

How Did Institut Pasteur's NGS Core Facility, Biomics, Manage the Coronavirus Disease 2019 Crisis?

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In 2020, research entities at the Institut Pasteur (IP) in Paris, as elsewhere around the world, were closed because of the coronavirus disease 2019 (COVID-19) pandemic. However, IP core facilities, laboratories, services, and departments working on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and priority projects were authorized to continue working both on site and remotely. Given the importance of its role in SARS-CoV-2 genome-sequencing initiatives, the IP Biomics core facility was fully functional during the first (*i.e.*, March–June 2020) and second (*i.e.*, November–December 2020) national lockdowns. We describe here how Biomics successfully implemented an emergency management plan to deal with this health crisis. We highlight the internal deployment of the institutional business continuity plan (BCP) through a series of actions. We also address the impact of the COVID-19 crisis on Biomics staff and collaborators. The added value of quality management and the limitations of risk management systems are discussed. Finally, we suggest that the Biomics infrastructure and the BCP described here could be used for benchmarking purposes, for other next-generation sequencing core facilities wishing to implement/improve their processes, and for future major crisis management.

KEY WORDS: OMICS sequencing, management, coronavirus, SARS-CoV-2, NGS

INTRODUCTION

Since 2014, the core facilities of the Institut Pasteur (IP) have been fused into the Center of Innovation and Technology. In 2017, Center of Innovation and Technology became the Center for Technological Resources and Research (C2RT).¹ This technological center provides access to cutting-edge technologies supporting IP research projects. It is home to 4 technology and service units and 12 technological platforms. The expert staff working in these facilities provides research teams with access to state-of-the-art technologies, training in their use, and up-to-date information about technological and methodological developments.

The Biomics core facility is the C2RT structure at IP for next-generation sequencing (NGS).² Its mission is to facilitate scientific discoveries by providing expertise in both short- and long-read NGS technologies. Biomics provides sequencing services and is involved in collaborative NGS projects. It works with the entire IP community, which consists of 136 teams on the Paris campus together with the 33 members of the IP International Network. It

also addresses other needs in terms of NGS solutions for both national and international academic organizations and specific needs for private companies. Biomics is moving toward a collaborator and innovator core facility model.³ It acts as an incubator for new technologies and research and development (R&D) activities for NGS technologies at IP.^{4–7} Given its mission and its role in the support of COVID-19 projects, Biomics could not shut down during the pandemic and even remained open during lockdown. We describe here the tools and methods used by Biomics to continue and maintain its activities. This study highlights the impact of the pandemic and lockdowns not only on project support, teaching, and training activities but also on user satisfaction and the members of the Biomics platform. The objective is to share this experience and to demonstrate the power of managerial adaptation to deal with uncertain situations.

MATERIALS AND METHODS

Biomics consists of 3 interdependent and complementary groups: the wet laboratory, the dry laboratory, and the support laboratory. Each group possesses specific skills. The **wet-laboratory group**⁸ consists of 1 supervisor and 5 technicians responsible for sample processing (RNA/DNA registration, quantification, quality control, and storage), library preparation, and sequencing. Biomics is equipped with the Covaris and Primadiag technologies for library preparation. For sequencing solutions, we use principally

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Illumina and Pacific Bioscience technologies. The **dry-laboratory** group⁹ consists of 1 supervisor and 2 bio-informaticians responsible for NGS data analysis and management. Preliminary analysis, demultiplexing, and quality control for fastq files are systematically performed for all projects. Secondary analysis (*e.g.*, variant calling, differential analysis) is performed internally, and a Sequana pipeline is available on request.^{4, 5} The **support-laboratory** group¹⁰ includes the Head of Biomics, 1 logistics technician, and 1 transverse project manager. This staff is responsible for coordinating IP International Network, national, and international projects. It is also responsible for ethical and regulatory issues and for supervision of the quality management system (QMS) based on International Standards of Organization (ISO) 9001 requirements. All the Biomics groups work on genomics, genotyping, epigenomics, transcriptomics, and metagenomics. In addition to these 5 scientific fields based on nucleic-acid sequencing, Biomics is involved in education, training, and R&D activities (see **Fig. 1** below). Both the versatility of its human resources and technological diversity of its machines, tools, and methods enable Biomics to provide diverse solutions for NGS projects.

Communication activities are efficient, regular, and based principally on face-to-face and group meetings. They also involve the use of videoconferencing tools and channels available online. Bimonthly meetings are attended by all the Biomics staff, and weekly meetings are organized by the wet- and support-laboratory teams. The dry laboratory usually holds daily meetings during joint working sessions. Each of these meetings is open to all Biomics staff members, but attendance is not compulsory for all groups. Biomics members also attend the annual review management audience and the annual QMS progress report session.

Rapid communication is achieved *via* Slack software. Finally, a virtual private network (VPN) is used to facilitate communication with and between people working from home.

Biomics' Project Management by the QMS

Within this organizational structure, sequencing, R&D, training, and teaching are all managed in the so-called “project mode.” For this purpose, a custom-developed, in-house open-access tool is available from <https://biomics.pasteur.fr/>.¹¹ This tool can be used for inquiries, project submission, and monitoring the progress of all ongoing projects. This interface plays a fundamental role in keeping all project submitters updated on the status of their projects. In accordance with ISO9001 certification, standard operating procedures and guidelines are established for all processes and for all project steps. In addition, for sequencing projects, depending on the demands and the proximity of the user, Biomics staff may perform the project (Biomics projects) or allow short-term visits so that the users can perform their own experiments (autonomous projects). Biomics encourages user autonomy by providing technological resources (including sequencers) in a communal room and by delivering small private online courses *via* the IP massive online open course platform.¹²

RESULTS

Management Adaptation at Biomics During the COVID-19 Pandemic

Fighting emerging infectious diseases is 1 of the 3 priorities of the strategic plan of IP for 2019–2023. During the COVID-19 pandemic, a BCP was set up and rolled out in the various departments and units of IP. Institutional decisions were published and updated by both the human resources department and a dedicated BCP team. Several effective measures were taken as part of the BCP. The main aims of these measures were to ensure the safety of the employees and to limit virus transmission. The IP working-from-home system was expanded to allow the majority of the staff to work remotely. Access to the campus was authorized for only 2 categories of staff: 1) those responsible for critical/priority activities, corresponding to the national reference centers, the urgent response to biologic threats laboratory, research units working on COVID-19, animal facilities, technological platforms, priority activities at the IP medical center, and research and communication support staff and 2) scientific staff members involved in projects identified by the scientific management team as priority projects. The occupational health department established and published updated recommendations concerning health and safety measures at various sites on campus. Many free training sessions were made available online to

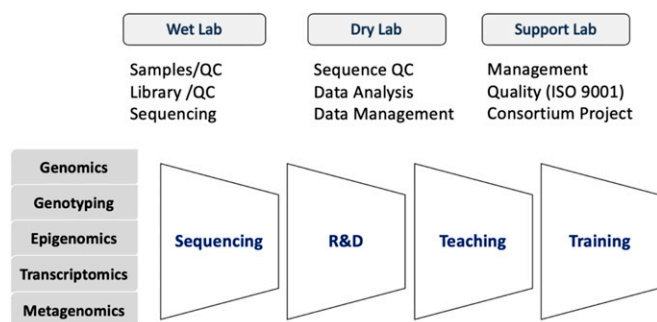


FIGURE 1

Matrix representation of the Biomics core facility. Biomics is composed of 3 groups: the wet laboratory, the dry laboratory, and the support laboratory. These groups are interdependent and have expertise in 5 scientific fields: genomics, genotyping, epigenomics, transcriptomics, and metagenomics. Sequencing, R&D, teaching, and training are the main missions of the platform.

enable the staff to continue developing new skills. Several online tools were made available to improve communication between staff members working on- and off-site and to maintain a sense of team spirit (e.g., web campus portal, internal IP newsletter, e-mailing campaigns, and videos regularly posted on social media by the Director General of IP).

Biomics is actively involved in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genome-sequencing projects, and therefore remained fully active during the lockdowns. We describe below the institutional deployment of the BCP and emergency management plan (EMP) within Biomics through the following decisions and actions undertaken during the pandemic.

The Establishment of a Joint On-Site/Off-Site Work Environment

Biomics team managers alternated between working from home and working on site to decrease the number of staff physically present on site while ensuring adequate supervision and coordination. There was at least 1 manager on site every day, making it possible to continue coordination activities during this rather unusual period. Unlike the wet-laboratory team, which manages operational production and sequencing projects on site, the dry- and support-laboratory teams could complete their daily tasks remotely, provided that they had access to a computer and a VPN

connection. The number of technicians working on site was halved and a rotation was implemented to ensure the respect of social distancing measures. The communication between staff, whether they were working on- or off-site, was maintained by the use of online tools for the regular 3-group meetings and instant exchanges. For example, Slack software was used principally for the sharing of information relating to ongoing projects, whereas Skype and Microsoft Teams were used for business activities and regular meetings, respectively.

Review of Priorities: Rapid Communication, Adaptability, and Flexibility

Tasks and goals were prescriptively reviewed to adapt to the reduction of on-site resources. During lockdowns, only 1) NGS projects relating to SARS-CoV-2, 2) projects identified as being of high priority by the scientific management of the IP, and 3) projects initiated immediately before lockdown were carried out. This prioritization was rapidly communicated by e-mail to all Biomics users and collaborators and was published on the Biomics website.² Bioinformatic analyses, the implementation of new small private online courses, and manuscript/grant writing were performed by the staff working from home. These measures were timely and ensured that resources were entirely dedicated to targeted actions in the short term. In addition, given the variability of the working environment in these conditions, staff working on site or from home was accorded greater temporal flexibility.

Key Facts About Emergency Management at Biomics

Biomics is now in a position to evaluate the efficacy of its BCP and EMP, as reflected by:

- i) The progress of projects initiated during the first lockdown (see **Fig. 2A**),
- ii) The number of projects completed, relative to 2018 and 2019 (see **Fig. 2B**),
- iii) Progress in terms of publications and the acquisition of funding,
- iv) The implementation of online courses and training on the massive online open course platform of the institute,
- v) The degree of customer/user satisfaction with the Biomics platform (see **Figs. 3 and 4**), and
- vi) Opportunities to acquire new knowledge through online training and e-learning.

During the first lockdown, the number of NGS projects decreased by 20% relative to the same period in the previous year. However, priority projects were successfully completed within 7 d, whereas other projects were completed within 66 d. This period was longer than that for previous years, in which similar projects were completed within 35 d (see **Fig. 2A**). The completion of priority projects

A

From March to June	2019	2020	
Project type	All	Priority	Non Priority
Project number	58	10 (7 on COVID)	29
Completion time (mean number of days)	35	7	66

B

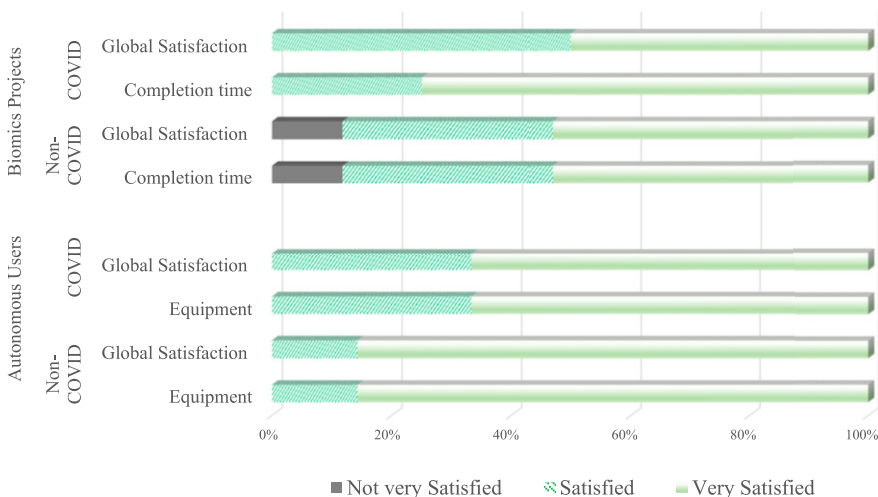
	2019	2020
Total number of runs	415	428
<i>Biomics projects</i>	277	270
<i>Autonomous projects</i>	136	158
Number of samples treated	6783	8148
All project types (service and R&D)	174	150

FIGURE 2

Impact of the pandemic on Biomics projects. (A) Differences in mean completion time between priority and nonpriority projects during the first lockdown. (B) Number of sequencing runs, samples, and projects completed annually by Biomics staff or autonomous users (years are indicated on top of each row).

FIGURE 3

Impact of the first lockdown on satisfaction among Biomics collaborators. Satisfaction was assessed with the LimeSurvey online survey tool. This tool was used to assess satisfaction with completion times, equipment availability, and global satisfaction with the services provided from March to June 2020. Users whose projects were performed by Biomics staff (Biomics projects) were targeted, together with autonomous users (using Biomics equipment). Satisfaction was assessed for COVID-19 (priority) and non-COVID-19 projects.



within such a short time required considerable investment from staff members, as this period of 7 d was considered the limit of feasibility for Biomics. Such efforts were possible only because of the urgency of the situation and on a short-term basis, making it possible to revise the mean time required for project completion. Urgency was applied in this situation to make it possible to meet the major need for COVID-19 project management while continuing to drive other priority projects' efficiency. The activities of Biomics remained globally stable throughout 2020 (see Table 2B). The number of projects completed by Biomics in 2020 (150) seems to be slightly lower than that for 2019 (174), but the number of treated samples increased (by 17%, from 6783 to 8148), as did the number of runs performed autonomously by Biomics users (from 136 to 158) (see Fig. 2B).

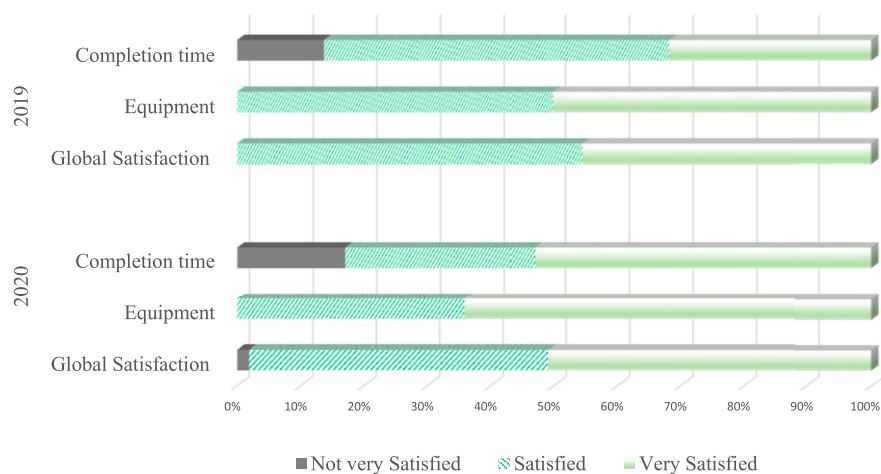
On our side, no impact on the quality of the submitted samples has been observed since the beginning of the pandemic. It should be noted that for each of our processes, we have specific guidelines in which the qualitative and quantitative characteristics of the nucleic acids to be submitted to the platform are specified. Our customers and collaborators are informed by the content of these guidelines during the project kick-off meeting or in the project initiation phase. Besides, to guarantee the quality of the provided service, the quality control and the quantification of nucleic acids are systematically checked at Biomics.

Two e-surveys were performed to improve our understanding of the impact of the COVID-19 pandemic on the interaction of Biomics with researchers and its customer service efficiency. The first covered the lockdown period from March to June 2020. It was targeted at 44 users and was analyzed from the feedback of 25 respondents. The second covered the entire year of 2020, was targeted at 162

users (all of autonomous and nonautonomous), and was analyzed from the feedback of 53 respondents. Autonomous users were fully satisfied with the available equipment and global interactions with the Biomics core facility team during the first lockdown (see Fig. 3). Indeed, this survey provided users with an opportunity to express their concerns about delays in the response to their requests, the quality of their data or results, the assistance/help/tips provided by Biomics staff, and the training activities provided by Biomics.

Two different types of behavior were observed among researchers seeking NGS solutions/services at Biomics. As COVID-19 projects were prioritized, maximal levels of satisfaction (100%) were reported among users with COVID-19 projects, with the level of satisfaction being slightly lower (88%) for researchers working on non-COVID-19 projects. This second group seemed to be less satisfied with the time taken to complete their projects and with the global core facility service. Nevertheless, global satisfaction levels remained high over the first lockdown period. The second e-survey, which covered the whole year, indicated that levels of Biomics customer satisfaction remained stable relative to 2019 despite the COVID-19 crisis (see Fig. 4 below). The 2019 satisfaction survey was targeted at 67 nonautonomous users and was analyzed based on feedback from 22 respondents.

Indeed, 100% of respondents were fully satisfied with the available technologies in both 2019 and 2020, and there was only a very small difference in satisfaction between the 2 y for the time taken to complete projects: 83% of collaborators were satisfied in 2020 *vs.* 87% in 2019. This difference is probably due to the prioritization of COVID-19 projects, resulting in a longer completion time for nonpriority projects. For the same reasons, 88% of respondents were globally satisfied in 2020 *vs.* 100% in 2019.

**FIGURE 4**

Satisfaction of Biomics users in 2019 and 2020. Satisfaction was assessed with the LimeSurvey online survey tool. The survey was performed to assess the services rendered throughout the year. All Biomics users working on all types of project were targeted.

Limitations of the BCP

During the lockdown periods, several challenges were encountered in the implementation and deployment of both institutional and Biomics BCPs. These challenges extended from materials, methods, and tools for working remotely to aspects relating to physical and mental well-being. For instance, there were too few laptop computers for all staff that had to work from home. Several desktop computers were therefore transferred to the homes of IP workers, and this required organizational efforts from Biomics. Similarly, VPNs were not always easy to use, because Internet connections were variable, and interruptions were frequent. This jeopardized teamwork by limiting access to common resources and software. In addition, the risk of cyberattacks increased during lockdown, increasing the need for vigilance. These challenges made some employees feel stressed and isolated, particularly because of the uncertainty concerning long-term working from home. Some employees also suffered from back and neck pain due to poor working conditions at home. Employees with children found themselves in particularly stressful situations, as they had to care for their children while working. This led to an increase in multitasking, generating fatigue and a lack of performance and productivity.¹³ For some employees, this experience also led to feelings of anxiety, guilt, and distress. Conversely, staff working on site lost time daily because of the precautionary measures implemented through the BCP but also because of changes in the management of their everyday lives and the constraints imposed on the population. It is clear that this new experience had a considerable impact on the employees' social, private, and professional lives. The abrupt change in professional culture (*i.e.*, working from home, the use of new tools and methods, revision of objectives) pushed them out of their "comfort zone." Some employees found adapting to this situation motivational, providing an

opportunity to improve things and to make them feel better about themselves. Employees adapted to the new situation, regularly changing the spaces and rooms in which they worked at home to avoid routine. Others, particularly those working from home occasionally, used this situation as an opportunity to increase their knowledge of NGS technologies and to get into work more easily without traffic jams. However, this situation was also destructive in some cases, leaving some employees with a feeling of incapability, sometimes leading to complete demotivation and depression. The Biomics managers developed their roles in the support of their teams during this period. For this purpose, the individual group meetings of the wet, dry, and support laboratories were maintained. Conversely, the first whole-team meeting was not held until 50 d into the first lockdown. Some employees reported misinformation and a lack of updates on the progress of work from other groups. After feedback from colleagues, this information was reported, and team meetings were scheduled once weekly thereafter. Based on the feedback from staff members during the first round of questionnaire surveys on the impact of the COVID-19 pandemic on work/life balance (April 2020), it became clear that this emergency situation was not easy to deal with within the COVID-19 BCP. As events were dictated by the health crisis, the consequences were unexpected, abrupt, imposed, and global. The difficulties were also due to IP being considered a crucial site for the French state. Employees alleviated the negative impact by dealing with daily stress, getting into new habits, and learning how to manage the private, professional, and social aspects of life during lockdowns.

During the second wave of the pandemic, IP again had to implement working from home to minimize the spread of COVID-19 cases. Unlike the first lockdown period, the second lockdown was considered more as an opportunity for changing working methods. This allowed employees to

focus on their productivity without necessarily having to juggle their professional and private lives as schools remained open. Working from home was better appreciated, and the relationship between staff members and their managers evolved from contractual conditions of employment to a perspective of trust. Feelings of isolation were minimized by implementing greater flexibility in terms of access to work on site on request. Employees appeared to enjoy the work-life balance provided by this new remote working experience.

DISCUSSION

In response to this unexpected crisis, the Biomics core facility had to react rapidly and make decisions very quickly to ensure an efficient maintenance of its activities. Because the lockdown measures imposed had never been used before, the institutional BCP was applied together with well-known EM techniques to resolve many issues.¹⁴ As described throughout this article, Biomics had established organizational, operational, and managerial adaptation measures to maintain its activity. We provide evidence here that the COVID-19 pandemic had no global impact on the Biomics sequencing service (based on an analysis of the number of completed projects *vs.* user satisfaction over the last 2 y). Sequencing activities at Biomics contributed to several SARS-CoV-2 and other priority projects. Despite the urgent nature of the priority projects, including the COVID-19 projects (7-d turnaround time), the quality of the samples submitted by the collaborators as well as the quality of the results delivered by Biomics were very satisfactory. In fact, the satisfaction survey shows a maximum level of satisfaction (100%) from the priority project leaders. Nevertheless, on-site teaching and training activities had to be postponed.

With hindsight, multiple factors contributed to the continuation of sequencing projects. First of all, thanks to both existing and established guidelines and standard operating procedures, and the project management tools and methods described above, task reorganization was rapid and straightforward. The technical staff displayed considerable flexibility, making the rotation of on-site workers possible. Moreover, Biomics did not restrict itself to the use of a single operating model in the completion of sequencing projects.¹⁵ Indeed, the platform had 2 models of sequencing-data delivery: a model involving brief visits of researchers and users (autonomous projects) and projects carried out by the Biomics staff (Biomics projects). This made it possible to make progress with sequencing projects, mitigating the impact of the pandemic and lockdown. The use of a single model would certainly have hampered the production of scientific knowledge in such circumstances. It became clear that the preparation of effective management

systems in advance results in efficient solutions with added value in the context of crises. These observations also highlight the added value of ISO9001 standards for academic research platforms.¹⁶

The risk management system is the key requirement for the latest version of ISO9001 (published in 2015). Several external and internal risk categories are treated in the Biomics risk management system, including risks relating to information systems, staff absence, and environmental and economic changes. However, there are some situations that cannot be anticipated. Indeed, even if risk management is well deployed in the framework of this standard, the COVID-19 pandemic situation exceeded the usual or anticipated levels of risk for the various categories. It is recognized that organizations cannot foresee every eventuality.¹⁷

As shown above, successful EMP deployment according to general principles was effective and resulted in an efficient maintenance of the principal activities of Biomics. Nevertheless, the impact of the EMP extends beyond advancing the work and the satisfaction of customer expectations. Indeed, as highlighted by the feedback from Biomics staff, the first lockdown period posed specific mental and physical health issues for on-site workers and for those working remotely. However, the employees seemed to be more confident during the second national lockdown, particularly those working from home. Similar positive changes in the working-from-home experience were also reported by global IP surveys and surveys performed by other organizations around the world.^{18, 19} For instance, the European Foundation for the Improvement of Living and Working Conditions recently reported that the level of concern had decreased for some items in the second round of its e-survey, particularly among groups of respondents benefiting from support measures implemented during the pandemic.²⁰ Following the emergence of variants of the coronavirus since the end of 2020 and the beginning of 2021, France is once again under the threat of an imminent confinement. As a result, the EMP as well as the processes described in this manuscript will be very strongly deployed again in the near future. Moreover, at the time of the revision of this manuscript, the third containment is announced (March–April 2021) for 16 French departments, including Paris, where our IP is located. It is therefore not questionable that the same BCP will be deployed to ensure normal operation of the facility. Our experience in coping with this pandemic helped us to re-evaluate our managerial tools and methods together with the services provided. Many of the changes made will undoubtedly be retained after we emerge from the current health crisis. This atypical experience has better equipped Biomics to face current and future challenges.

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