Gyrolab in a GxP environment: the Merck Serono experience

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INTRODUCTION

The Immunoassay & Abs Group (NCD / DMPK-Bioanalytics, Merck Serono Ivrea, Italy) started employing 2 Gyrolab platforms (Fig.1) for GxP activities in 2010. The one year and half of experience and the workflow that has been put in place in order to comply to the GLP, in particular the Thermo Watson LIMS integration, will be described.
The platforms have been used so far for PK methods development and validation, PK and TK routine analysis (non-GLP and GLP) and Clinical PK routine analysis of New Biological Entities (NBE), i.e. new protein-drugs in development (see Table 1 for methods developed and applied since Feb/2010).

Fig. 1

Table 1

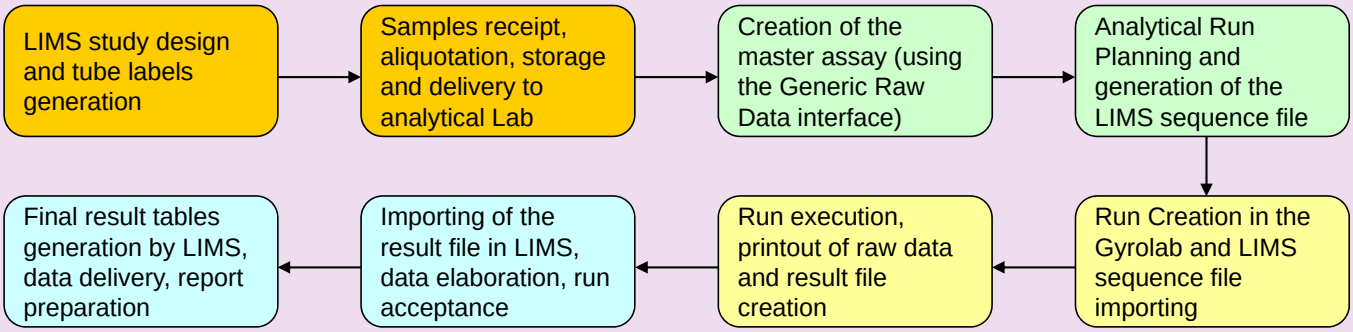
Methods developed since February 2010	Fc fusion protein (total M.W. about 160kDa) in monkey serum	Protein (about 20kDa) in dog serum	Fc fusion protein (about 160kDa) in human serum	Protein (about 20kDa) in human synovial fluid	Fc fusion protein (total M.W. about 80kDa) in monkey serum	Fc fusion protein (total M.W. about 80kDa) in human serum
Status	Developed for technology evaluation	Developed for technology evaluation	Developed. Not validated	Validated and used for clinical study (Phase I)	Validated and used for preclinical studies (PK/TK analysis)	Validation on going, to be used for clinical study (Phase I)
Method range	12.8 – 30,000 ng/mL	50 – 400,000 pg/mL	4.0 – 4,000 ng/mL	150 – 50,000 pg/mL	2.0 – 1,000 ng/mL	1.0 – 200 ng/mL
LLOQ	12.8 ng/mL	50 pg/mL	4.0 ng/mL	150 pg/mL	2.0 ng/mL	1.0 ng/mL

METHOD DEVELOPMENT AND VALIDATION

All the new immunoassays undergo the following steps:
- Labelling of reagents and screening
- Optimization of the main method parameters
- Assay Qualification
- Method Validation (Accuracy & Precision, Selectivity, Sensitivity (LLOQ), Dilution Linearity, Sample Stability, Robustness)

THE WATSON LIMS INTERFACE AND THE SAMPLE ANALYSIS WORKFLOW

During the early phase of the method development, data reduction and data interpretation are carried out by Gyrolab SW (Gyrolab Evaluator, XLfit, Gyrolab Viewer). During the method validation and the routine analysis, the only official data management system allowed is Thermo Watson LIMS 7.3.
Gyros AB developed a dedicated LIMS custom interface of the Gyrolab SW fully compatible (input-output) with the Watson LIMS. MerckSerono collaborated with Gyros for the design and the production of a specific Report format fulfilling the GLP requirements for the paper raw data. The full workflow (from study generation to data release) is showed in the following scheme:



The whole process is LIMS driven and fully validated. All the phases are audit trailed. Multi CD runs can be created. The result report generated is an unalterable pdf to be printed and signed by the analyst. The data reduction is standardized.

CONCLUSIONS

Immunoassays using the Gyrolab platform have been successfully implemented in a GxP environment, integrating the whole analytical process within the Watson LIMS 7.3. The main advantages of the Gyrolab automated nanoliter scale technology (small volumes of samples, reduced incubation time and lowered matrix effect, fast assay and high throughput) were integrated with the GLP requirements and with a 21 CFR Part 11 compliance data management (Watson LIMS).
In the Immunoassay & Abs Group in Ivrea, most likely, the next applications will be the immunogenicity method development (Preclinical and Clinical) and immunoassay reagent qualifications/QC (e.g. Ab affinity constants calculation).

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