The **LAB2LAB™** Advantage

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Introduction

It is essential for medicinal chemists to have access to analytical instrumentation for reaction monitoring and product analysis. For reasons of convenience and productivity, instruments need to be in close proximity to chemists' work areas. The high capital cost and maintenance overheads associated with such instrumentation makes it unattractive to install and support LC-MS in every medicinal chemistry lab.

In the Horsham Sector of Novartis Global Discovery Chemistry we have initiated a project, **LAB2LAB**, with TTP LabTech to develop a system for connecting remote medicinal chemistry labs on different floors of the building to LC-MS instruments in a central Analytical Chemistry lab.

Operation

The initial phase of the **LAB2LAB** system integration was to link six medicinal chemistry laboratories to one Agilent HPLC. The flow of samples is controlled by a Router which connects the labs to a temporary storage area (Buffer), and to the HPLC. When this phase was complete and we were satisfied with its operation a single Waters Acquity UPLC-MS instrument was then added. This instrument is used for reaction monitoring and so the throughput of samples increased dramatically (100+ per day). The final phase of this part of the project was to add a second Acquity UPLC-MS to the **LAB2LAB** system. The second UPLC-MS was the same configuration as the first, and is running identical methods. The three analysers now supported in excess of 250 sample submissions per day. Both the Agilent and Acquity analysers were existing instrumentation owned by Novartis and neither required modification to enable them as part of the **LAB2LAB** system. The chemist prepares the sample for analysis in a 500uL Matrix tube (which has a 2D barcode on the base) and seals it with a septum cap. The chemist scans the tube barcode and logs the sample details into the **LAB2LAB** software deployed onto a lab PC. The sample is then transported pneumatically to the Router where it is distributed to the Buffer or appropriate analytical instruments depending upon the methods associated with the sample chosen by the chemist. Once the sample has been analysed, associated results data is collected and returned across the network to be captured into the ELN. **LAB2LAB provides the chemist with a 'virtual instrument' in every laboratory, capable of running a variety of methods.** We used the time taken from the chemist physically submitting a sample vial to data being available in the ELN as one metric of system performance.

In our environment of drug discovery, the flow of samples to an analytical instrument is dependent on several factors including the difficulty of the chemistry, the type of synthetic reaction, and the number of chemists working on a particular project. Thus the flow of samples varies during a typical day, see Figure 1, but data shows it is consistent across the department in the usage of each sender, Figure 2.

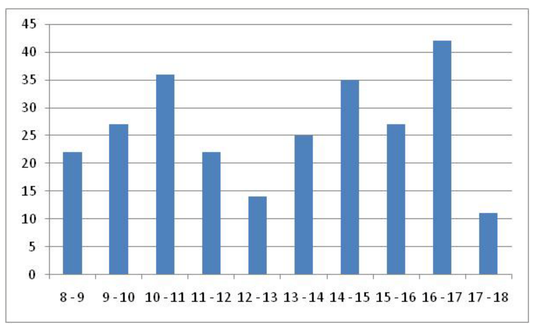

Figure 1. Typical sample submission

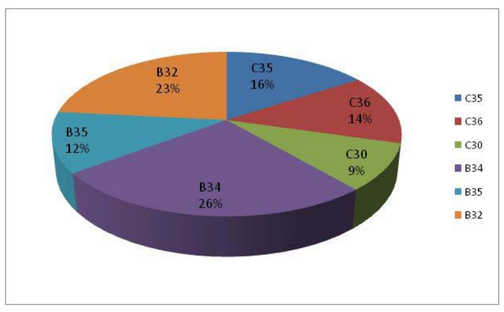

Figure 2. Typical Sender usage

When the analysis of a sample was complete, the time the data appeared in the ELN was recorded. The UPLC-MS uses a 2 minute method specifically for reaction monitoring, however, with the equilibration period, the sample has a residence time of 3 minutes 45 seconds in the instrument. The histogram shows the distribution of time taken to obtain data in the ELN for the samples run on 01/17/2011. A total of 180 samples were run on this date.

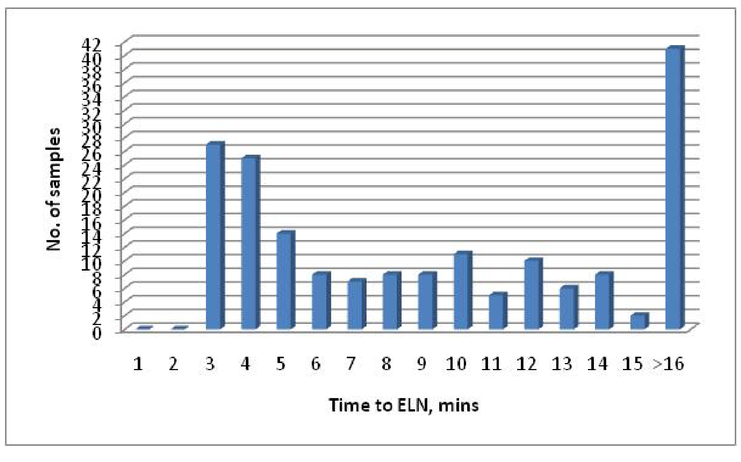

Figure 3. Histogram of time taken to obtain data in ELN

Benefits

For each day, it is possible to obtain the average time taken to obtain data, and this is plotted below in Figure 4 against the number of samples run.

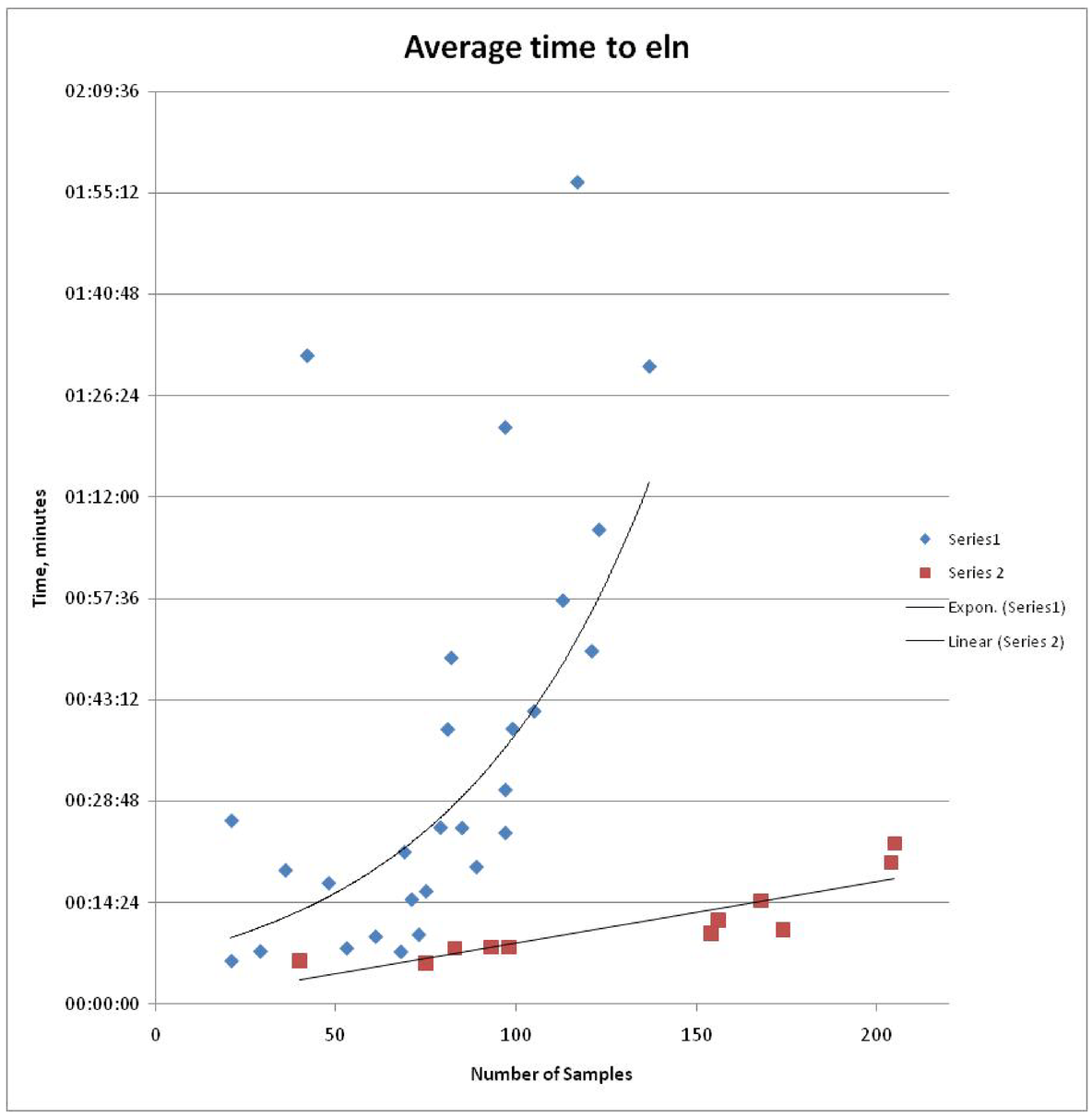

Figure 4 . Average time taken for data using **LAB2LAB** (2010)

The data in Figure 4 shows the response of a single UPLC-MS (Series 1) and two UPLC-MS instruments (Series 2) in managing the queue of samples. The first UPLC-MS instrument was installed in October 2010, and the second instrument added in December 2010. The data includes samples which have been submitted for multiple methods, and also those submitted for runs other than the 2 minute method. In addition, the outliers show the effect on queue times of taking an instrument offline for maintenance. Clearly, as the number of samples per day increases to more than 100, a single UPLC-MS instrument struggles to cope. The addition of a second analyser within **LAB2LAB**, which manages the queuing and distribution, can be seen to reduce the queue time significantly, and more than 250 samples per day are being run with an average queue time of < 30 minutes.

The **LAB2LAB** advantage may be summarised as:

- Efficient use of scientists' & instrument time as samples are sent to shortest queue.
- Safe, secure transport of samples
- Samples identified by barcode, giving sample tracking, location and status
- Status of instruments and queue reported to Med Chem
- May be installed in existing labs onto existing instrumentation
- Simple to expand system
- Does not prevent instruments being used offline from LAB2LAB
- Clustering instruments provides control of methods, fluids and maintenance
- Long transportation distances are possible
- Cost effective

Collaboration

This project is a collaboration between Novartis and TTP LabTech, and we wish to acknowledge the contribution made by Clive Aldcroft, Kamlesh Bala, Ian Clemens, James Neef and Jamie Scott (Novartis), and Grant Gardner, Tim Bedford, Chris Knights, Brian Clifford, and Paul Wogan. (TTP LabTech).