

Good laboratory practices and L.I.M.S. system: the challenge for a Next Generation Sequencing and bioinformatic research laboratory

Introduction Next Generation Sequencing (NGS) platforms have radically changed the field of genomics and are routinely applied to a variety of functional genomics problems. Although NGS has markedly accelerated multiple areas of genomics research it is a massively parallel process and generates unprecedented volumes of data which present challenges and opportunities for data management, storage, and, most importantly, analysis and interpretation. The Molecular Biodiversity Laboratory (MoBiLab), located in Bari at the CNR-IBBE, is a NGS research infrastructure, realized within the LifeWatch European infrastructure for Biodiversity. In MoBiLab, skills and advanced facilities for molecular and bioinformatics analyses are integrated to provide the scientific community with services and counselling for molecular biodiversity studies. MoBiLab has started the set up of a quality management system based on Good Laboratory Practices (GLPs) accompanied by a Laboratory Information Management System (L.I.M.S.) in order to assure the highest levels of reliability, reproducibility and traceability of the results. **Methods** GLPs are considered a quality system aimed at ensuring safety, reliability and reproducibility of the non-clinical tests on chemicals intended for the use on human, animal and environment. GLPs are mandatory in OECD countries for preclinical tests, but may be also considered as a reference for laboratory management systems outside their main scope, that can be referred to as “GLP-like” quality systems. The L.I.M.S. is a computer system capable of handling the Acquisition stages-Processing-Storage of all data generated by a laboratory and/or processes, minimizing the risk of errors and increasing the information security. **Results** The internal quality system of MoBiLab has been designed by taking into account the progressive evolution of Good Research Practices. The team has first outlined a description of the main process by means of a Supplier-Input-

Process-Output-Customer-like flowchart which includes the person in charge for the activity and the related documented information (Standard Operation Procedures, SOP, and records). After having identified the SOPs, researchers were provided with a template and with the instructions to draft them. In parallel, management procedures were defined by the whole team, drafted, and supported by flowcharts and other quality tools. MoBiLab, in collaboration with the Italian company Eusoft, started to develop and optimize a L.I.M.S. platform for managing all the laboratory activities through a suite of integrated modules. The platform is structured starting from the SIPOC-like flowchart and the modules are developed and customized in agreement to the SOPs. A CAPA (Corrective Action/Preventive Action) system is also going to be implemented within the LIMS.

Conclusions and Perspectives The implementation of some Lean tools in the production process of the MoBiLab will be the next task of the project.

1 **Good Laboratory Practices and L.I.M.S. system: the Challenge for a Next**
2 **Generation Sequencing and Bioinformatic Research Laboratory**

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17 **Introduction**

18 Next Generation Sequencing (NGS) platforms share a common technological feature
19 consisting in the massively parallel sequencing of clonally amplified or single DNA
20 molecules that are spatially separated in a flow cell. This design is far from the classical
21 Sanger sequencing based on the electrophoretic separation of chain-termination
22 products generated in individual sequencing reactions. NGS platforms have radically
23 changed the field of genomics allowing both resequencing and de novo sequencing of
24 whole genomes and are routinely applied to a variety of functional genomics problems,
25 including, but not restricted to, global identification of genomic rearrangements,
26 investigation of epigenetic modifications, single nucleotide polymorphism (SNP)
27 discovery, transcriptome profiling and metagenomics. Although NGS has markedly
28 accelerated multiple areas of genomics research, it is a massively parallel process and,
29 thus, generates unprecedented volumes of data, which present challenges and
30 opportunities for data management, storage, and, most importantly, analysis and
31 interpretation. The Molecular Biodiversity Laboratory (MoBiLab), located in Bari at the
32 CNR-IBBE, is a NGS research infrastructure, realized within the LifeWatch European
33 infrastructure for Biodiversity and funded by the PONa3_00025–BIOforIU project. In
34 MoBiLab skills and advanced facilities for molecular and bioinformatics analyses are
35 integrated to provide the scientific community with services and counselling for
36 molecular biodiversity studies. The laboratory is fully equipped with operative
37 platforms based on the most innovative NGS technologies and powerful resources for

38 data storage and computational analysis. These facilities allow to obtain detailed
39 taxonomic and genetic/functional information from environmental, food or clinical
40 samples. The design and application of massive meta-barcoding or shotgun DNA
41 sequencing protocols for the analysis of prokaryotic and eukaryotic genomes and
42 transcriptomes of individual organisms and for the investigation of eukaryotic,
43 prokaryotic and viral microbiomes living in different environments, including human
44 host, represent the main MoBiLab topics. Recently, MoBiLab has started the set up of a
45 quality management system based on Good Laboratory Practices (GLPs) accompanied
46 by a L.I.M.S. management system in order to assure the highest levels of reliability,
47 reproducibility and traceability of the results, a process that is also expected to foster
48 their potential exploitation.

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50 **Methods**

51 Good Laboratory Practices (GLPs) GLPs are considered a quality system aimed at
52 ensuring safety, reliability and reproducibility of the non-clinical tests on chemicals
53 (drugs, cosmetics, pesticides, food additives, etc) intended for the use on human, animal
54 and environment. GLPs are mandatory in OECD countries for preclinical tests, but may
55 be also considered as a reference for laboratory management systems outside their
56 main scope, that can be referred to as “GLP-like” quality systems. Applying a GLP-like
57 quality system allows a research laboratory to maintain, under control staff structure
58 (role, accountability and responsibility, skill and competence), research study
59 development, management of substances under test, test vehicles, materials and
60 equipment, facilities, automated systems and documentation, according to clear and
61 strict rules. Such a management system ensures the quality of the research outcomes:
62 uniformity, consistency, reliability, and reproducibility. Laboratory Information
63 Management System (L.I.M.S.) The L.I.M.S. is a computer system capable of handling the
64 Acquisition stages - Processing - Storage of all data generated by a laboratory and/or
65 processes. With the LIMS the laboratory can have a single platform to manage all tasks
66 and thus focus more on the laboratory business without wasting time in paper
67 management and minimizing the risk of errors. In general, the security of information
68 and the reduction of errors in data entry and costs represent the main L.I.M.S
69 advantages.

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71 Results

72 The internal quality system of MoBiLab has been designed by taking into account the
73 progressive evolution of GRP (Good Research Practices), but also considering that the
74 “customers” of their research services are laboratories already working under the
75 principles of GLPs. A PI, three researchers, a technician and a quality consultant have
76 constituted a working group meeting fortnightly via videoconference. The team has first
77 outlined a description of the main process by means of a Supplier-Input-Process-Output-
78 Customer (SIPOC)-like flowchart, which includes the person in charge for the activity
79 and the related documented information (Standard Operation Procedures, SOP, and
80 records). After having identified the SOPs needed for the operational processes,
81 researchers were provided with a template and with the instructions to draft them. In
82 parallel, management procedures were defined by the whole team, drafted, and
83 supported by flowcharts and other quality tools whenever needed. SOPs were ranked
84 with respect to priority; few SOPs were not considered since are not required for these
85 specific research activities (e. g.: management of test systems) and bioinformatic SOPs
86 are in progress. Recently, MoBiLab, in collaboration with the Italian company Eusoft,
87 started to develop and optimize a L.I.M.S. platform for managing all the laboratory
88 activities through a suite of integrated modules. The platform is structured starting from
89 the SIPOC-like flowchart and the modules are developed and customized in agreement
90 to the SOPs. The main functionalities implemented in the system will be the followings: -
91 grouping of all samples of the same project; - analytical steps categorized in the system;
92 - control of execution of all stages with warning in case of failure of one phase;-
93 automatic entry of the results produced by the instruments; - recording of raw data;
94 managing files related to tests; - automatic integrated reporting; - traceability of
95 instruments and materials used in the analytical stages; management of the
96 maintenance schedules of instruments; - management roles and qualifications based on
97 the organization chart. A CAPA (Corrective Action/Preventive Action) system is also
98 going to be implemented within the LIMS.

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100 Conclusions and Perspectives

101 The implementation of some Lean tools in the production process of the MoBiLab will be
102 the next task of the project. Lean Production (a.k.a. Toyota Production System) is a wide
103 methodology developed in manufacturing to reduce waste and improve product quality.

104 A Value Stream Mapping (VSM) will be outlined to identify value-added and non-value
105 added activities, in order to improve the process flow. Workplaces will be optimized
106 with the “5S” method, and “poka-yoke” systems for identification, traceability, and
107 handling of samples and data will be introduced. The lean approach will be strictly
108 connected with the LIMS system, leveraging its features to ensure the best control. The
109 GLP-like system and the Lean approach will allow the MoBiLab to improve the
110 efficiency, limiting waste of time and materials and reducing error opportunities, and
111 the effectiveness, guaranteeing traceability and reproducibility of results.