RESEARCH ARTICLE

Measures to increase value of preclinical research - an inexpensive and easy-to-implement approach to a QMS for an academic research lab [version 1; peer review: 1 approved, 2 approved with reservations]

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Abstract

Background: Increasing concerns emerge regarding the limited success in reproducing research results. This is a major problem for science, society and economy. Driven by industry or scientific networks, several attempts to combat this crisis are initiated. However, only few measures address the applicability and feasibility of implementation of actions into an academic research environment with limited resources.

Methods: Here we propose a strategy catalogue aiming for a quality management system suitable for many research labs. Our proposal is guided by its inexpensiveness and possibility of rapid installation. Moreover, we restrict presentations of our actions on those for what we received a positive feedback by the users regarding its applicability. For this we used eLabFTW, an electronic lab book, as hub for all other components of our quality management system (QMS). Storage of lab journals and project management will be done there as well. Standard operation procedures have been introduced. Those will be stored in eLabFTW too. Furthermore, we implemented a bio bank for safer long term storage of bio samples and cryo-cultures of cell lines. Next we set up a lab meeting as feedback mechanism for the QMS. In a final step we implemented an automated pipeline to be used for example for drug screens.

Results: With this effort we want to reduce individual differences in work techniques, to further improve the quality of our results. Although, just recently established, we can already observe positive outcomes in quality of experimental results, improvements in sample and data storage, stakeholder engagement and even promotion of

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new scientific discoveries.

Conclusions: We believe that our experiences can help to establish a road map to increase value and output of preclinical research in academic labs with limited budget and personnel.

Any reports and responses or comments on the article can be found at the end of the article.

Keywords

QMS, Quality Management, SOP, Automation, Lab book, electronic lab book, Cell banking, database

This article is included in the **Research on Research, Policy & Culture** gateway.

This article is included in the **Preclinical Reproducibility and Robustness** gateway.

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Background and Goal

Due to its immense documentation load, the establishment of a quality management system (QMS) certified with ISO 9001 standard¹ in biomedical research labs is challenging. This is particularly true for academic labs where usually staff is changing rapidly and the progress for individual careers is often the dominator for operator's decision making. However, it is shown, that a lack of quality management and transparency are two reasons for the ongoing reproducibility crisis²⁻⁴. We implemented a slim line QMS that should lead to an increase of confidence in our scientific lab outcomes by optimizing internal processes for elevated transparency and reproducibility.

Methods

We introduced several technological tools to optimize processes, which combined, will form the QMS (Figure 1) of our lab.

Experience with freeware solution for electronic lab documentation

Transparent data management is a cornerstone for research integrity. As the basis of our work we set up an electronic documentation system to document all lab activities of all lab members. We chose **eLabFTW**⁵ in the current version 3.4.8, an open source solution to track experiments with a powerful and flexible database. In the used version it provides all features necessary to provide the grounds of conformity with the principles of good research practices as proposed by the German research Foundation (DFG). This includes, not exclusively, the installation of a non-delete policy for created entries. The relevant software code can be found on **GitHub platform**⁶. eLabFTW is made up from two parts. One is called 'experiments' and is the lab journal part of the software, the other is called 'database' and lets the user create text entries in self defined data types. The journal part of eLabFTW will be used by each researcher to document their research, and for project management. Created entries cannot be deleted and changes to these entries will automatically be logged. The database part will be the backbone of our QMS. We decided to share reading and search authorization for all entries amongst all registered personal accounts in our working group to increase transparency and to stimulate the critical interaction. Data storage, backup and archiving of eLabFTW data files can be easily implemented in regular executed local data management

policy. All finished experiments will be time stamped (digital signature), and will be blocked for editing from any user by the server itself. This will secure the written text and attached primary data (pictures, raw data from lab machines etc.) from later manipulations, as they are now unchangeable and undeletable.

Establishment of coherent protocol and lab tool documentation system

SOPs (standard operating procedures) are a main principle of most QMS. To our experience, even within one working unit, for one given experiment various self-developed, self-adapted protocols are in use at the same time. By implementing a binding SOP policy for all users, defining the accountability of the data to qualify for the use in external presentation such as in a scientific publication, we aim to enhance process coherence in order to increase intra-lab reproducibility success. As first step, a template for SOPs was created and its categorization and storage were implemented in the electronic lab documentation system followed by the establishment of a writing procedure for how to complete the template was developed. Any person can then write a draft of a new SOPs, but creation of the SOPs and QMS implementation are managed by selected authorized identity (in our hands a governmental- certified technical assistant to ensure conformation with regulation processes), to avoid duplicates or development of multiple parallel versions of one subjects. Approved, newly established SOPs then are categorized by name, a standardized alphanumerical identifier, and version number. Then all new SOPs get uploaded to the database of the electronic lab book. If applicable, SOPs are electronically linked with each other if their execution/specification depends on each other. In the last year 91 unique procedures and recipes have been standardized. 31 of them have been revised at least once, to either correct them, or adapt them to new findings or necessities. Every new employee will be sent a package of our most used methods and receipts as well as SOPs related to his proposed project, prior to their first day of work, so they have the chance to already get familiar with the methods in theory.

Moreover, virtual one-to-one project development meetings have been integrated in our e-documentation system by weekly, time-stamped progress reports of each lab member. Those are

Blocks of the introduced QMS

Figure 1. Blocks that form the QMS and their function inside of it. SOP: Standard operation procedure, QMS: Quality management system.

composed of structure items common for academic research projects featuring presentation of new results, problems experienced, suggestions of problem management and update on current literature. Leadership provides feedback on each parameter within a timely manner to secure up-to-date project management. Importantly, apart our open visibility of progress reports and feedback to all team members ensuring full transparency for all stakeholders, we have set up visibility-restricted sub projects. Those more restricted groups are intended to exchange work-in-progress documents between the individual user and the leadership, that have certain impact on the “outside-presentation” of the lab, such as presentations or manuscript drafts. We found this virtual project development-meeting platform enables efficient time management of the leadership and has been proven suitable to be conform with guidelines to minimize social contact, that have been stated by governments worldwide to fight the Covid-19 pandemic.

Bio Bank

According to FAIR principles, when publishing research results, used material and created bio samples (tissue, cell pellets, DNA, RNA, plasmids, etc.) need to be held in stock to allow for future replications of the experiments performed or to share lab tools with the community. By establishing our lab bio bank, we aimed to provide a centralized storage facility for bio samples both for experimental and clinical research projects. The bio bank consists of a -80°C deep freezer and a liquid nitrogen tank. Both contain labelled boxes with designated positions for bio samples. Stored samples are characterized by a unique identifier. Long term preservation is supported by using freezing approved label technology and designation with printing instead of handwriting. The entire needed lab infrastructure to install our bio bank is a standard set up in each lab and does not require extra investments. Due to the anticipated large and constantly increasing number of bio samples included in the storage, we decided not to integrate the storage data into the database of eLabFTW but used a separate SQL database as the digital complement of the physical bio bank. Nevertheless, samples and experiments can be cross referenced in both platforms using the unique identifiers of the samples in the experiment section of eLabFTW, thereby securing complete and intertwined electronic documentation in our QMS. All lab members can search for samples in the digital database. However only three people have write access and can add and delete entries. Only those three people can access the physical bio bank, to add and remove samples. With this setup we aim to minimize sample loss and mix up, as well as ensure proper labelling of the samples.

Quality assessment of cell models

As for many research labs, most of our projects fundament on *in vitro* experiments. For most of the cancer research projects, we perform our work by using the standard disease model type: the cancer cell line. Meanwhile paying particular attention to create the most-accurate-as-possible recapitulation of the pathophysiology of the disease by using 3D cultures, we furthermore surveil our technical quality of the applied biological test matrixes. This includes a) the confirmation of authentication through short tandem repeat analysis (STR) of cultured models every 6 months, b) the use of as-young-as-possible cell models (monitoring cell

passage number); c) surveillance and - if necessary - clearance of mycoplasma contamination (PCR-based mycoplasma detection) and d) adherence to culture procedures as defined in SOPs. The STR analysis is outsourced to an in-house service. There Quantitation was performed using the Quantus™ Fluorometer (Promega) and the QuantiFluor® dsDNA Sample Kit (Promega) following manufacturer's instructions. A multiplex PCR of 21 STR loci (PowerPlex® 21 System Kit, Promega) was performed in a total reaction volume of 12.5 µl with 0.5 ng template DNA. Thermal cycling conditions were followed as described by the manufacturer. Capillary electrophoretic separation was performed on the ABI Prism® Genetic Analyzer 3130 equipped with a 36 cm Capillary Array/POP-4 (Applied Biosystems, Darmstadt, Germany) following manufacturer's instructions. Data acquisition and analysis was performed using the ABI Prism 3130 Collection software (Applied Biosystems) and GeneMapperID® v.3.2 software (Applied Biosystems, Darmstadt, Germany). For STR and mycoplasma test we invest less than 20 USD in total. We believe that the adherence to chronic execution of those simple methods is an economical, feasible and robust measure to sustainably reduce the creation of low-value cancer cell line data.

Feedback and update communication platform

A monthly gathering of all participating and interested stakeholders secures the communication of updates and feedback mechanism of the QMS. The date and location for the meeting is circulated well in advance to ensure high frequency of participation of invitees. The feedback platform is open for all stakeholders independently of profession, profession hierarchy and amount of involvement in hands-on lab work. Each time a protocol of the meeting is generated in form of meeting minutes-like listing including specification of attendance. Although sometimes time consuming due to extent exchange of opposing opinions on topics, we hypothesize the impact of this outreach effort to involve all participants in the policy development extends further then the QMS. We believe such a platform increases the teamwork atmosphere and group belonging hereby increasing work atmosphere. We also think this is a valuable tool to fight occurrence of inequality and discrimination in our working group. The generated meeting minutes will be used to permanently alter the QMS to guarantee the highest possible quality. For that they will also be uploaded to the electronic lab book.

Automation for lab work execution

Automation is a standard in industry labs and clinical diagnostics. We implemented a robotic liquid handling instrument (Beckman Coulter Biomek FXP) connected with automated plate reading for performing pharmacology testing on a cancer cell (Vargas-Toscano *et al.*)⁷. We chose this method as our implementation trial since this is one of our most frequently used lab procedures. Our validation experiments based on manual repetition of the experiment proves that the functionality of our automation assay. Besides the accurate execution, the possibility of direct data reporting into the electronic lab documentation system and the possibility of electronic surveillance of executed pipetting for error reduction makes the inclusion of automation a valuable measure to increase reproducibly and transparency of our work. We hypothesize that robotic assays increase the value and

innovation of our work. As such, the application of the screening identified a repurpose of a FDA approved neurotransmitter drug to inhibit growth of brain tumor cells. Given the recent high-profile publications revealing the importance of neurotransmitter signaling for the biology of brain cancer⁸, our QMS coincidentally enabled us to contribute to current line of cancer research that we had not purposely addressed without it. Given the existence of low-cost pipetting automation, more economically feasible options instead of the Biomek solution are available. Here, single-dose pumps in particular come to mind. These are of course not as comfortable as robotic systems but fulfill the need of standardized pipetting. Used pumps can be bought for less than 1000 USD.

Results and discussion

In our experience the approach of using an all-digital lab book with shared reading rights and automated storage of raw data, does not only guarantee data management according to FAIR⁹ or increase the transparency according to the Hong Kong principles¹⁰, but also helps to increase motivation of the team in general and thereby improving scientific development of the users. From all 17 lab members (at the time of publishing this), only 4 are not using the electronic lab book for recording their experiments. Those are members who are at the end of their projects and were therefore encouraged to keep their old method of recording, for consistency. Yet also those people use the database part of the electronic lab book, as well as the SOPs.

The use of SOPs, which were uploaded to the electronic lab book, lead to the standardization of particular processes in the lab. Before researchers performed several experiments with protocols from other or former labs. This leads to lack of reproducibility inside of the lab. Now a higher consistency of experimental results is given, as all researchers perform each experiment in only a single way, minimizing individual differences.

Compared to shared freezers used in the lab, central administration by only a few people highly reduces the loss of samples and mix-ups. Furthermore, the bio bank and its digital complement, with the possibility of linking it to the electronic lab book, make it very easy to find all samples used in all experiments. Since the Bio Bank is relatively freshly implemented, we cannot give results for the improvement of storage over longer periods of time yet. Until now the model of a digital copy of the bio bank, combined with limited access to the physical bank is holding up. All samples that got stored in the bio bank are still unmistakably findable. We argue that due to the QMS we fulfill the requirements for storage of data and samples, according to good scientific practice guidelines, as proposed by DFG¹¹.

STR and regular mycoplasma testing lead to rejection of low quality cell cultures, ensuring higher significance of results derived from experiments with those cells (Table 1¹²). Especially for metabolics or pharmacoproteomics experiments, a contamination with mycoplasma can lead to wrongful results. In our experience, even the most skillful and experienced cell culture scientists cannot avoid the introduction of unrecognized contamination. With the introduced QMS, in our lab we identified cancer cell models have established subclones with different genetic background due to inter cell line contamination. Those subclones were designed as a different cell line instead of a subclone. The introduction of the QMS leads to significant project adjustments and in some case to termination of experiments. We also put on hold a scheduled submission of a manuscript draft for publication due to cell line miss-identification.

The implemented communication system already proved its worth by leading to updated and refined versions of some SOPs. Given the deliverables of the meetings have significant influence on future lab procedures, we have experienced a significant increase in involvement and commitment of responsible lab members in this effort. A regular non-science oriented lab

Table 1. Short tandem repeat (STR) profile of contaminated brain cancer cell line mix assumed to be BTSC349 (mix), which got contaminated with BTSC268 cells. For comparison and a reference for the scientific community, STR profiles of parental lines are provided as well. STRs with mixes of both cell lines are marked. For original data as supplied by in-house service, see underlying data¹².

STR	BTSC349	BTSC268	Mix	STR	BTSC349	BTSC268	Mix
D3S1358	14, 16	14, 15	14, 15	vWA	17	14, 18	14, 18 (17)
SD1S1656	15	15.3	15.3	D21S11	29	29, 30	29, 30
D6S1043	7, 19	11, 15	11, 15 (7,19)	D7S820	10,11	9, 10	9, 10 (11)
S13S317	12	8, 11, 12	8, 11, 12	D5S818	12	11	11 (12)
PENTA E	17, 18	12	12 (17, 18)	TPOX	8	8, 12	8, 12
D16S539	11, 12	9, 13	9, 13 (11, 12)	D8S1179	13, 14	11, 13	11, 13 (14)
DS18S51	12, 14	12, 13	12, 13	D12S391	21	21, 24	21, 24
D2S1338	17, 18	23, 24	23, 24 (17)	D19S433	12, 15	14	14 (12, 15)
CSF1PO	11, 12	12	12 (11)	FGA	20, 25	21, 22	21, 22 (20)
PENTA D	11, 13	10, 14	10, 14 (11, 13)	AMEL	xy	x	x
TH01	9, 9.3	6, 8	6, 8 (9.3)				

meeting creates an opportunity for easier expression of general matters thereby facilitating interpersonal communication amongst stakeholders. The virtual one-to-one project development report-feedback loops provides an opportunity to timely manage diverse research branches with moderate resources needed at each time.

As the technologically most advanced component of our QMS, we implemented an automated pipetting system in our lab routines. We believe that the robustness and transparency of the data generation, as well as the simplicity of its use in supporting repetitive work procedures are the reasons for high attractiveness to many lab users. Our initial results applying this industry-like assay on drug resistance testing on cell models are very encouraging. However, conclusive evaluations on whether data quality is improved requires further projects comparing manual pipetting-derived data with corresponding data retrieved from the robot tool. Such a project is currently underway.

Summary

We present a rapid-to-implement, feedback approved method guide for initial steps to improve value of preclinical lab deliverables in a budget-restricted academic research environment. Given the increasing concerns on the value of preclinical

research, we believe our activities are in line with current goals of funding authorities, academic self-governance and help to improve trust and recognition of science in society. We hypothesize that side effects of a QMS can also reduce inequality/discrimination amongst stakeholders.

Data availability

Underlying data

Zenodo: STR Analysis results BTSC 349, BTSC268 and mix of both. <http://doi.org/10.5281/zenodo.3901446>¹²

This project contains the following underlying data:

- 15-1-Wiss2020-01-16.fsa (BTSC 349 short tandem repeat analysis)
- 15-3-Wiss2020-01-16.fsa (BTSC268 short tandem repeat analysis)
- 15-4-Wiss2020-01-16.fsa (Mixed cell line short tandem repeat analysis)

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](#) (CC-BY 4.0).

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Summary:

The article describes an experience with a quality management system (QMS) within an academic basic biomedical research laboratory. The subject is relevant to the life sciences in general, as concerns with research quality are on the rise, and describing the development and implementation of a QMS within a lab is a worthy contribution; however, we believe the article would benefit from major changes in its structure to make its objectives, methods and results clearer.

Main concerns:

- Who is the intended audience for the article? If this is meant to be a template or example to be followed by laboratory researchers in general, we believe that more information about the concept of QMS and the process of developing it are probably warranted. On the other hand, very specific information about cell culture automation and STR profiling, such as that presented on Table 1, is only of interest to a very specific audience. If the article aims to be a description of QMS in cell culture labs, that would be a valid goal as well, but in this case this topic should be covered in more detail, and the text in other sections should be changed in order to reflect this aim.
- What are the objectives of the article? If the goal is to describe the effects of the QMS system on some aspects of quality, more data is needed to adequately assess its impact. If the goal of the article is to present the development of the QMS, that is fine as well, but the methods and results sections should then be restructured to reflect that goal – in this case, the methods should explain the decision process leading to QMS implementation, while the

results would present the system as it was implemented. In either case, a more detailed description of each block of the QMS is warranted, either as methods or as results, depending on the objective of the article.

- What is meant by quality and by reproducibility? Both terms can be read with many different interpretations, so including definitions would help to avoid misinterpretations of the goals of the article. Note that the QMS seems to address multiple facets of these concepts, so clarification might be necessary within each block of the QMS. In particular, most lab researchers are not familiar with the literature on quality management, so a more in-depth review of these concepts is needed in the introduction.

Title and abstract:

- Given the direct and practical content of the article, we suggest the title would be improved by removing the first part (i.e. "Measures to increase value of preclinical research") and leaving only the second one.
- While the abbreviation QMS is defined in the abstract, we believe it should not be used in the title, in which it cannot be defined. Instead, we suggest using the unabbreviated form.
- The whole abstract could be shortened and made more direct, particularly in the Introduction and Methods section.
- If the system has already been implemented (as seems to be the case), why are some sentences in the future in the methods section of the abstract (e.g "These will be stored...")?
- The abstract "Methods" subsection contains information not available elsewhere in the full text article (i.e. "Moreover, we restrict presentations of our actions on those for what we received a positive feedback by the users regarding its applicability"). Moreover, such feedback data is never presented in the article.
- The "Results" subsection does not seem to contain any result, irrespective of what objective is intended (as described above).

Introduction:

- If the article is targeted at a life sciences audience, however general or specific, we would not expect most of them to be familiarized with quality assessment vocabulary or literature. With that in mind, we suggest including an operational definition of QMS. Additionally, there has been some debate about its implementation in the basic academic research lab; thus, describing this context and reviewing the literature on the subject would also be beneficial to the readers.
- On a more specific development of the previous point, we suggest including a brief description of your motivations for engaging in this endeavor. Was this a requirement by a superior instance, such as the institution or a funding agency? Was this a bottom-up initiative from the researchers? This could both (a) help to reach readers that could identify with the same issues but were not aware of them and (b) help to contextualize the adopted strategies in a broader landscape of previous experiences.
- Independently of the goal or targeted audience, for a case-study such as this one, it is vital that the introduction includes a description of the lab setting for which this QMS was

developed. This includes the number of people and their positions in the lab (such as students, technicians, postdocs, etc), the group's research interests or focus areas and the institutional environment (such as governmental vs. private funding, discovery-based vs. applied, etc). While some of these features can be inferred from other sections of the text, they should be presented upfront in the Introduction.

- The three references cited on “that a lack of quality management and transparency are two reasons for the ongoing reproducibility crisis” do not seem to fully support the sentence, as they do not directly mention quality management. That sentence should either be corrected or clarified to better represent the cited articles.

Methods:

- The issues raised as general comments should have a strong impact on the structure of the methods section. If the goal is to describe the creation of the QMS, the decision process to create each component of the system should be included here. If the goal was to assess the QMS itself, a more objective description of the QMS itself is warranted, but new sections on data collection would be required. In each subsection of the Methods, we found one or a combination of these strategies, which causes the section to lack coherence and makes the reader unsure about what the objectives actually were.
- From our understanding, Figure 1 is intended to be a summary of the QMS system. However, it does not completely correspond to what is described in the text. On one hand, the “lab meeting deciding core rules of QMS” shown in the first block of the figure is not described in the Methods section; on the other the “Quality of Cell Cultures” subsection is not reflected in the figure.
- In the description of standard operating procedures (SOPs), it is not clear for what processes they are being developed. Listing at least the most used SOPs would greatly improve our understanding of the strategy; one cannot understand for example, how specific a process is described in each of the 91 SOPs. Ideally, the authors should share some examples in the article, and perhaps include a template as a supplementary material.
- The description of one-to-one meetings probably deserves its own subheading and should not be under the SOP subsection.
- As mentioned previously, the quality of cell culture assessments subsection seems out of context and should only be included if the authors mean to reach a very specific audience (e.g. labs mainly working with cell cultures). If they mean to use cell culture as an example of the QMS implementation, we would suggest describing it in the Results section and relating each step of the process to the QMS blocks that are described in the methods.
- In the Feedback and Update section, there are three consecutive sentences with “hypothesize”, “believe” and “think” as verbs. That said, do the authors have data on the subjects touched upon? If so, they should present it – otherwise, they might be excessively speculating on the impact of their intervention.
- Also in this section, the link between the meetings and the claims of reduced inequality and discrimination is not clear. Please clarify.

- When describing automation, a result is mentioned: “i.e. the application of the screening identified a repurpose of a FDA approved neurotransmitter drug to inhibit growth of brain tumor cells...”. This does not belong in the Methods section and should be moved to the Results. Moreover, the causal link between automation and the mentioned results is not obvious and could be better explained by the authors.

Results and discussion:

- As mentioned above, the structural questions about the objective of the paper addressed in the General section of this report should have an important impact on the “Results and discussion” section of the article. In general, we found it to be better structured than the “Methods” section. In particular, we appreciated the description of some quantitative results and recognition of some limitations. That said, the section is still scarce on providing actual measures of impact of the QMS implementation – and, if this is meant to be the goal of the article, should include more data on the subject.
- In the first paragraph, the authors mention an increase in team motivation and improvement of scientific development of lab members, while the second paragraph states that “now a higher consistency of experimental results is given”. Do the authors have any data to base these statements on? If so, it should be shown (and details of this assessment should be included in the methods). If not, these conclusions might not be warranted.
- We suggest including more information when describing the implementation of the electronic laboratory notebook. For example, this particular product requires server installation, which might not be accessible to many biomedical researchers. Did you have assistance from an IT department of your institution? Moreover, how was the process for the 13 people who were able to completely migrate to this system? Did they have to stop their experimental schedules to implement all changes at once or was it gradual?
- The description of cell culture contaminations (Table 1) is very specific and not understandable for readers with no experience with STR profiling. If this is to be presented, it definitely needs a general description of how the results should be read and interpreted. That said, perhaps the best option would be to leave this information out of the main text of the article and present it as supplementary material.
- To support the claims of this being a QMS for resource-restricted research groups, more information regarding the implementation cost of all blocks of the system is needed. Exemplifying the financial costs of the cell culture assessment assays is a welcome contribution; this, however, could be expanded in other parts of the QMS, not only in terms of financial costs but also of human resources and time requirement.
- In various points, but especially when discussing meetings (i.e. “a non-scientific oriented lab meeting creates an opportunity for easier expression of general matters...”), it would be useful to know whether the authors’ impression is indeed shared by all of the lab personnel. Do they have any kind of questionnaire/feedback data to know whether this opinion extends beyond the authors themselves?

Summary:

- We suggest toning down the conclusions presented here. Given the methods and results presented as they are, there is little data to support the claims of fast, easy or low-cost implementation of the QMS. To substantiate this claim, more details relating to cost, speed

and implementation challenges should be provided in the previous section.

- The same recommendation holds for increased value of preclinical lab deliverables – unless the authors present more data on the impact of QMS implementation, this conclusion might not be warranted.
- Once more, it is not clear what the hypothesis of a reduction of inequalities (also mentioned in the methods) and discrimination is based on, as this does not seem to follow logically from QMS implementation.

References:

- In general, we do not believe the study provides an adequate reference list. It is insufficient to provide context to the methods used or to the discussion presented.
- Reference 4 has the wrong title and links to an unofficial source. It should be corrected to the publisher's version.
- There is a typo in Reference 10: it should read OSF Preprints.
- Reference 12 is listed with two “publishers”: F1000 and Zenodo. From the link, we infer that Zenodo is the correct one.

Is the work clearly and accurately presented and does it cite the current literature?

No

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Partly

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

No

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Metascience and behavioral neuroscience.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 29 Jul 2020

Michael Hewera

Dear Clarissa Carneiro and Olavo B Amaral,

We thank you a lot for your very detailed review of our publication.
Most of your suggestions have been introduced in the revised version of the article.

Best regards,
Michael Hewera

Competing Interests: No competing interests were disclosed.

Reviewer Report 27 July 2020

<https://doi.org/10.5256/f1000research.27020.r65763>

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Judith J. de Haan

Utrecht University, Utrecht, The Netherlands

Frank Miedema

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It is an interesting manuscript that shows that research groups can improve the quality of their experimental work without spending lots of money. It is great that researchers feel the need to improve their own practice, even if that does not immediately lead to more publications or more funding, but because it will improve the reproducibility of their work and contribute to the quality of the whole research field they are working in.

Some suggestions for improvement:

- The level of details in this paper vary a lot, on the one hand it is very detailed (the amount of DNA and volume for the reaction to check cell line stability), but the level of information on the bio bank is very limited.
- It seems that the authors try to write a 'case report' about their own lab and at the same time try to give recommendations for other labs. It might be more valuable to make a clear distinction between those two goals. Maybe write it as a case report and then provide recommendations in the discussion part. Maybe distinguish the recommendations too, material wise recommendations (check cell lines, buy a pipet pump of ~1000 USD), (data) storages recommendations and attitude recommendations (have regular lab meetings about quality, make sure all lab members use the same digital notebook and SOPs).

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Human cellular immunology, virology.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 29 Jul 2020

Michael Hewera

Dear Judith de Haan and Frank Miedema,

Thank you for reviewing our publication.

Following your suggestion, we adapted the level of detail, by adding some information to the bio bank part of the text.

Best regards,

Michael Hewera

Competing Interests: No competing interests were disclosed.

Reviewer Report 17 July 2020

<https://doi.org/10.5256/f1000research.27020.r65819>

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Jan Vollert

Pain Research, Department of Surgery and Cancer, Imperial College London, London, UK

The authors present the quality management system they have implemented in their lab and lay out specifics and improvements to their previous processes. The reader would benefit from more elaboration of the motivation that initiated the change, a better structure in before/after comparisons, and a primer in quantifying compliance and satisfaction of the users.

Specific points:

- *"However, it is shown, that a lack of quality management and transparency are two reasons for the ongoing reproducibility crisis²⁻⁴."*

While I fully agree with this statement, I think the reader would benefit from some elaboration on this topic: why and how do QS and in particularly organised documentation, increase reproducibility?

- eLabFTW: it would be interesting to lead the reader through your decision process, as I assume other labs will consider similar options as you did. Why did you choose this one over the others?
- The central element of this manuscript – the reporting on some bits on the motivation of the researchers to finally approach this step would be interesting, which could also allow for a better before/after comparison. Which processes have improved by the introduction of the new system, where do the users experience early benefit, where are the users rather reluctant?

I appreciate that some information on the before is given in the results section, but think that a separate, earlier header on "before" would improve the structure.

- Similarly, the reporting of enthusiasm within the group is relatively vague – maybe you could even add a small anonymous survey within the group which bits are most and least liked. This can quantify the impact of the system at least a bit.
- Minor point: I am always at risk of doing this myself, but I would recommend refraining from using terms like "significant influence" as the word "significance" is so strongly tied to p-values in research papers.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Not applicable

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Pain Research, Placebo, Improvement of Clinical and Preclinical Trial Design

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 29 Jul 2020

Michael Hewera

Dear Jan Vollert,

Thank you a lot for your very quick response!

Following your advise, we added a short part about the process of choosing eLabFTW as our electronic lab book and changed the several "significants".

We really liked your idea of small surveys, but think it would have been only feasible, if we also did the same one before the installation of the QMS.

Inside of the team we do have our feedback meetings, to get these responses.

Unfortunately we cannot publish our meeting minutes as data though.

Best regards,

Michael Hewera

Competing Interests: No competing interests were disclosed.

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