc.*	*Not used*
15	M	Accept acknowledgement type	Always AL
16	M	Application acknowledgement type	Always AL

Seq.	M/O/N	Element name	Content
17	*N*	*Country code*	*Not used*
18	M	Character set	UNICODE UTF-8
19–21	*N*	*Misc.*	*Not used*

Table 9. SPM for OUL^R22 Messages

Seq.	M/O/N	Element name	Content
1	*N*	*Set ID*	*Not used*
2	M	Specimen ID	This field contains a unique identifier for the sample as referenced by the placer application in the OML^O33 message.
3	*N*	*Specimen parent IDs*	*Not used*
4	M	Specimen type	Specifies the specimen type as referenced by the placer application in the OML^O33 message.
5–29	*N*	*Misc.*	*Not used*

Table 10. OBR for OUL^R22 messages

Seq.	M/O/N	Element name	Content
1	M	Set ID - OBR	Always 1
2–3	*N*	*Misc.*	*Not used*
4	M	Universal service identifier	Identifier of required test as referenced by the Placer application in the OML^O33 message.
5–6	*N*	*Misc.*	*Not used*
7	M	Observation date/time	Date when result has been released from the approval queue. Format: YYYYMMDDHHMMSS.
8–24	*N*	*Misc.*	*Not used*
25	M	Result status	Supported values: F — Analysis was successful; valid results are available. X — A problem or error occurred during analysis; no valid results could be produced.
26–33	*N*	*Misc.*	*Not used*
34	M	Technician	Contains the identification of the user who released the results from the approval queue.
35–47	*N*	*Misc.*	*Not used*

Table 11. ORC for OUL^R22 messages

Seq.	M/O/N	Element name	Content
1	M	Order control	Always OE (Order/service released).
2	M	Placer order number	Order id assigned by the placer application as referenced in the OML^O33 message.
4–8	*N*	*Misc.*	*Not used*
9	M	Date/time of transaction	Date/time when result has been released from the approval queue. Format: YYYYMMDDHHMMSS.
10–25	*N*	*Misc.*	*Not used*

Table 12. OBX for OUL^R22 messages

Seq.	M/O/N	Element name	Content
1	M	Set ID - OBX	Ascending IDs starting with 1 Increments of 1 for each OBX record related to the same OBR record.
2	M	Value type	Supported values: ST – String result for overall analysis result ED – Encapsulated data to transfer files RP – Referenced pointers to transfer URL to cloud hosted results
3	M	Observation identifier	Application name
4	*N*	*Observation sub-ID*	*Not used*
5	M	Observation value	Result of the analysis. For possible values, refer to section “Observation values”, page 13.
6–10	*N*	*Misc.*	*Not used*
11	M	Observation result status	Supported values: F – Analysis has been successful, valid results are available X – A problem or error occurred during analysis, no valid results could be produced
12–19	*N*	*Misc.*	*Not used*

The NTE element (Table 13) is used to transmit flags to inform the user on deviations that occurred during the processing of the sample.

Table 13. NTE for OUL^R22 Messages

Seq.	M/O/N	Element name	Content
1	M	Set ID – NTE	Always L
2	*N*	*Source of comment*	*Not used*
3	M	Comment	Name of the flag. For the list of all flags refer to section "Flags" page 14.
4	M	Comment type	Always RE

This segment is only reported if OBX-5 Observation Values = DEVIATIONS. The NTC element is repeated after every OBX element.

After each result message, the LIMS acknowledges receipt with an ACK message.

Observation values

First OBX element – overall analysis result

The first OBX segment transmitted within an OBR segment contains the overall analysis result. This OBX element will always be transmitted. Value Type = ST.

Observation Values:

- OK – Analysis has been performed. A result could be obtained.
- DEVIATIONS – Analysis has been performed. A result could be obtained. One or more deviations during processing of the sample occurred.
- FAILED – No result could be obtained.

For Observation Value = DEVIATIONS, the list of flags will be transmitted using the NTE element. All NTE elements for that specimen are repeated after every OBX record.

Second OBX element – variant calling file

This OBX element will be transmitted for Observation Values OK or DEVIATIONS. Value Type = ED.

Observation Value contains the MIME package including the variant calling file (*.vcr).

Third OBX element – variant calling report

This OBX element will be transmitted for Observation Values OK or DEVIATIONS. Value Type = ED.

Observation Value contains the MIME package including the variant calling report (*.pdf).

Fourth OBX element – GeneRead Link process report

This OBX element will be transmitted for Observation Values OK or DEVIATIONS. Value Type = ED.

Observation Value contains the MIME package including the GeneRead Link process report (*.pdf).

Fifth OBX element – QCI™ Interpret report

This OBX element will be transmitted for Observation Values OK or DEVIATIONS, and when a QCI Interpret Analysis has been requested. Value Type = RP.

Observation Value contains the URL to the QCI Interpret report.

Flags

QC Flags

QC flags are set if a certain error condition or deviation from the recommended process occurs.

Table 14 below shows the definition of QC flags for the GeneRead QCI Targeted Gene Panels workflow. Any changes of the workflow may affect the flag definitions.

Table 14. Definitions of QC flags

Sub-workflow	Description	Flag
DNA Extraction	Kit has expired	DE_Kit expired
DNA Extraction	QIAcube® run failed	DE_Run failed
DNA Extraction	QuantiMIZE QC call is “Low”	DE_QC low
DNA Extraction	QuantiMIZE Assay QC failed	DE_QC failed
DNA Extraction	Concentration too low	DE_Conc low
DNA Extraction	For at least one test with big primer pool concentration is too low	DE_Conc low for 1 test

Sub-workflow	**Description**	**Flag**
DNA Extraction	QuantiMIZE run failed	DE_QC run failed
DNA Extraction	Sample or experiment canceled	DE_Canceled
Target Enrichment	GenePanel kit has expired	TE_Kit expired
Target Enrichment	GenePanel PCR run failed	TE_Run failed
Target Enrichment	AMPure® Beads kit has expired	TE_Beads expired
Target Enrichment	Different cycle number used than recommended	TE_Diff cycles
Target Enrichment	Size distribution not as expected	TE_Size not ok
Target Enrichment	Concentration too low (<0.5 ng/µl)	TE_Conc low
Target Enrichment	No concentration measured	TE_No conc
Target Enrichment	No size distribution determined	TE_No size
Target Enrichment	Sample or experiment canceled	TE_Canceled
Library Preparation	Size Selection/Library preparation kit has expired	LP_Kit expired
Library Preparation	Library preparation (end repair, adapter ligation) has failed	LP_Run failed
Library Preparation	Enrichment PCR run has failed	LP_PCR failed
Library Preparation	Size selection run has failed	LP_SiSe run failed
Library Preparation	Size distribution not as expected	LP_Size not ok
Library Preparation	Concentration too low (< 0.25 ng/µl)	LP_Conc low
Library Preparation	No size distribution determined	LP_No size
Library Preparation	Sample or experiment canceled	LP_Canceled
Sequencing Template Preparation	Kit expired	STP_Kit expired
Sequencing Template Preparation	Make droplets failed	STP_MaDro failed
Sequencing Template Preparation	Emulsion PCR run failed	STP_PCR failed
Sequencing Template Preparation	Pooling and Breaking run failed	STP_PoBr failed
Sequencing Template Preparation	Enrichment run failed	STP_Enrich failed
Sequencing Template Preparation	Sample or experiment canceled	STP_Canceled
Sequencing	Run failed or canceled	SE_Run failed
Sequencing	Cross contamination detected	SE_Cross cont
Sequencing	Experiment canceled	SE_Canceled
Data Analysis	Analysis failed	DA_Failed
Data Analysis	Analysis rejected	DA_Rejected
Data Analysis	Analysis canceled	DA_Canceled

Examples

Test order for sample with single test

Request (LIMS → GeneRead Link)

```
MSH|^~\&|||Middleware||20150908093623.878+0200||OML^O33^OML_O33|42160
1|P|2.5.1||||||UNICODE UTF-8\r

SPM||S1||FFPE\r

ORC|NW|O1|||||||20150908093623\r

OBR||||101X\r
```

Acknowledge (GeneRead Link → LIMS)

```
MSH|^~\&|||||20150908093624.054+0200||ORL^O34^ORL_O34|421701|P|2.5.1|||||
|UNICODE UTF-8\r

MSA|AA|421601|Message will be processed\r
```

Response (GeneRead Link → LIMS)

```
MSH|^~\&|^Middleware||^LIMS||20150901143519||OUL^R22^OUL_R22|2401|P|2.5.1||
|AL|AL||UNICODE UTF-8\r

SPM||&&8814193837420317004_0||Sample\r

OBR|1|||101X|||20150901143346||||||||||||||||||F\r

ORC|OE|^^4659851137639925299_0|||||||20150901143346\r

OBX|1|ST|101X||DEVIATIONS||||||F\r

NTE|L||CrossContamination|RE\r

OBX|2|ED|101X||^AP^Octet-stream^Base64^QkVHSU46VkNBUkQNClZ...KDQ==||||||F\r
```

```
NTE|L||CrossContamination|RE\r

OBX|3|ED|101X||^AP^Octet-stream^Base64^JVBERi0xLjMKJcTl8uX...GCg==||||||F\r

NTE|L||CrossContamination|RE\r

OBX|4|ED|101X||^AP^PDF^Base64^JVBERi0xLjQK...ZWYKNTIzNQolJUVPRgo=||||||F\r

NTE|L||CrossContamination|RE\r

OBX|5|RP|101X||||||||F\r

NTE|L||CrossContamination|RE\r
```

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