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PRACTITIONER'S REPORT

Applying Quality and Project Management methodologies in biomedical research laboratories: a public research network's case study

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Abstract Quality principles and Project Management (PM) methodologies have long been ignored in non-regulated scientific research, even though they have been widely used in industrial and business applications, improving management and results and reducing costs. A groundbreaking project named Quality and Project Management OpenLab was implemented by a network of Italian National Research Council institutes, with the aim to realize and disseminate within the scientific community an innovative way to plan and organize research activity, inspired by Quality and PM principles and customized for needs and requisites of biomedical research laboratories. The results show better use of time and project consistency. Our experience of working side by side with Quality consultants clearly shows that the proper and accurate application of Quality and PM methodologies to intellectual and scientific production can facilitate and strengthen research, providing tools to make it faster and more efficient without imposing any undue constraints.

Keywords Management of science and technology · Quality methodology · Knowledge management · Project Management

Abbreviations

DoE	Design of experiment
FMEA	Failure mode and effect analysis
GLP	Good laboratory practice
GMP	Good manufacturing practice
ICH	International Conference on Harmonization
ICT	Information and Communication Technology
PDCA	Plan–do–check–act
PM	Project Management
QMS	Quality Management System
qPMO	Quality and Project Management
TQM	Total Quality Management

Introduction

Quality methodologies have been widely used for decades in industrial and business fields. One of the central concepts in a Quality approach is the importance of how the final result is achieved. This attention easily leads to effectiveness, intended as guaranteed results, prevention, and safety, and to efficiency, in terms of rigorous resource

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management. In the commercial field, these aspects are strong drivers of strategy development and related tools. Under the aegis of Quality, significant methods have been collected and developed covering almost all areas in business and production (see ISO 10014:2006), from management systems to production control, from project and innovation management to statistical tools. However, Quality Management has not so far received proper attention from the scientific community, with the prejudice that they might be an impediment to creativity and that reaching and maintaining Quality standards might be very expensive in terms of money and time.

In recent years, the scientific world has been clearly experiencing a revolution: the attention of the scientific and social community is not focused solely on the final results, but also on the process utilized and other related issues such as the reliability, safety, and efficacy of the discoveries, and the efficient and effective use of resources. As an example, Quality Management in scientific R&D is emerging as an essential tool to ensure valuable and robust outcomes, within a framework of best practice [1–9]. A proper deployment of the Quality approach has long found its application in drug discovery and development through the standards of good practice (good laboratory practice, GLP); however, a culture of Quality is still lacking in non-regulated scientific research. Moreover, it should be noted that even GLP, which controls and rules scientific experimentation, leaves unaddressed most management issues as well as continuous improvement. This was also the case of good manufacturing practice (GMP), the international standards for pharmaceutical production, now facing an evolution to a Quality Management System (QMS) (see International Conference for Harmonization—ICH Q10 Guidelines). In line with the need of integrating Quality standards within biological research, recent EU calls for research projects either require or strongly suggest a transversal Quality Management work package (WP) to ensure the training, control, and application of Quality methods. Recent examples of the application of International Organization for Standardization—ISO 9001:2008 standards in research structures have indicated many advantages in terms of governance, control, efficiency, and results [10–14].

A group of ten researchers and technologists of the Italian National Research Council (CNR) plus an external Quality consultant constituted a knowledge network, with the aim of realizing a Total Quality Management (TQM) model for biomedical research laboratories. The project, named "Quality and Project Management OpenLab" (qPMO), was designed and developed applying Quality, Project Management (PM), and team-working methods from the very beginning. The strength of such a project is that it was intended as a research project and run by scientists, deeply involved in research activities, working side by side along with a Quality expert. According to their own experience, scientists had the opportunity to define the research needs and objectives and to identify the proper Quality methodologies for their needs. The final goal is to generate, validate, and disseminate a model of TQM easily suitable for a biomedical research laboratory. In the following, we show how the team has worked, the methods by which the project has been built and conducted, the objectives that have been fixed, the principal advantages experienced, as well as the results regarding the main topics.

Methods

For the development and realization of the project, we used both PM and Quality methods, as follows:

Brainstorming, consisting of a short time (20–30 min) of free contributions, aimed at collecting the largest possible number of results [1, 15]. Results of brainstorming can be processed by applying filters. In this case, focused on a very rapid choice among many proposals, two types of filters were used. Because different solutions can be better compared with the characteristics and limitations of the system, rather than among themselves, *constraints and preferences* [1, 16] were chosen. It is helpful to use a "Table of Constraints" to manage and summarize results. Proposals are listed in lines, constraints in columns; a final column summarizes the compliance to constraints of each proposal with a logical AND. Proposals compatible with all constraints are kept; proposals that do not meet even one constraint are marked with "no" and rejected; proposals that have a dubious compatibility are marked with a "?" to be kept for further analysis.

Decision Matrix (*or Grid*), a useful tool when a decision has to be made among many proposals [1, 16]. First of all, the aim of the decision must be clearly defined. Then, the team must identify the criteria that are used to characterize each solution. Preferences are used as criteria for the brainstorming output. In the decision matrix, each criterion is given a weight (1 = lowest to 5 = highest) based on its importance in the final decision, and each proposal is assessed against each criterion (1 = lowest to 5 = highest). The sum of the weighted assessments gives the final score for each proposal.

Debriefing, realized using a table in which each participant in turn can express (in mandatory order) one aspect as good and one as needing improvement [1, 17]. The debriefing results are quickly analyzed by the team during a subsequent meeting.

Meeting minute, formal records following with a simple and clear scheme, divided into three parts: description of the meeting, summary of the topics covered, list of actions (past and present) [1, 17].

Project charter, a formal document used in PM to describe the purpose, context, resources, and expected results of the project [1, 15, 17].

Gantt chart (also known as a Bar chart), a simple tool to plan a project. On a chart, time is shown along the X-axis; each activity is represented as a bar or a line [1, 15, 17, 20].

Plan–do–check–act (*PDCA*), also known as the Deming circle, an iterative four-step management method used in business for the control and continuous improvement in processes and products [18, 19]. It is the foundation of TQM and the Quality approach.

Failure mode and effect analysis (*FMEA*), a risk analysis developed in aerospace and automotive fields and then used in industrial fields [21–23].

Design of experiment (*DoE*), a statistical method to analyze the interactions among experimental factors in order to identify their optimal combinations. Minitab (www.minitab.com) was used to carry out the statistical analysis for DoE.

Results

Setting up the project and objectives

To define the topics to be developed within the qPMO project, the technique of brainstorming was used, oriented toward collecting the largest possible number of research fields. Constraints and preferences were also identified by the team in order to refine the proposals that emerged from brainstorming. Among constraints, the need for immediate results and compliance with the priorities of the funding program were identified; most preferences were focused on management, visibility, networking, and exportability. The brainstorming session produced sixteen proposals, all regarding the application of Quality principles and methodologies to a biomedical research laboratory. Afterward, during a coached team meeting, some proposals (proposal no.: 4, 5, and 14) were combined, leading to a new one, number 17 (Table 1).

Proposals can be clustered into six main fields, all having as their main goal supporting the research activities using Quality and PM methodology (Table 1):

- the setting up of dedicated offices within the pilot research institute (proposal no. 1, 2, and 6);
- the generation of models aimed at optimizing: administrative processes (proposal no. 3, 12, and 13), research or Quality training (proposal no. 10, 11, and 16), and laboratory and project efficiency (proposal no. 7, 15);
- the development of ICT tools (proposal no. 17);
- the application of Quality methodologies (FMEA, etc.) to support technology transfer process for the development of in vitro diagnostic tools (proposal no. 8, 9);
- the generation of guidelines for laboratory procedures (proposal no. 14).

The range of subjects identified was then reduced to seven (proposal no. 6, 7, 8, 13, 15, 16, and 17) by applying

Table 1 Selection of the proposals emerged from brainstorming by applying two constraints

No.	Proposals	Constraint 1: first results available in 6 months	Constraint 2: compliance with the priorities of the funding program	Selected
1	Project Management office	No	Yes	No
2	Grant office	No	Yes	No
3	Model of administrative management	No	Yes	No
4	Quality Management database for small model organisms	–	–	–
5	Database of validated laboratory protocols	–	–	–
6	Scientific dissemination office or program	Yes	Yes	**Yes**
7	Model of PM methodologies applied to research project	Yes	Yes	**Yes**
8	Quality methodologies (i.e., FMEA, DoE) to support technology transfer	Yes	Yes	**Yes**
9	Quality methodologies to support the development of IVD tools	No	Yes	No
10	Model for assessing the ability of a laboratory to train researchers	Yes	No	No
11	Model for improving research training	No	No	No
12	Model/s of contract/treatment for temporary researchers	No	No	No
13	Model for supplier management	Yes	Yes	**Yes**
14	Guidelines for cell culture and other laboratory procedures	–	–	–
15	Model of Quality Management System for a research laboratory	Yes	Yes	**Yes**
16	Training on Quality	Yes	Yes	**Yes**
17	Web site for protocols, guidelines, models	Yes	Yes	**Yes**

Bold indicates positive evaluation of proposals

constraints, filling in Table 1, and discussing the results. Finally, chosen preferences were applied and the decision matrix tool was used to arrive at the final ranking, in which the highest scores were obtained by proposals 17, 8, 13, and 15 (Table 2). The ranking obtained was brought to further discussion to be validated, and one of the proposals (no. 13) was excluded due to an emerging constraint not evidenced in the first analysis, that is, the need to involve the CNR administrative department, which was not part of the research project. In substitution for it, we decided to expand the proposal regarding the application of Quality methodologies in research (proposal no. 8) and include a new proposal based on the application of DoE methodology to multivariable assays, after having carefully analyzed in terms of constraint and preference criteria.

Each approved proposal was considered an independent WP and assigned to a working group of one of the four participating institutes:

1. *Management of knowledge*: Definition of guidelines for research laboratories and development of a Web platform for the cataloguing and dissemination of guidelines, experimental procedures, model systems, and molecular tools used in biomedical research (corresponding to proposal 17);
2. *Management of experimental procedures*: Quality methodologies for technology transfer support (corresponding to proposal 8);
3. *QMS for a research laboratory* (corresponding to proposal 15);
4. *Management of multivariable assays*: Application of DoE, corresponding to the newest proposal.

We have chosen to define a simple QMS model, easy to be used and validated, and to deepen separately some aspects regarding documentation, experimental procedures, and assay management. Successively, we integrated the outcomes obtained by the four working groups into a TQM model for a generic research laboratory. For this reason, possible and expected synergies among WP subjects were addressed at the coordination level, i.e., by means of periodic meetings among the four working group.

The planning of each group was delineated by using PDCA method (Fig. 1), thus detailed by a Gantt and described in a Project Charter. The final definition of the project was ready in 1 month, submitted to upper management, and formally approved during the kickoff meeting about 1 month later. As a result of the proper setup of the project, the four working groups started to accomplish their planned milestones in advance with respect to the initial timetable; as an example, the results of the first 6 months show better use of time and project consistency (Table 3).

The working strategy

Once the qPMO network had been created, the first issue was to ensure adequate technological support to allow the effective exchange of information and materials, maintaining a direct contact, and the generation of substantial

Table 2 Application of the decision grid to the seven selected proposals

		Selected proposals													
		6. Scientific dissemination		7. PM methodologies applied to research project		8. Quality methodologies to support technology transfer		13. Model for supplier management		15. QMS for a research laboratory		16. Training on Quality		17. Web site for protocols, guidelines, models	
Preference criteria	W	A	Score	A	Score	A	Score	A	Score	A	Score	A	Score	A	Score
Available indicators for saving time or money	4	2.5	10	4	16	5	20	5	20	5	20	3	12	3	12
Better visibility and communication	3	5	15	3	9	4	12	3	9	5	15	3.5	10.5	4.5	13.5
Affordable with workforce	4	4	16	4	16	4	16	3.5	14	3	12	4	16	5	20
Exportable model	5	4	20	5	25	5	25	5	25	4	20	4	20	5	25
Already in the wish list of the board of directors and grant revisor	3	4	12	3	9	5	15	5	15	5	15	3	9	4	12
Integration degree with other funded projects	5	4	20	2	10	3	15	5	25	4	20	4	20	5	25
Total			93		85		103		108		102		87.5		107.5

W, weight of criterion; A, assessment of proposal versus criterion; score, W × A

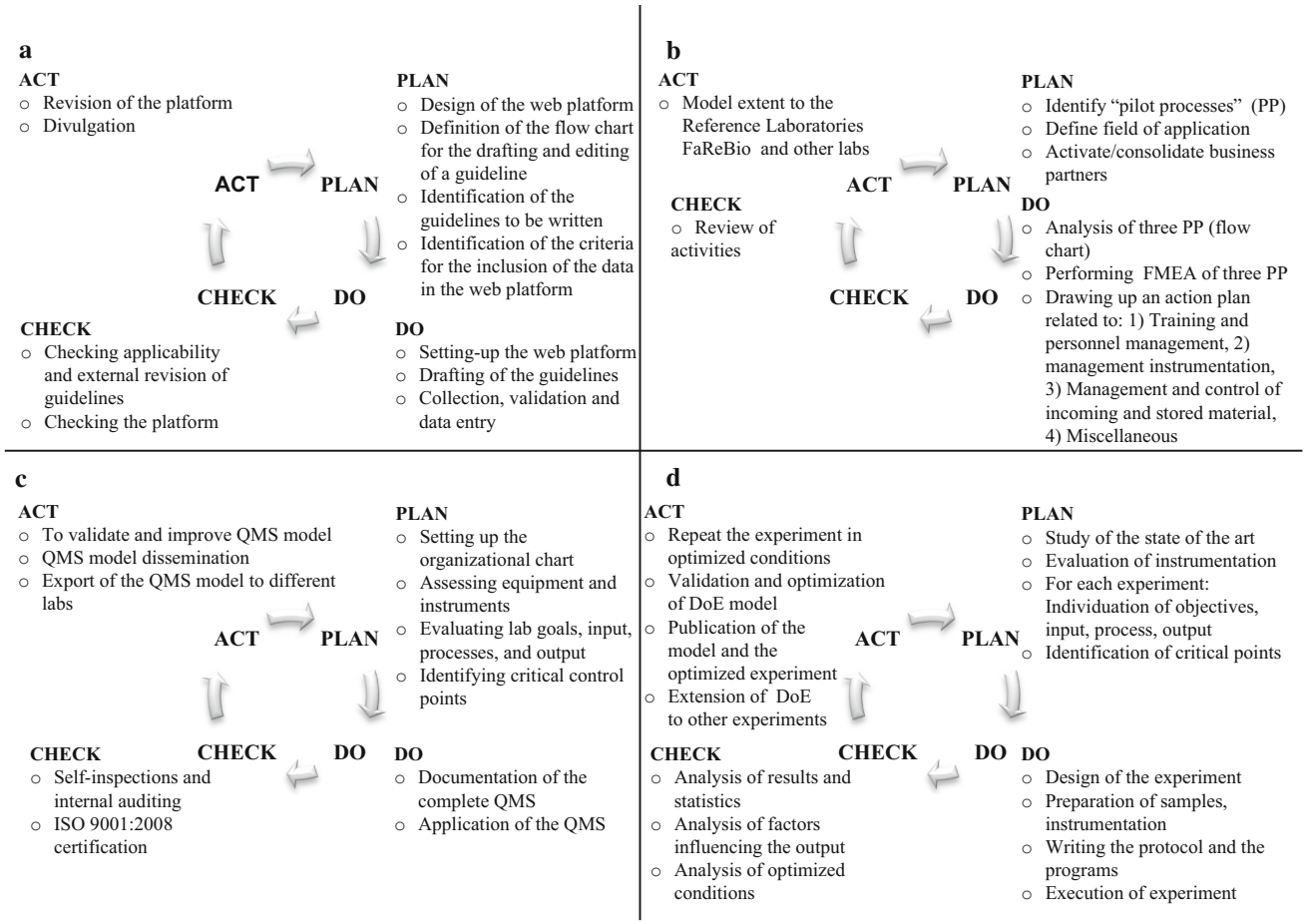

Fig. 1 Planning of the four WPs. The *four panels* show the application of the PDCA cycle for defining and planning activities for the four WPs: WP1 management of knowledge (**a**), WP2 management of experimental procedures (**b**), WP3 QMS for a research laboratory (**c**), and WP4 management of multivariable assays (**d**)

synergies. To address this aspect, it was decided to hold meetings via videoconference and to share and manage documents via a cloud service. Team building has been pursued via different practices, among them weekly or fortnightly videoconferences and some multi-day retreats. The periodic meetings were managed by the aid of team-working tools, such as sharp meeting planning, regular minutes of meeting, resource management, adequate records, and sharing of information, both in the project coordination and within the same working group. Furthermore, the technique of debriefing was used to take care of the first opportunity to work in a team, picking up cues from the participants to focus and improve teamwork. Among positive aspects were enthusiasm, participation, concrete proposals, discussion, agreement, and new ways of organizing discussion and projects (i.e., management of interventions and respect of the meeting agenda). Judged to be in need of improvement were technical aspects, communication, and focus on constraints and goals.

Description of the four work packages and main results

For each of the four WPs of the project, the main results achieved are reported (Table 4). The complete description of the final results obtained by the working groups at the completion of the project will be described in separate, dedicated papers.

WP1: management of knowledge

The objectives are (1) identification of adequate standards for the drafting of guidelines in biomedical research, according to Quality principles, and for the description, cataloguing, and sharing of scientific data; (2) definition of guidelines for specific activities in a biomedical laboratory and for the design and validation of experimental procedures; (3) development of a Web platform for the collection, cataloguing, and dissemination of the scientific information provided by researchers working in biological

Table 3 WP forecast results after 6 months versus actual results achieved

Workpackage	Actions and goals		Forecast (month 6)	Actual (month 6)
WP1	Plan	Operational flow for drafting guidelines	Month 3 of the project	Month 2 of the project
Management of knowledge		Web site design	Month 5 of the project	Month 4 of the project
	Do	Drafting of guidelines	2 out of planned 8	3 out of planned 8
		Web site setup	50 % done	75 % done
WP2	Plan	Partner	50 % (1 out of 2)	50 % (1 out of 2)
Management of experimental procedures		Pilot process (flow chart)	100 %	100 %
	Do	Process analysis (FMEA)	30 % done	100 % done
		Documentation (FMEA report)	0 %	10 %
WP3	Plan	Organization chart; Quality policy; Quality objectives; products and customers; processes flow chart and network	65 % done	100 % done
Quality Management System (QMS)	Do	Quality manual	40 % done	70 % done
		Procedures	0 %	5 % Final documents
				15 % Drafts
WP4	Plan	Pilot process	Month 1 of the project	Month 1 of the project
Management of simple to high-throughput assays		(1st experiment)		
	Do	1st Process flowchart	Month 6 of the project	Month 4 of the project
		Design of first experiment	100 %	100 %
		Sampling procedure; execution	75 %	100 %

fields inside the CNR. These goals address the need, both nationally and internationally, to enhance the wealth of knowledge present within the CNR and structure adequately processes for its diffusion and preservation, encouraging the generation of new knowledge. The identification of guidelines is one of the basic steps for the training of personnel and the Quality certification of a laboratory [24–26]. Whereas a great attention has been dedicated to the identification and applications of guidelines in clinical or preclinical studies, the non-regulated scientific research has not yet developed a common sensibility to this topic. To manage this point, we developed a general guideline for the drafting of guidelines firmly based on Quality principles and methodologies, in which specific key questions, particularly pertinent to non-regulated research, were explicitly addressed (Digilio et al. in preparation). We validated the operational flow identified for drafting guidelines, by defining 13 guidelines divided into five principal areas of interest (Table 5). All of them have been successfully applied in CNR research institutes. At the same time, we developed the Web platform http://quality4lab.cnr.it for scientific data management, designed following the project Web sites—Best Practice Guidelines [27]. For the optimal organization of the contents (experimental procedures, molecular tools, and model systems), we generated specific templates for data entry. We have completed the beta testing of the platform that is now available to CNR researchers who want to register and upload their scientific contents. According to international Quality principles, scientific data will be subjected to review and can be published only if they accomplish specific validation criteria. The final aim is to provide powerful tools to promote identification and diffusion of standard procedures for research laboratories, to increase the efficiency of laboratory activities, giving new opportunities to researchers for disseminating their scientific activity, and to create networking, and increasing cohesion and collaboration among CNR institutes and with others institutions.

WP2: management of experimental procedures: Quality methods for technology transfer support

Starting from the application of a risk management method, such as FMEA on a "pilot process," a pattern for the implementation of Quality methodologies has been generated. In this context, FMEA is also useful to drive the adaptation of laboratory processes to an industrial approach, when a technology transfer is envisaged, helping to anticipate and deal with production aspects and requirements. We chose to analyze a process consisting in three main sub-processes that have been first described using a flowchart, followed by a quantitative assessment of the risks associated with the most delicate operations and the definition of improvement actions. Particular attention has been paid to adapt the FMEA risk index to the research context, because most of the operations carried out in the laboratory are not automated.

Table 4 Main results achieved by each WP and by the transversal activity of scientific dissemination

Activities	Final results
WP1	Operational flow for drafting guidelines
Management of knowledge	13 Guidelines for research laboratories
	Web platform: http://quality4lab.cnr.it
WP2	Analysis of an experimental protocol (three phases)
Management of experimental procedures	Control plan
	Scheme for FMEA in research laboratory
WP3	Software Help4Lab
Quality Management System (QMS)	QMS release and application
	QMS certification
WP4	DoE application on four medium- and high-throughput experiments
Management of multivariate assays	DoE application on three simple-assay experiments
	Optimization of four protocols
Project scientific dissemination	1 Paper on peer-reviewed journal
	5 Communications to both national and international meetings
	15 Seminars in scientific institutes (CNR institutes, Universities, IRCSS)
	1 Degree thesis in Biological Sciences
	1 Lesson in Training Courses

Table 5 Guidelines written according to the operational flow identified and validated in different CNR research institutes

Guidelines
Basic
Management of experimental procedures
Writing the laboratory notebook
Management of reagents and materials
Personnel management
Instruments
Equipment management
Sea urchin aquarium management
Facilities
Cell culture
Glass-washing and solution preparation center
Animal house
Research activities
Working with *D. Melanogaster*
Working with *P. Lividus*
Quality methodology
FMEA
DoE

In particular, the three main sub-processes analyzed include 102 steps (elementary operations). As a result, a set of improvement actions was generated covering most laboratory aspects, such as management of instrumentation and materials or training of personnel involved. The risk priority number (RPN), calculated for each process operation, showed an initial value greater than the fixed threshold in more than 50 % of the steps and has been reduced to 0 after the implementation of corrective actions identified. These results are compatible with the case of non-automated activities where some aspects, such as human error, can greatly affect the process. Thus, according to general guidelines (see WP1), we drafted two guidelines for staff management and equipment management. On the other hand, in order to keep under control all correctives action for the specific processes analyzed, we draw up a control plan referred to incoming materials and processes. The control plans generated have brought useful information for management of laboratory and can be used as the statement of work in a newly established laboratory. However, we found it somewhat difficult to work with a language and a scheme not intended for life science, which we understand is a limitation to the diffusion of these useful tools in research laboratories. For this reason, we are currently working on a FMEA model suitable for a research laboratory (Mascia A. et al. in preparation). Furthermore, the use of a common language oriented toward results is expected to facilitate technology transfer, thus promoting interaction between research and industrial applications.

WP3: QMS for a research laboratory

The main goal is to ensure the Quality Management of a research laboratory, working in the area of biomedical research. Specifically, we have selected a research laboratory working with marine animal models (mainly the sea urchin *Paracentrotus lividus*) in the scientific area of drug discovery and embryonic development as pivotal laboratory. From among various others (GLP, ISO 17025, etc.), we chose to implement the ISO 9001:2008 Quality system. We had to pay careful attention to its design and application in the research laboratory, since QMS translation from the manufacturing system was not simple, and there was the need to not impose any constraints on the research work. Furthermore, because of the absence of specific background, the "Plan" and "Do" phases were particularly challenging (Fig. 1). As specified by the ISO standard and in agreement with the heads of the laboratory, we first defined the Quality policy. Next, we identified operational and support processes to be managed, stakeholders, recipients, and suppliers. Once these concepts were translated and fixed for the selected laboratory, we were able to complete the Quality manual. We also generated the procedures, operating instructions, guidelines, and forms to

cover all laboratory aspects. We have applied this QMS during 4 months of activities of the pivotal laboratory and performed a self-inspection and internal auditing of the QMS (Check stage, Fig. 1c). In parallel, we have generated an *ad hoc* modular software to manage instruments, Quality, and safety documents (Help4Lab, currently under the process of copyrighting). Following the upgrading of the QMS and the setting up of the software, we were able to obtain the UNI EN ISO 9001:2008 certification (#585SGQ00, IAF no. 34, 38), as final validation of the system.

A proof of concept of the efficacy of the QMS application in the pivotal laboratory would derive from the evaluation of the selected quantitative indicators (i.e., staff motivation grade, number of non-conformity, number of published scientific paper) after 1 year from the certification, during annual internal audit. However, we have already experienced a drastic improvement in the efficiency of the sea urchin supply and housing related to the number of successful experiments. Indeed, one of the established indicators of the QMS regards the management of the sea urchin housing in the aquarium; the efficiency of aquarium management is evaluated through the ratio (*R*) defined as number of experiments divided by number of sea urchin supplying activities (by free-diving or purchasing) over a year of activity. We have considered the following correlation between *R* and the efficiency of aquarium management: *R* less than or equal to 1 means "poor," *R* between 1 and 2 means "limited," *R* between 2 and 3 means "acceptable," *R* between 3 and 4 means "good," and *R* more than 5 means "excellent." During the first 6 months of application of the QMS, this indicator has been "excellent." As a confirmation of the good management of the aquarium: from the application of QMS none of the programmed experiments had to be postponed or canceled due to lack of suitable biological material (sea urchin embryos). We expect that this validated QMS model with the support of the intranet management software would be a new alternative for organizing labor, motivating the staff toward a continuous improvement in shared operations, and enhancing communication between all management levels and personnel. Such a system would also ensure the reliability of the results of research laboratories and increase the prestige of the laboratory and the public research institution itself.

WP4: management of multivariable assays

The main goal of this activity is to use experimental design to set up and optimize both simple and high-throughput biological assays and to generate some DoE models suitable for different kinds of experiments, to be transferred to scientific community. The DoE approach allows experiments to be efficiently designed so to identify the key factors influencing their outcome, the interactions between them, and the best combination that permits to maximize the output [28, 29]. We decided to use DoE in a field close to its original area of application, biomedical research. For each experiment, we defined the experimental plan, using a matrix of experimental conditions based on DoE requirements. The execution of the experiments as designed followed, and we evaluated the corresponding output values to determine the best combination of physicochemical conditions necessary for output maximization and to identify the most influential factor or combination of factors. The conditions optimized using DoE were chosen for an experiment that was a key part of a recent publication [30]. The DoE methodology has been first applied to the following medium- and high-throughput experiments: (1) enzymatic assay of tryparedoxin peroxidase (TXNPx) activity and (2) thermal stability of nucleic acids and proteins (3 experiments).

The reaction between *Leishmania major* TXNPx and H_2O_2 has been determined by competition approach utilizing the H_2O_2 with horseradish peroxidase (HRP) [30]. HRP activity was studied, depending on three factors: (a) pH of the reaction buffer, (b) ionic strength of the reaction buffer, and (c) stock of HRP. Higher activity was found at buffer 0.1 M, pH 7.4.

The thermal stability of mitochondrial (mt) RNA transfer (tRNA) was determined by thermofluor experiments depending on five factors: (a) type of fluorescent dye, (b) dye concentration, (c) RNA concentration, (d) type of salt, and (e) salt concentration. The highest thermal stability was obtained in the presence of high concentrations of dye, of RNA and of salts (Fiorillo et al. in preparation).

DoE methodology has been applied also by the other qPMO working groups to non-automated multivariable assays such as: (1) toxicity assay to determine the amount of a reagent that could affect cell viability in different culture conditions and cell density, (2) transfection protocol for neural progenitor cells, which are known to be very hard to transfect, and (3) reactive oxygen species (ROS) detection assay in cell culture. The first two assays have been used for the analysis of the effects of specific genes ectopically expressed on stemness and neural differentiation. For the transfection protocols, we performed a first screening DoE, identifying the factors impacting on the output (transfection efficiency) and the important interactions between them, followed by a optimization DoE identifying inside the chosen interval of parameters the better combination which permits to maximize the output (Mancinelli et al. in preparation). We also defined a general guideline for the application of DoE to set up and optimization of scientific protocols. The management of

multivariable experiments using a DoE methodology allowed in most cases one-step optimization of the set of experimental conditions tested and showed three important advantages with respect to the OFAT (one factor at time) method used by most researchers, where only a variable at a time is varied, keeping all other variables fixed. First, DoE increases in the robustness and the reliability of the data and of the analysis, because the presence of a matrix of conditions including replicates and randomization of the experiments leads to high-Quality and high-reliability results. Second, DoE lowers the time used for the optimization of the experiment and finally yields information on the whole chemical–physical landscape of the experiment.

Overall the four WPs contribute to the creation of the "concept laboratory," which is referred to as a qPMO model (Fig. 2). The tight interaction between the working groups is a key element of the project. To report a few examples:

The indications for writing a guideline (WP1) have been also used to write prescriptive documents for FMEA (WP2), QMS (WP3) and DoE (WP4);

FMEA application to a laboratory protocol (WP2) led to several references regarding management of materials, instrumentation, and staff, which can be seen as an analytical scheme of similar requirements of the ISO 9001 standard, so to be directly used in the QMS design (WP3).

Both groups working on WP1 and WP3 synergized to identify requirements for protocols to be considered validated, respectively, for the QMS (WP3) and for the publication on the Web site (WP1).

Different laboratories in various CNR institutes and external organizations have expressed interest in one or more models developed by the qPMO team. The final qPMO models will be made available through a dedicated Web site (see WP1) to all institutes in the public research institution and to the scientific community in general. One of the initial targets of the project was to disseminate Quality culture in the scientific community. We started from giving invited lectures in university courses, because, agreeing with Davies [6], we thought that the younger generation of scientists need to know Quality principles and tools to face challenges of cooperation, reliability, and integrity of the scientific research and results. We participate to a TT support project to share our experience, we presented talks and posters to national and international events, and we are preparing several papers for presentation of detailed WP results (Table 4).

Discussion and conclusions

Overall, the entire project is designing a general TQM model in biomedical research, in which simplified and customized models of Quality methodologies are developed and experimented with the final goal of being easily transferred to other laboratories.

Our activity can be divided into two main streams: (1) setting up the project and coordinating it during its development and (2) management and activity in the four WPs. Regarding the project coordination, we can highlight some undisputable advantages: the use of Quality and PM tools allowed the entire project to be set up in 1 month and to be designed around a well-identified target. Project outline and documentation, so defined, was easily reviewed by upper management to rapidly take a formal decision. Then, the traced roadmap helped each working group foresee a clear pathway, specific tasks, deliverables, and the related

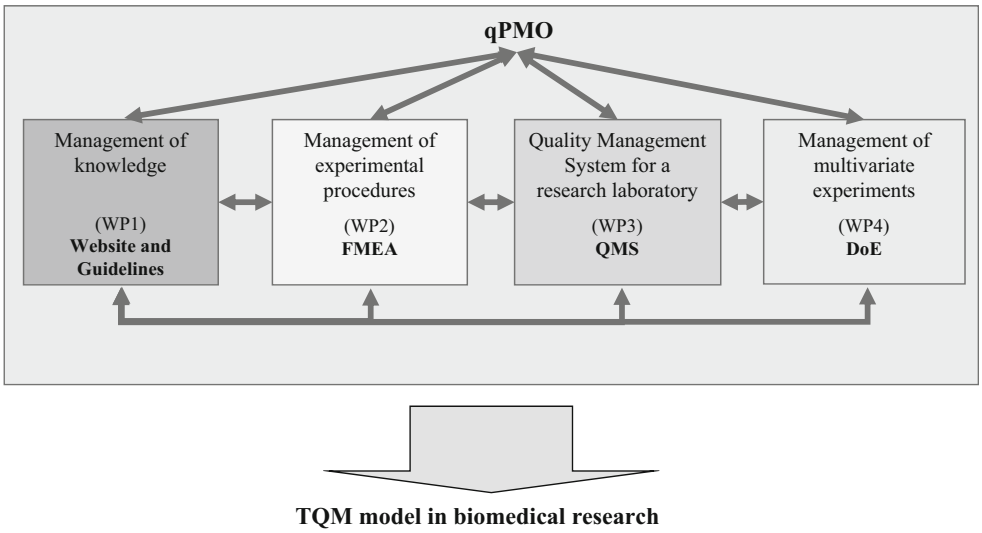

Fig. 2 The qPMO model. The qPMO network develops four WPs, each one focusing on a specific aspect of the integration of Quality and biomedical research. WPs cover most Quality aspects of a biomedical research laboratory, and the products achieved can be transferred to other research laboratories. High interconnection and interoperability among WPs is a key element of the project and contributes to the creation of a "concept laboratory," based on TQM

schedule. The use of free informatics tools for teleconference and file sharing and a neat organization of meetings and labor actually helped in overcoming the physical distance among the four sites involved. This modality has been very useful for creating a real team that is more than the sum of the single individualities and to cause each one to feel truly and deeply involved in the project. Moreover, each of the four teams took advantage of the experience and the results of the others, preserving and even fertilizing a common view of the entire TQM model. This way of proceeding allowed the team to maintain and, in some cases, even anticipate the activities timeline.

Regarding the second main stream, i.e., experiencing different Quality methodologies, the application of the four ones chosen is marking the way for their use in research. Basic principles have been carefully studied and understood before being interpreted and translated into a language familiar to scientific researchers. This study has allowed us to exploit the methodology's potential of organizing, structuring, and finding efficiency in the research laboratory. Using well-known and already experimented standards, models, tools, and schemes, we saved economic, time, and intellectual resources that can be reserved for pure research. After overcoming this obstacle, the value and utility of this approach can be easily appreciated, even by people predisposed to thinking that it can be proficiently applied only in corporate and industrial fields. This goal has been made possible thanks to the strong cooperation between researchers and a Quality expert, working together in a research project. As first results show, an early capability of integration among the four working groups demonstrates the high interconnection and interoperability of the four chosen subjects and the capacity to cover most Quality aspects of a research laboratory. This synergy among the four working groups is not surprising when considering that the Quality approach, chosen from the first setting of the project, is holistic, i.e., comprising the entire (research) system and looking out for mutual relationship between different aspects. In this sight, the project has taken into account in tight relation all the most important categories of a laboratory management: resources and materials, instrumentation and tools, documentation and methods, and human resources. These four categories can easily be referred to the 4-M of Kaoru Ishikawa [31]. More specific results from each WP will be available in separate, dedicated papers. Furthermore, the first experiences of dissemination have received great interest, demonstrating that Quality approach meets latent or even unexpressed needs of scientific researchers and laid the groundwork for future collaborations.

In conclusion, our experience clearly shows that a proper and accurate transfer of Quality culture from areas of high development (such as automotive, manufacturing, services) to intellectual and scientific production can facilitate and strengthen research, providing new tools to make it faster and more efficient without imposing constraints on the research work. Among these, we wish to emphasize the standardization of procedures, awareness, and control of management issues, identification of key levers for improving management and technical procedures, effectiveness of how experiments are designed, and improved use of resources with similar or better results.

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