FeatureCloud

Privacy preserving federated machine learning and blockchaining for reduced cyber risks in a world of distributed healthcare

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Deliverable D3.2
"Manuscript on Quality management process"

Work package WP3
"Guidelines, standardization, and certification"

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Acronyms and definitions

AI	artificial intelligence
concentris	concentris research management GmbH (Germany)
CT	computer tomography
DM	Document Management
GND	Gnome Design SRL (Romania)
IDIR	Institute for Diagnostic Image-processing in Radiology
ISO	International Organization for Standardization
MA	Management
MDx	Molecular Diagnostics
ML	machine learning
MUG	Medizinische Universität Graz (Austria)
patients	In this deliverable, we use the term "patients" for all research subjects. In FeatureCloud, we will focus on patients, as this is already the most vulnerable case scenario and this is where most primary data is available to us. Admittedly, some research subjects participate in clinical trials but not as patients but as healthy individuals, usually on a voluntary basis and are therefore not dependent on the physicians who care for them. Thus to increase readability, we simply refer to them as "patients".
PE	Project Execution
PP	Project Planning
QM	Quality Management
QMS	Quality Management System
RI	Research Institute AG & Co. KG (Austria)
SBA	SBA Research gemeinnützige GmbH (Austria)
SDU	Syddansk Universitet (Denmark)
SOP	Standard Operating Procedure
TUM	Technische Universität München (Germany)
UM	Universiteit Maastricht (The Netherlands)
UMR	Philipps Universität Marburg (Germany)

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1 Objectives of the deliverables based on the Description of Action

The objective of WP3 is amongst others, to develop a guideline for a standardized software development process within the academic context and to compile a documentation guideline for MDx-ready software (**Objective 1**), which makes a conversion from academic projects into MDx software feasible. The goal of these guidelines and recommendations is to ensure that the error rate in the diagnostic process is as low as possible. In particular, as described in **Task 1**, we developed a concise quality management process according to ISO 13485 standard. A concrete implementation of such a process for the FeatureCloud project was previously demonstrated by the quality report submitted D3.1. Moreover, these guidelines will promote further the realization of regulatory requirements, training, and enable a control of these requirements to ensure product safety. Finally, the guidelines will be made publicly available to ensure the same standards for software that will be developed on top of FeatureCloud by third parties.

2 Executive Summary / Abstract

2.1 Methodology

Requirements for quality management are defined in ISO 9001 (Management and Devices, 2015) and in ISO 13485 (Management and Devices, 2016). However, while ISO 9001 is generic and can be used in very different fields, ISO 13485 is specific for quality management in medical device development. The main differences are that ISO 9001 requires the organization to demonstrate continual improvement, whereas ISO 13485 requires only that the certified organization demonstrate the quality system is effectively implemented and maintained. Additionally, the ISO 9001 includes customer satisfaction, which is not relevant for ISO 13485. There are also some other differences in ISO 13485, e.g., that the promotion and awareness of regulatory requirements is a management responsibility, that risk assessment and management need to be carried out (according to ISO 14971), as well as some others. Unfortunately, ISO 13485 is most likely outside of what is feasible for research groups in universities and other research organizations. So far, there is not much guidance available on how to work between the two extremes of not having any quality management system at all and having a full-blown quality management that complies to relevant standards. Therefore, we have been studying the corresponding standards and adjusted those requirements towards a quality management system for the development of software in academia that will potentially be transferred to medical devices. Our aim has been to embrace most of the benefits and facilitate the technology transfer as much as possible whilst keeping the overhead in a range that is well manageable – all in the context of universities or similar organizations that engage in research on software in the medical setting.

2.2 Main results

We proposed establishing an academic quality management system for machine learning systems in medical research, which has the potential to greatly facilitate and speed up such technology transfer for medical software, such as implemented in the FeatureCloud project, in a controlled and predictable way. Being aware that a full quality management system is not feasible for most research organizations, we proposed a subset of crucial elements of a quality management system which we are convinced will provide a valuable benefit while keeping the effort in a range that can easily be handled in most academic settings. Our proposal is centered on procedures for document management, project planning and execution, as well as some surrounding administrative procedures. Depending on the specific needs of a project, the set of elements of a quality management system work best may differ. The fact, however, that a quality management system is set up and that the elements are deliberately chosen is probably a key factor for facilitating technology transfer.

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2.3 Progress beyond the state-of-the-art

State of the art:

- Modern machine learning (ML) approaches have shown huge potential when applied for diagnosis, prognosis, and monitoring of diseases and therefore opened up a new era in health care and precision medicine
- The design and development of medical devices – including software as a medical device – have to comply with quality management standards that ensure the safety and quality of the medical devices in clinical practice. Industrial standards, here the ISO 13485, exist and focus to establish industrial standards and regulations (Management and Devices, 2015, 2016).
- However, a full quality management system as described in these standards, is not feasible for most research organizations, which hinders a smooth knowledge and technology transfer to manufacturers.

Beyond the state of the art:

- We propose an implementation guideline for academic organizations incorporating the essential components of a QMS.
- A carefully assembled QMS with diligently chosen elements will greatly facilitate knowledge and technology transfer in a controlled and predictable way.

3 Introduction (challenge)

3.1 Motivation

Artificial intelligence (AI) offers new opportunities to transform healthcare, in particular, modern machine learning approaches have shown huge potential when applied in various fields of medical research and therefore opened up a new era for precision medicine (Hawgood *et al.*, 2015). In the last decade, Universities and other research organizations supported and encouraged by public funding agencies have spent huge efforts on the development and enhancement of such predictive software models, algorithms, and systems as medical devices for clinical research and application.

Subsequently, a manifold of studies have proven ML to be advantageous for disease diagnosis, prognosis, and monitoring of diseases (Fatima and Pasha, 2017; Center for Devices and Radiological Health, 2019). In cancer research, for instance, ML is used to gain deeper insights and understanding of the genetic alterations that are required for cells to develop various stages and severity of cancers (Jeanquartier *et al.*, 2016; Batra *et al.*, 2017; Wiwie *et al.*, 2019) and thereby enable tailored prognoses and monitoring of diseases. Moreover, computational models on clinical variables and electronic health records are used to assess individualized health risks, for instance to identify high-risk patients for sepsis in intensive care units (Desautels *et al.*, 2016; Calvert *et al.*, 2019) or the analysis of longitudinal data for the early detection of heart failure.

Once the outcome of this development is mature and robust enough to be used in routine treatment or diagnosis, there is a need to bring this knowledge to clinical practice. Therefore, a straightforward technology transfer to a manufacturer of medical devices would be beneficial (Riemenschneider *et al.*, 2018). While the knowledge and technologies to develop powerful AI driven medical decision support systems exists, a manifold of pressing problems hinder its transfer to clinical practice. Particularly, modern systems medicine approaches integrate all facets of private data such as electronic health records (EHR) (Shickel, Tighe and Bihorac, 2017), laboratory results (Goecks *et al.*, 2020), medical imaging (Anwar *et al.*, 2018), molecular data (Hauschild, Baumbach and Baumbach, 2012), or pathway information (Jeanquartier *et al.*, 2016; Batra *et al.*, 2017; Wiwie *et al.*, 2019). However, data exchange within and amongst institutes is perceived as insurmountable posing a roadblock hampering big data-based medical innovations.

Additionally, the design and development of medical devices – including software as a medical device – have to comply with regulations and standards that ensure the safety and quality of the medical devices in clinical practice (Organization and Others, no date). This includes standards

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concerning quality management, but also software development life cycle standards including agile methods such as Scrum (Schwaber and Beedle, 2002) or Kanban (Anderson, 2010), and risk management, for instance, which are not common in academic research work (Zamith and Gonçalves, 2018). This technology transfer usually means that the intellectual method and know-how are transferred, but all artefacts that were created during the academic research are discarded. Manufacturers will need to understand the principles of the new method, train their staff on this, and maintain design and development records when creating the final product. This will include design documents, meeting minutes, and other documents created during the development. Because the focus during the research in academia is typically more on the content than on documentation and formal procedures, these are often not in a status that supports the manufacturers very well in the technology transfer. Manufacturers are required to implement each software as a medical device according to strict regulatory guidelines, see Mark and Wylie for a comparison of the US and EU guidelines (Maak and Wylie, 2016). This causes a significant overhead in the time and effort that they have to invest before the product is ready for the market (Sharma *et al.*, 2013). In this article, we propose recommendations for research organizations that have the potential to significantly reduce the barrier for the transfer of software to industrial manufacturing, in particular for software that is intended to be used in the context of a medical device. It is guided by standards that are common for medical device development, but does not have the intention to shortcut any steps of the regular medical device development – this will always have to be done according to the strict rules and regulations that apply. Nevertheless, some of the basic thoughts that stand behind the regulations for medical software will help software development in research organizations reaching higher quality and standards.

One of the fundamental requirements towards the development of medical devices (and thus also as medical software) is the establishment of a quality management system in the organization, such as FeatureCloud. This is required for good reasons, two of the most important being traceability (i.e., being able to understand what happened when and why it happened) and reproducibility (i.e., make sure things happen the same way each time they happen). Having these established for software when technology transfer is initiated has the potential to tremendously facilitate and speed up the transfer. Some of the other reasons a quality management system is required for medical device development are also beneficial for research organizations when developing software. Examples are: responsibilities are clear, new team members can be phased in quickly, it is made sure that people know what they are working on and how this contributes to the project goal.

The requirements that are relevant for quality management in medical device development (e.g., as defined by the International Organization for Standardization, ISO 13485 (Management and Devices, 2016) and the Code of Federal Regulation, CFR Title 21 (Us Fda, 2017)) are however quite significant and most likely outside of what is feasible for research groups in universities and other research organizations. So far, there is not much guidance available on how to work between the two extremes of not having any quality management system at all and having full-blown quality management that complies with relevant standards. We have been working on requirements towards a quality management system for the development of software in academia that will potentially be transferred to medical devices. We have aimed to embrace most of the benefits and facilitate the technology transfer as much as possible whilst keeping the overhead in a well manageable range – all in the context of universities or similar organizations that engage in research on software in the medical setting.

Two things are important to keep in mind for this: first of all, the ideas presented here do not provide a shortcut when developing medical software. Any development of medical software must strictly follow the regulations that are relevant in the specific country or region. Therefore, our considerations presented here are supposed to provide a starting point that is intended to be adapted to specific requirements as needed. This is well in the mindset of most quality management systems: if there is a good reason to change something, change it – but be sure to consider all relevant aspects and document the reasons and the changes.

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3.2 QMS for medical software research

3.2.1 Scope of the QM system

A major aspect to be clarified when setting up any quality management (QM) is the scope of the activities. In principle, QM is set up on an organizational rather than a project level. One of the key benefits of a QMS is that it provides projects with guiding principles for the setup, documentation, and more. The organization sets up the QMS, the projects (and other procedures in the organization) comply with this, to ensure organization-wide quality and standards.

Universities and other research organizations often have some QMS set up for the entire organization, mostly focussing on the quality of research and education. However, because of the range of topics such a QMS has to cover for the specific task of developing software that will be used in a medical context, common University regulations are typically neither helpful nor sufficient. A university-wide QMS may cover topics such as staff hiring, waste disposal, publishing guidelines, and commitment to scientific standards. However, it is lacking specific requirements necessary in a customer-centered setting, such as for medical software development and defined in ISO 13485.

Traditionally, a QMS is defined by a company or organization to be applied in each project. In the academic setting, we recommend setting up a QMS for instance at the level of a research institute itself, an organizational unit such as a department, or subunit like a research group. For clarity, in this manuscript, we will use the general terms organization, unit, and subunit interchangeably. Which level is most appropriate may differ on a case to case basis. However, it is important to make a dedicated decision before starting to set up such quality guidelines.

3.2.2 Content of the QM system

The QMS of an organization or research unit serves to define procedures and structures that are implemented in the organization in a way that they can be seen and understood by everyone. It describes the basic structure of an organizational unit and defines procedures that are implemented in this organization. Procedures in this context may be administrational processes, like how to train employees, but could also be technical processes, like how to store and archive documents. For each procedure, the QM system documents inputs, outputs, responsibilities, and activities, see Figure 1.

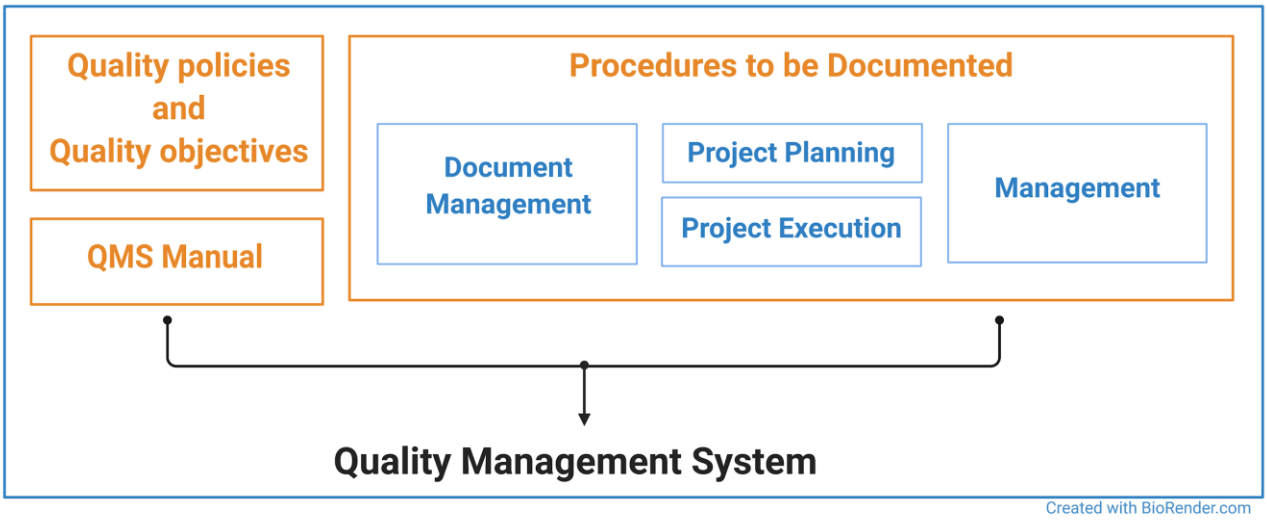

Figure 1: Quality Management System

For an organization that works on projects - and in the scope of this document we assume that research organizations work on "research projects" - the QMS should give guidance on how projects are executed. This includes in particular the basic structure, documentation, technical setup as well as responsibilities and roles within the projects. With this guidance and policy in the

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organization that requires compliance with the guidance - the organization sets the stage such that its projects are executed in a controlled and defined way.
For many purposes in a research environment, a good QMS however should be guidance, not a corset. This means that the QMS will allow a significant degree of freedom in terms of deviating from the processes. It will, however, ask to provide a good reason for the deviation and, most of all, to document the reasons and the decision, including documentation of the new path chosen. This will allow us to adapt to different conditions while maintaining a solid level of traceability and reproducibility. In addition, the working methods that are necessary for a qualitative implementation and documentation that each person involved in the project commits to, need to be described. Therefore, the QMS is addressed to all personnel involved in a project. Ultimately, by participating in the project, they commit themselves to comply with the working methods and regulations defined in the QMS.

3.2.3 Quality policies and quality objectives

ISO 13485, which is an international standard for QM systems for medical devices, requires documenting the quality policy and the quality objectives of an organization on the highest level of the QMS - other QMS standards have similar requirements. While this is not required for research groups or similar organizations, we do recommend taking the time to think about quality policy and quality objectives. Having clear quality policies and quality objectives will help everyone to understand what drives the organization and how the organization intends to reach its quality goals (Management and Devices, 2016).

A quality policy describes the high-level attitude of the organization concerning quality. A quality objective is a measurable goal that is derived from quality policies. Quality policies describe what distinguishes this special organization from other organizations and what drives the organization on a high level. Personnel must be aware of the relevance and importance of their activities and how they contribute. The quality policies are the place where the overall goals are stated, allowing them to put their work in the context of these overall goals.

For the specific case of a research organization implementing some limited QMS, this should also be the place where the organization documents to what extent it plans to make the QMS mandatory (policy) and how it intends to enforce this decision. This is not relevant for manufacturers of medical devices because they have no choice - they simply have to make sure that the QMS is fully implemented. For organizations in the scope of this article, full implementation is not mandatory - but it should be a deliberate choice where and to what extent the QMS will be used.

3.2.4 Quality manual

The quality manual is the document that contains the core of the QMS - the definition of the scope of the QMS and the description of procedures and structures in the organization. It can be considered as “instructions for use” of the QMS. Ideally, it should be possible to hand a copy of the quality manual to a person entering the organization and with this enable that person to work according to the QMS (in reality, this is typically not possible due to the size and complexity of a QMS).

A quality manual should be created for every QMS, no matter how simple or complex it is, and no matter in which environment it will be used. This is the place to document things like:

- Scope of the QMS (For whom is it relevant? Which Procedures are covered? etc.)
- Structure of the QMS (One document? Multiple documents? How are multiple documents organized? etc.)
- How and where are the procedures of the QMS stored, maintained and archived

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Typically, a quality manual does not contain all the descriptions of all procedures that are covered, but rather contains references to other documents that contain these descriptions. This usually makes it much easier to find and read the description for specific procedures and also allows updating the description of parts of the QMS rather than only the entire QMS as one big block.

3.3 Procedures to be documented

The goal of this article is to give guidance on what subset of a QMS is helpful to implement to facilitate technology transfer from research to a manufacturer of medical devices. So far, we have discussed the general aspects of a QMS; the following sections list and briefly describe which procedures that we consider to be most important in this context. Established standards for QMS, require a significantly larger set of procedures, and there are always good arguments for including or excluding a certain set of procedures (Management and Devices, 2015, 2016). We consider our recommendation as a starting point that can - and should - be adapted if there is any good reason to do so.

3.3.1 Document management

One of the most important things to aid the technology transfer to move forward from research to an industrial, full-blown medical product is documentation. It helps tremendously to have reliable, well-defined, structured, and (within the given possibilities) complete documentation.

The most basic part of this is to know where and how documents are stored and managed. Documents may be stored in a file system, in a source code management system (like git or subversion), in a content management system, a dedicated document management system, and so on. If every project decides on its own how to store documents, it will make management and retrieval of documents much more difficult within the scope of the organization. Therefore, it is advisable to use the same document storage for all documents relevant for the organization. This should be decided once and documented in the QMS. The documents that make up the QMS should be stored the same way, so the decision on the storage needs to be made very early when setting up a QMS.

Other things that should be covered by this part of a QMS are for instance

- How are documents identified consistently and unambiguously?
- How can users access and modify documents?
- How will previous versions of a document be available?
- Is any approval needed when creating/storing a new document or a new version?
- If approval is needed, who needs to approve and how is this done?
- How can a user be sure to have the current version of a document?
- Will documents be discarded at any time?

Defining a set of procedures that cover these topics and others that are relevant for the handling of documents make up the document management part of the QMS. This may also include the choice of a specific format or software for the work with documents.

A distinction is often made between "documents" and "records", where roughly spoken "documents" describe what is planned and "records" describe what happened. Procedures may differ in some points, as records probably never should be changed after they were stored. For the sake of simplicity, we do not distinguish in the scope of this article.

3.3.2 Project planning

Having some kind of project planning is tremendously helpful, even in a research-oriented organization. It not only dramatically increases the likelihood of successful project completion, but it

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also makes it much easier to understand what happened in a project and why it happened - which in turn supports the technology transfer significantly.

Therefore, we propose to define a set of procedures on how to handle project planning as part of a QMS proposal. Remember that this does not mean that every tiny project has to implement a full-blown project planning, it only clarifies, when to do which kind of planning and sets guidelines for the implementation.

Things that should be covered here are for instance

- A procedure to systematically choose which parts of the QMS will be applied to the project (might be a limited subset for very small projects)
- A procedure that requires projects to check if everyone has the same understanding of the project goals
- A procedure that requires projects to define the roles and responsibilities within the project
- A set of documents that needs to be created for each project
- Special focus has to be set on risk assessment and management (according to ISO 14971)

3.3.3 Project execution

Every project has its own set of circumstances, boundary conditions, internal and external requirements, and so on. This often leads to each project being executed differently. While this may or may not be beneficial for each project, it usually makes technology transfer much more difficult - as part of the transfer, all of the specific setups for the project need to be understood. Having some level of standardization for all projects in an organization and having this standardization documented consistently will make the transfer much easier. Besides this, it also provides many benefits that may not be visible to the individual projects at the time they are started - having a higher chance of avoiding pitfalls using experience from previous similar setups is one of these. Therefore, we recommend defining procedures for project execution as part of our QMS for research organizations.

More specifically, we recommend at least to define procedures for the following:

- Requirements management. Each project should at least spend thoughts on which inputs to consider for requirements, how to prioritize requirements, how to document requirements, how to handle changes in requirements. A set of procedures that tells projects how to spend these thoughts in a more formalized way should be part of the QMS.
- Definition of the development environment and tools: It is probably not helpful to have all projects use the same development environment and set of tools. But it is helpful to require the projects to decide on what to use in a structured way and to document this decision. Include the procedures on how to make the decision and what to document in the QMS.
- Development process: like before, the most important thing is that the selection of a specific development process (Scrum, Kanban, Waterfall, ..) is done consciously and that the reasons for the decision are documented.
- Completion of the project: It must be clear when a project is finished. Again, this may depend strongly on the individual project, some may be finished after successful testing, others simply when time is over - the important thing is that everyone has the same understanding of when this is the case. Therefore, there should be a procedure that requires each project to define the criteria for completion and document this decision.
- Documentation: the level of documentation created during the development (code comments? design document? test documentation? etc.) may be subject to different needs; however, it is a good idea to have strong guidelines here, as documentation is typically an unpopular activity and tends to be neglected.

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3.3.4 Management

The success and quality of a venture or project largely rely on the competencies of the contributing scientific and administrative personnel and their access to resources. Therefore, it is inevitable to provide them with the necessary knowhow and competencies, through appropriate processes such as education, training, skills, and experience, for instance. To ensure the consistent quality of all projects within an organization, the corresponding QMS should document such processes.
More specifically, we recommend at least to define procedures for the following:

- QMS training: All of the effort put into establishing a QMS is useless unless the staff involved in the projects and administration know about this QMS. It is essential that every person is aware of the QM system and knows where to find the QMS documents associated with their work and how to act accordingly. Therefore, it should be documented how the management will ensure appropriate QMS training for new employees but also initiate recurring update training for all personnel when the QMS is changed. Moreover, it is important to determine who is responsible to ensure that every employee has the required QMS competencies and how training is implemented. This will ensure that a QMS will be implemented in practice. However, while according to QM system standards like ISO 13485 such training processes require meticulous documentation of participation for each employee, we suggest that this is not mandatory in the academic environment (Management and Devices, 2016).
- Qualification of personnel: The management is responsible to ensure that all staff is qualified for all tasks they are given. This may include hiring staff according to the requirements of the project and ensuring necessary training. The QMS should define procedures and responsibilities for this.

4 Discussion and Conclusion

Computer and data science approaches have opened a new era in health care and precision medicine such as diagnostics, prognostics, and monitoring. The development of such biomedical and health algorithms is very time-consuming and the knowledge and technology transfer to clinical practice requires to rigorously obey the quality requirements defined in international standards. In this article, we discussed the difficulties of this process from research to commercial manufacturing with particular focus on software that is intended to be used in a biomedical and clinical context. Only a few research organizations have started to implement such processes (Sapunar *et al.*, 2016). To the best of our knowledge, here we propose the first guidelines establishing a limited quality management system for research organizations, which has the potential to greatly facilitate and speed up such technology transfer in a controlled and predictable way. The intention of the developed guidelines is not to simplify the certification process, but to support the manufacturer with gathering all required documentation for the certification process from the academic partners. Being aware that a full quality management system is not feasible for most research organizations, we proposed a subset of elements of a quality management system which we are convinced will provide a significant benefit while keeping the effort in a range that can easily be handled by most organizations. Our proposal is centered on procedures for document management, project planning, and execution as well as some surrounding administrative procedures. Depending on the specific needs, the set of elements of a quality management system works best for an organization that may differ from what we propose. The fact, however, that a quality management system is set up at all and that the elements are deliberately chosen is probably a key factor for facilitating technology transfer. Our proposal provides a starting point for this, lowering the hurdle for many research organizations to set up some quality management.

5 Practical Proposal for a QMS Implementation

The concepts of a QMS system are hard to grasp on a theoretical level. Therefore, we will present in the following a practical example of a QMS implementation in academia.

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The Institute for Diagnostic Image-processing in Radiology (IDIR) is a fictional organization for the development of medical software focussing on the processing and interpretation of medical imaging technologies such as Computer Tomography. This fictional organization could also be a clinical partner in the FeatureCloud consortium, thus, the example could be directly transferred for the partners in FeatureCloud. However, the process should be generic enough to be applicable also outside the FeatureCloud consortium. We assume a size of roughly 100 employees - the size has a strong impact on what is feasible for the organization. To ensure structured processes and quality throughout the institute, they intend to set up an institution-wide quality management system. This example will give an idea on how a QMS for a real world organization such as a research institute could be implemented. Note that it is beneficial to define a QMS on an organizational level which will define more general aspects and processes. If such an organizational QMS does not exist, smaller organizational units can implement a QMS which will focus on specific aspects within the unit. In the following, we will give examples for information that could be included for the different sections of a potential QMS for the IDIR, see Figure 2 for an overview of the QMS components for IDIR. We therefore will use the terms organization and organizational unit interchangeably.

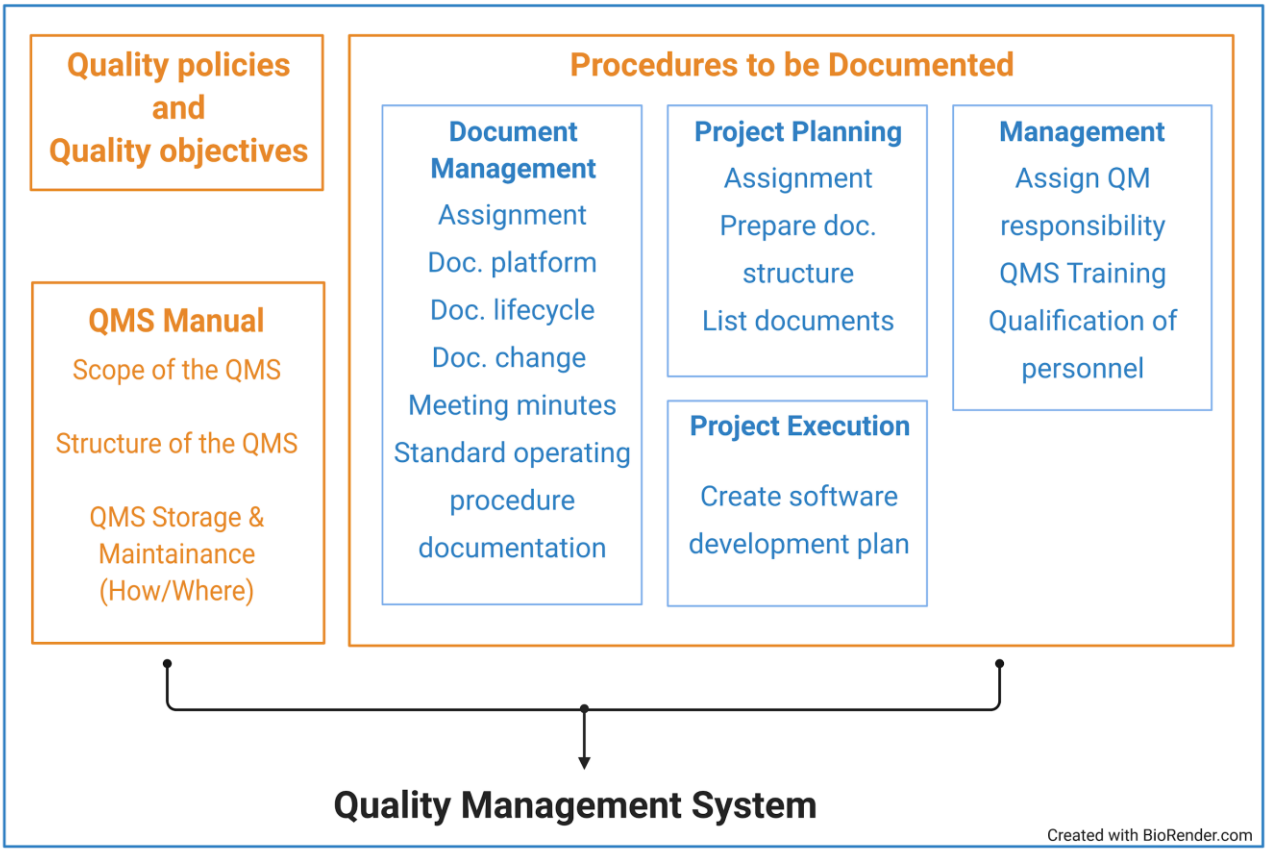

Figure 2. This figure shows the building blocks for the example quality management system of the IDIR institute.

5.1 Quality policies and quality objectives

An integral part of a QMS system is the definition of quality policies and objectives of the organization. While quality policies describe the high level aims and attitude of the organization, quality objectives will define measurable goals that are derived from these policies. For instance, the IDIR might define the quality policies in the following way:

Our institute is striving to **revolutionise the way we utilize medical imaging for information mining** with a focus on medical applications. Our efforts are therefore tailored to processing and interpretation of imaging generated by technologies such as computer tomography (CT) or positron

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emission tomography - CT. Moreover, we aim to ensure that all **advancements will be publicly available to benefit society**. Major objectives are the combination of this information with computational and artificial intelligence to optimize clinical diagnostics and therapy optimization for various diseases.

Consequential the IDIR dedicates all its efforts to the following objectives:

- We aim to develop algorithms that enable the integration and analysis of medical images (as specified previously) and regularly publish open source software packages and medical applications that support various aspects of interactive data interpretation for academic and medical research.
- We aim to build computational models that utilize medical imaging to optimize clinical diagnostics for tumours of for instance internal and external organs. Moreover, we will integrate these models into user friendly software tools and applications to make them publically available to support medical decisions.
- An integral objective of this institute is to facilitate a seamless knowledge and technology transfer to industrial partners for commercial release.
- Therefore, the IDIR commits to implementing the academically tailored QMS as described in the following. This document is accessible to all organizational groups and employees in the IDIR and it is mandatory to adhere to the described standards and recommendations. Exceptions must have a reasonable explanation and require a written justification.

5.2 Quality manual

As described before, the Quality manual is the central component of the QMS. It defines its scope and describes key procedures and structures in the organization.

For the IDIR, the QMS defines standard procedures and processes such as documentation and responsibilities that are relevant for all groups and employees in the institute. In particular, projects that contribute to the above described objectives are encouraged to implement the QMS in their work.

The QMS of the IDIR is described in a set of documents highlighting different aspects and processes within the QMS. A central document management describes procedures involving various aspects of documentation and management thereof. For instance, the clarification of responsibilities (DM -1), the technical and organisational aspects of document storage (DM-2), document lifecycle from creation to disposal (DM-3), and changes affecting other documents and processes(DM-4). Moreover, it should comprise meeting minutes (DM-5) and generally defines the standard operating procedure for documentation (DM-6). Additionally, the QMS should include a number of documents for project planning and execution. For example, standardized processes could describe assignment of responsibilities within a project (PP-1), technical aspects of document storage (PP-2) and a list of documents created for a project (PP-3) as well as a procedure for a software development plan (PE-1). Finally, procedures for different aspects of management can be determined, such as assigning responsibility for the quality management (MA-1), the implementation of training (MA-2), organization of regular QM update meetings (MA-3) and the annual QM review (MA-4).

Moreover, the quality manual will give a detailed description of the location, maintenance and lifecycle of the different documents within the QMS.

5.3 Procedures to be documented

The following information is documented and available to every employee in the local intranet of IDIR.

5.3.1 Document management

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General requirements

Procedure DM-1: assignment

The document management process is a very important part of the QMS and is therefore described in more detail below.
The first step is to appoint a person responsible for documentation, the documentation representative, to ensure that responsibilities for the implementation of the document management procedures are clear. One of the tasks of this person is to take care that the following setup of the QMS is appropriately documented, e.g. minutes are written for meetings. Furthermore, the range of tasks of the documentation representative should be determined depending on the institute and its objectives and be appropriately assigned.

Procedure DM-2: documentation platform

Then a documentation platform is needed that contains several functions.

- The most important thing is that documents are not lost. Even documents marked as deleted must be retrievable at any time. This is of great importance in order to be able to track the entire work process.
- This is partly solved with the second property that such a platform should have, namely versioning. This ensures that old versions of documents are not lost, so that it is possible to track the progress of the project. Good versioning can also solve the problem of documents that need to be deleted. The latest version is marked as deleted and the document and its versions can still be found.
- The third characteristic for a good documentation platform is that everyone who reads and edits the documents also has the necessary access. However, it is equally important that documents cannot be changed by everyone, but only by authorized employees.
- The last characteristic is that a good platform should have a system that allows you to mark whether employees have read documents. This is to make sure that everyone has read the important documents needed for working on projects of this instance.

Procedure DM-3: Documentation lifecycle

Furthermore, the life cycle of the documentation should be defined. This typically consists of generating, editing, distribution, use, archiving and disposal. It should be precisely defined how the steps should be carried out to ensure that the documentation is uniform and consistent.

Procedure DM-4: Documentation change

The process of document changes should also be recorded in the QMS. This is because important steps must also be followed here. When making changes in the documents, it should be taken into account that changes also may affect other documents and processes. For this purpose, all objects that could be affected by the change should be identified first and whether they also need to be adjusted.
After this elaboration, the changes must be confirmed by persons with permission. Finally, the changes are implemented and the adaptation of documents that are affected by the change are also made.

Procedure DM-5: Meeting minutes

In most cases, each employee is responsible for documenting their work. However, in meetings where many people are working on a project, it can happen that the responsibility is not clear. It is therefore advisable to create a process for recording the meeting.

Procedure DM-6: Standard Operating Procedure documentation

Now that the basic structures are in place, the emphasis is on uniform documentation where possible. Since requirements for documents can change quickly and frequently, it is not recommended to integrate them explicitly into the QMS. For this the possibility exists to define specific details in "SOP" (Standard Operating Procedure) documents, which are referenced by the

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QMS, but not part of the QMS. This allows the documents to be modified without having to modify the QMS itself. The SOP documents should not define procedures or organizational structures, but rather be used for document templates etc.
All physical (paper) documents and records will be scanned and stored in the file system unless this is physically not possible. Paper documents may be discarded after this, unless this would result in a loss of information (e.g. dynamic range cannot be captured by scan).

#	Headline	Content
1	Title	The title should clearly and briefly summarise the topic of the SOP
2	Department, Date, ID	Department, date and ID are information that must be recorded regarding the affiliation
3	Purpose	Here is a brief summary of the reason why there is an SOP in this context
4	Scope	The scope describes to whom the SOP applies and the reason why this is carried out
5	Definitions	All terms used in the SOP are defined to avoid misunderstandings
6	Procedure	The actual procedure to be followed

Concrete example

Procedure DM-1: assignment

In this example, the head of the Institute for Diagnostic Imageprocessing in Radiology (IDIR) first appoints a person responsible for documentation, who acts as a document representative.
Since the document representative cannot take over solely the documentation, further responsibilities of the documentation still need to be clarified. While each individual and projects are responsible for documenting their work and adhering to the change policy, random checks can be made to ensure that they are carried out correctly within the guidelines of the QMS.

Procedure DM-2a: documentation platform

In addition, the Institute has chosen Apache's Subversion software as its documentation platform (Collins-Sussman, 2002). This platform meets the majority of the requirements, namely

- versioning,
- editing and access only by authorized users

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- renaming and deleting documents is versioned, thereby preventing data loss.

To check if all the necessary documents have been read by everyone, the institute has set up an email address. Whenever an employee has read a document, he/she/* sends a confirmation to this email address. These documents are managed and stored by the documentation representative.
To maintain structure, documentation within subversion is divided into categories. Categories like QMS, processes and other global topics such as sales should be included as a minimum and these categories should be expandable at any time. In these categories, related documents can then be stored in a structured manner. But also every project gets its own documentation folder to store related documents in the same place and to create a structure in which content can be easily found.

Procedure DM-2b: documentation platform (Code)

Since the code management is project-related, IDIR allows the projects to choose which code management system to use. The "main responsible person" for the project makes this decision; the decision must be documented in the "software development plan" (see procedure PE-1) However, IDIR recommends its staff to use Git to manage the code(Spinellis, 2012). By using Git, the properties required for code management are automatically maintained. There is also versioning and the possibility to store intermediate states in a referenceable way. Furthermore, no code is lost and several people can work on the same code. Any decision not to use Git should be documented in the "software development plan".

Procedure DM-3: Documentation lifecycle

The monitoring of the life cycle of the documents is in IDIR also performed by the document representative.

While the creation of project-related documents is the responsibility of the project leader, the following procedure applies to global documents.

First, each employee can request that documents be created or modified. This request is then checked by the document representative and the task of creation is delegated. After the document has been created, it must be approved by persons who have the authority to accept it. In the IDIR these are the leading positions and the document representative. These are versioned according to the regulations and released for reading by the employees. Old versions are marked as such and are then no longer accessible.

To guarantee consistent storage, backups are required, which are performed by the IT department at weekly intervals.

Procedure DM-4: Documentation change

The procedure of "DM-3: Documentation lifecycle" must also be followed for changes. Furthermore, it is necessary to validate which documents are affected by the change and adjust them if necessary.

Procedure DM-5: Meeting minutes

In general, the person who sets up a meeting is responsible for its documentation. However, this can be delegated before the meeting. In the documentation of the meetings, there is also the possibility to implement alternative documentation for project-related meetings, as long as they comply with the standards defined in the QMS. For all meetings that take place project-independently, the following procedure is required.

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Since the person responsible for documentation cannot be present at every meeting, the taking of protocols will be passed on in the group attending the meeting. Once all the participants have taken the notes, they start again from the beginning. At one-time meetings, someone is needed to take the notes voluntarily, and if no one volunteers, someone is appointed by the chairperson of the meeting.

This process can be adjusted within a project for alternative meeting protocol requirements. All adjustments should be documented.

Procedure DM-6: Standard Operating Procedure documentation

SOPs can be described as guidelines on how certain applications should be carried out. An SOP is always structured similarly. To illustrate this with a practical example, an SOP for meeting protocolling is shown below.

#	Headline	Content
1	Title	Standard operating procedures for the recording of meetings
2	Department, Date, ID	Institute for Diagnostic Image Processing in Radiology, 24. Apr 2020, SOP-74922947
3	Purpose	To provide a procedure to define the general guidelines to ensure the recording of meetings is done correctly
4	Scope	This procedure applies to all meetings held independently of projects and is recommended for each meeting protocol.
5	Definitions	ID - Identification Document representative - Working title for the person responsible for the documentation

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6	Procedure	First of all, a recorder is selected. If the document representative is not present, the procedure is as defined in the QMS. The recorder will first note the name of the department, the date, the meeting ID and the project name to which the meeting belongs. Furthermore, all attendees should be recorded by name. Now the content of the meeting should be recorded in key points. Afterwards, the protocol is sent to all participants and stored in the documentation platform

5.3.2 Project planning

The IDIR handles projects in a broad range of sizes, ranging from a few months for a single person to multi-year with an entire team. The requirements the QMS put up must therefore find the balance of being so flexible that they fit all these different projects and on the other hand so precise that it does not void the benefits of having a QMS.

Procedure PP-1: assignment

In order to make sure this works, the QMS requires every project to fill out a “project start” form asking for some project details. The specific “project start” form is stored in a SOP Document which may change over time, but the following fields always need to be in the document and are mandatory to fill – no matter how big or small the project is.

#	Item	Comment
1	Project name	A unique name helps to make sure everyone is talking about the same project
2	Main responsible person	Could be a “project manager”
3	Goal of the project	High level goal
4	Planned start and end date	
5	Success/termination criteria	Could be the finalized development of a “product”, the end of an available time window, a certain funding used up, …

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6	Planned resources	How many people for which time; any specific devices, suppliers, …
7	Any exclusions from procedures the QMS asks for – with reason	This is the place where the QMS can be tailored in a planned and systematic way

The filled-out "project start" form needs to be signed by the "main responsible person" and the head of the institute.
The head of the institute is responsible for this procedure. Responsibility will probably be delegated to the person who will be the "main responsible person", but at the time this process needs to be initiated, there is no assignment to this role yet. The assignment of the role "main responsible person" to a physical person is one of the results of this procedure.

Procedure PP-2: prepare document storage

As soon as the project has a name, a folder with this name is created in the institute's main "projects" file system. All documents and records that will be created for this project must be stored in this folder or subfolders. A set of subfolders (one level deep) is defined in an SOP and will be created for each project. (Note: this includes subfolders like "Administration", "Testing", "Requirements", …). Further substructures may be defined by the projects as needed. Note: The scanned "project start" form is one of the documents to be stored here. The "main responsible person" is responsible for this procedure, which must be completed within 2 weeks after the assignment.

Procedure PP-3: list of documents

The next procedure that the QMS defines is a creation of a list of documents that will be created during the lifetime of the project, together with a responsible person for each of these documents. Purpose of this list is to make sure that no document is forgotten and it is clear who takes care of which document. The list of documents may be updated during the project, items may be added or removed, and no management approval is needed for an update, but for each change, the affected responsible persons must approve and a reason for the change must be documented. The "main responsible person" must create the initial version of this list within 4 weeks of the assignment.
Typical documents that would be included in this list would be the software development plan (see below), the requirements specification, the user manual or a team member list.

5.3.3 Project execution

Again, due to the wide range of possible project sizes and types, the processes that the QMS defines need to find the right balance between flexibility and strict guidance. Projects can customize the procedures to a wide extent, but every customization must be documented.

Procedure PE-1: create software development plan

One document that each project must create is a software development plan. This document is the fundamental document for the technical planning of the project. It lies within the responsibility of the "main responsible person" that this document is created and maintained. A template for this software development plan is again stored in a SOP document that may be adapted to needs over time; however, the following points must be addressed in each software development plan:

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#	Item	Comment
1	Choice of development process	E.g. Waterfall, Scrum, Kanban, any custom approach or none at all
2	Description of development environment	Should be detailed enough to allow to re-create the development environment
3	Description of build and integration steps	Should be detailed enough to allow to re-create the final software
4	Description of requirements handling	Where do requirements come from, how are they prioritized, how are conflicting requirements handled, [how] are requirements documented
5	Plan for testing	High level, what level and what type of testing is planned (if no structured testing is planned at all, there is a reason for this – document it here)
6	Handling of changes	How will the project deal with changes during the development

This may seem like quite a lot of writing for a small project, but the individual items may actually be very short for such a project. A single person working on a bachelor thesis would probably choose not to use a formal development process. This person would document the requirements as part of the thesis, perform only punctual functional tests and decide spontaneously whether or not to consider a change. All these steps would be compatible with the QMS. Describing the build environment and the build and integration process however is important even in such a scenario, as otherwise it might be very difficult to make use of the results of the thesis.

The IDIR considers it an important benefit that following the QMS procedures implies such decisions (e.g. to minimize the efforts for an item) are taken consciously and are documented, so that it can be understood afterwards why such decisions were made. This makes it much easier to retrospectively understand projects, helping any technology transfer significantly.

5.3.4 Management

In order to make sure the QMS system is actually being used, it is important for the IDIR to make sure all staff are aware of the way the QMS works. It therefore defines the following mandatory processes:

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Procedure MA-1: assign quality management responsibility

One person in the institute is assigned the role of a quality management assignee. This person is the “owner” of the quality management documents and needs to approve any change to the QMS. Note: this approval is mainly to make sure that the quality management representative is aware of all changes and to avoid contradictions within the QMS. The head of the institute is responsible to make sure that the role is always staffed.

Procedure MA-2: implement training for new staff

All new staff need to read and understand the QMS as it is at the time they start working at the institute. A small test is conducted afterwards, with the main intent that people actually read the QMS. The supervisor of the new team member is responsible for the implementation.

Procedure MA-3: implement one department meeting each semester with QM update

Additionally, there is a short update session at the beginning of each semester in which the entire institute gets an update on any changes to the QMS and can provide feedback or improvement suggestions. The head of the institute is responsible for the implementation, but may delegate this to the quality management assignee.

Procedure MA-4: annual QM review

The IDIR at this time chooses not to implement any specific measures to enforce the QMS, it is optimistic enough to assume the procedures will be followed voluntarily. An annual QMS review is planned in which this policy and the effectiveness of the QMS will be reconsidered. The head of the institute is responsible to organize this meeting.

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