Towards unified tooling for easing the qualification of medical normed environments

Anthony Gelibert, Sébastien Jean, Denis Genon-Catalot, Gérard Santailler, Ioannis Parissis

Towards unified tooling for easing the qualification of medical normed environments

Anthony Gelibert*†, Sébastien Jean*, Denis Genon-Catalot*, Gérard Santailler† and Ioannis Parissis*

*LCIS
Grenoble Institute of Technology
Valence, France
{anthony.gelibert}{sebastien.jean}{denis.genon}{ioannis.parissis}@lcis.grenoble-inp.fr

†Nocosium SAS
2 rue Stalingrad
Vaulx-en-Velin, France
{a.gelibert}{g.santailler}@nocosium.com

***Abstract*—Medical confined environments are characterized by a very stringent set of standards and regulations, depending on a wide range of parameters. These are very difficult to handle because of the lack of appropriate tools to qualify before use, monitor during use and audit after use. Providing these tools requires to tackle the complexity of gathering all the different elements of the environment profile (building topology, standards and rules, instrumentation) in a single model which could be statically validated and dynamically checked against events. This article both focuses on introducing the context of medical confined environment regulation and issues faced when trying to design and implement qualification and monitoring tools, and on presenting the approach and work in progress.**

***Index Terms*—Requirements Engineering; Model-Driven Engineering; Medical confined environment; Qualification**

I. Context

Confined environments can be defined as space-limited areas, hosting a product or process, in which all uncontrolled transfers between the inside and the outside world are forbidden. In some cases, motivation is to protect the process against outside contaminations (such as in surgery). In other cases, it is much more to protect the outside against contaminations by the process itself (such as in virology).

Confined environment characteristics (such as use, manufacturing, high attendance, location…) imply strong constraints and, therefore are ruled by several design methods and use guides. These regulations lead to the definition of "normative layouts", consisting in a set of standards a given environment has to comply with. Moreover, the norms are not all opposable, some are only good practice or advice (such as the World Health Organization (WHO) documents [1]).

To illustrate the needs and issues related to our work, we will use a simplified "Centralized Reconstitution of Cytotoxic Drugs Unit (CRCDU)" (Fig. 1) all along the article. In these environments, users are expected to prepare drugs, under chemical hoods in a dedicated room, which will be used for antineoplastic treatments. Here, confinement protects preparations from external contamination by a gradual asepsis [2]. *Inter alia*, it consists in several pressure stages as well as by the rooms' conformance to several (and gradual) ISO levels (ISO 14644-1 [3] standard defines the allowed concentration of particles of various sizes). In France, depending on the context of implementation, a different set of laws, best practices [4]–[6] and norms [3], [7], [8] regulates these units.

The first room is a clearance room, remaining in a particular pressure level in order to protect itself from outdoor atmosphere (whose pressure is considered as a reference). An airlock allows users to dress, and thus acts as a first decontamination stage. Finally, users reach the preparation room with the highest pressure level and the lowest ISO class.

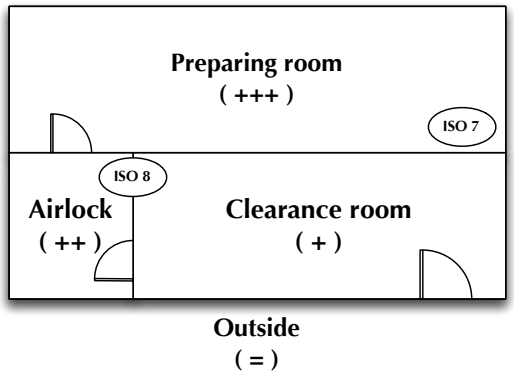

Figure 1. Illustration case: simplified CRCDU

II. Motivations and issues

Human and financial risks related to the design, or the use, of noncompliant environments lead to the need for qualification of such environments before commissioning, but also for their monitoring and auditing after the operation. To support this assertion, it is enlightening to remember that in France, there are more deaths each year by nosocomial infections than

by road accidents. There is a strong need for an integrated toolset, presented in Fig. 2, operating cooperatively all along the confined environment lifecycle (design, commissioning and use).

To summarize:

- upstream of any project checking (0), an analysis is required to proceed with the next two steps ;
- for each project:
  - during the design (1), it should be possible to qualify a confined environment by using only its technical data, to determinate, *a priori*, its conformance ;
  - during the usage (2), the need is to trace usage in order to follow the evolution of the confined environment and to keep its history for audit purposes.

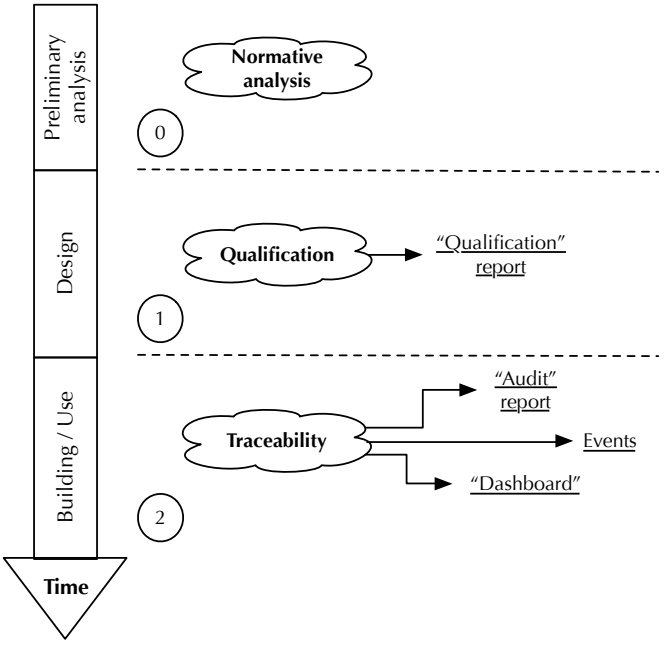

Figure 2. Required process

This section details the required features.

A. Analysis (0)

This is the entry point of the toolset, its preamble, the basis of all the process. The objective is to constitute the normative layout of a kind of medical confined environment and process it to extract the elements required by the qualification (II-B) and the monitoring (II-C). This operation will be done according to the type of environment or according to the "version" of the normative layout, evolving in the same manner.

In the chosen example, it is the analysis of the documents composing the normative layout of a CRCDCU (among which the documents [3]–[8]).

B. Qualification (1)

During the design phase (next section), it should be possible to qualify a confined environment by using only its technical data, to determinate, *a priori*, its conformance with its targeted usage. It is a typical case of Requirements Engineering (RE) [9]. To simplify, it is an engineering domain, targeting the checking of a product against its requirements ; all the process is considered from the requirements elicitation up to the product conformity checking. In this step, the objective is to produce a "qualification" report, which will provide the decision aids allowing to enhance and maximize the conformity of the project with its normative layout.

In our use case, considering the foreseen use of the unit, rooms (size, volume, relative layout…) and their instrumentation (sensors, actuators, external systems…), the qualification would consist in checking all required systems are present ("Heating, Ventilation and Air-Conditioning [HVAC]", access control…) and that they are properly configured.

C. Monitoring and traceability (2)

After commissioning, it is necessary to trace usage in order to follow the evolution of the confined environment and to keep its history for audit purposes. Monitoring then aims at delivering a "specialist-oriented" feedback, giving a clear and cohesive view of running operations to various users rather than trying to automate a complete normative usage analysis. Thus, a customizable "dashboard", displaying only the relevant information, could perfectly embody this feature.

In our example, this could consist in recording the evolution of the pressure in the various rooms, in checking that airlock system is properly running as air velocity and throughput are compliant to requirements…

III. Approach and Work in Progress

Our work focuses on the design of a unified process (called the "methology" in this section) to answer the need presented in Fig. 2. We drew the sketch of the process architecture in a previous paper [10] and conduced additional research to refine its operating and set its technical details. Figure 3 presents this enhanced version, based on model design and transformation, for which we are addressing steps 0 to 2.

The qualification tool (0 & 1) has to take some abstract representations as inputs, in other words, models of both technical data and applying standards. This leads to tackle an RE problem using "Model-Driven Engineering (MDE) [11]"; an approach called "Model-Driven Requirements Engineering (MoDRE) [12]". The realization of these models could be unified in a megamodel [13], interconnecting the metamodels of each component with the required weaving models and so on. As most of the time the normative layout also induces alternatives that lead to several solutions (i.e. building and instrumentation that conforms to it), a notion of "prominence" in the qualification process consequently has to be taken into account. These models (and the linked constraints) represent the abstract syntax and semantic of our modeling language for confined medical environments, the last point is the concrete syntax. As a reminder, this is the syntax (graphic or textual) that the user will manipulate and use to model their project. The challenge is to design metamodels flexible enough to support

the whole targeted domain while providing a framework strict enough to automate checking and data extraction operations. This means a trade-off between the ability to easily model the target and the expressivity required for the transformations generating the "qualification" report and the next step.

About the applied profile (2), its presence is required by the need to reengineer "high-level" model of the targeted environment and its "normative layout". Indeed, the environment profile used during qualification is too abstract to be used directly by the monitoring platform. A strict rule such as "two doors of an airlock cannot be opened simultaneously" has little concrete links within the "computer world": what is an airlock? What is a door? How should its state be read? The model produced by the user to assess their project should partially or completely be automatically reified in an easily manageable version by the monitoring platform. In our example (Fig. 1), this could lead to explicit constraint definitions like "P1 pressure sensor value should always be greater than P2 one", "opening indicators cannot be active at the same time"... Obviously, required information should be introduced in models, to identify P1, P2 and opening indicators. Profile generation is a requirements reengineering problem, consisting in automatically extracting relevant parameters from the abstract profile in order to configure the monitoring platform.

Concerning the traceability platform (3), among the complete set of exploitation constraints, the most important are: the qualification as "Medical Device" [14]; the data use in legal cases which requires integrity-guaranteed data [15]; the support of all the legacy systems already deployed in the targeted confined environment and the adaptability to a profile and an environment which will evolve over time. Here, the challenge is thus as much in the design of the tools themselves as in this specific context of deployment.

We are currently setting up the methodology on real cases. We are working on the analysis step (0). The design of the metamodels enabling to model the building and its instrumentation was the first step and now, we are handling the normative processing. The production of the normative layout and its analysis is a manual process, leading to extract a relevant megamodel which will be the core behind the modeling workshop. It is specialist-oriented work, requiring great knowledge of the concerned domain, provided by Nocosium. As stated in the previous section, we do not aim at a very sharpened concrete syntax and we work more on the methodology than on the user experience. The concrete syntax (presented in the Section II-B) is more an "engineering" problem which would be better tackled later by engineers because there are no real research locks. These further works should investigate the current business processes and determine how to integrate the modeling part in their workflow.

Our first application scenario is the CRCDU presented all along this article. This work enables us to achieve a kind of typology of the normative constraints. Indeed, we can discern several types of constraints depending on the verifications required to conform with. For example, the constraints based on the presence of a specific element (e.g. pressure sensor to ensure pressure monitoring) differ from constraints based on the configuration of a sensor (e.g. frequency of the pressure monitoring) or from functioning constraints (e.g. the calibration of pressure sensors). The means to check them are different.

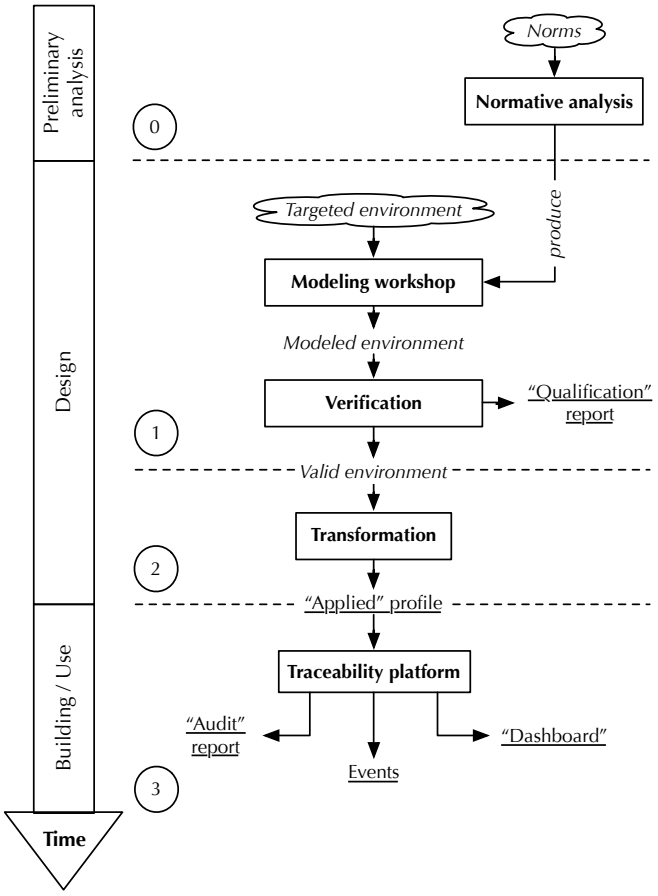

Figure 3. Proposed approach

So, we are currently analyzing the CRCDU "normative layout". For each norm, we classify the constraints and report them into the megamodel or later in the methodology. The produced metamodels are Nocosium's property and will not be presented in this publication.

IV. Discussion

Requirements engineering is a transversal thematic spanning over several scientific fields, not necessarily technical, like in contributions examining the adequacy of a process of requirement validation with a company's workflow. In this thesis, we adopt a fully technical stance and we assess its feasibility, efficiency and limits. Hence, we have to compare our contribution to the other technical approaches for requirement engineering.

The contribution presented in this paper is downstream of typical IT approaches for requirements engineering, like the "Knowledge Acquisition in automated Specification (KAOS)" method [16]. These works aim at identifying the inconsistencies and the conflicts in the targeted requirements for a given project.

This is not our case: we adopt the point of view of the "maitrise d'ouvrage" for which the normative layout cannot be altered. We aim at checking the project against the normative layout. In the same search area, we can also quote the PhD work of Nicolas Sannier [17], on the coherency analysis and the conflict detection, between the various versions of the same norm. Once more, this work is upstream our own objectives.

We can also quote the PhD thesis of Panesar-Walawege [18] aiming at analyzing the conformity of safety-critical systems with the relevant IEC norm, by the UML modeling of the norm to extract the list and calendar of the artefacts to produce. However, we handle different (although complementary) aspects. We will not check if the "maitrise d'ouvrage" produces the required elements but if the project is conform. To put it shortly, it is almost, an opposition between syntactic and semantic analysis.

To conclude, there is not much research on global approaches of requirements engineering (from conception to audit) targeting normed environments.

V. Conclusion

Confined environments are controlled working zones where all unmanaged transfers between the inside and the outside are forbidden. We intend to define a methodology to qualify the normative conformity of an environment, then checking the durability of such compliance over time. The first steps of this process will be validated at the end of the engaged PhD thesis.

Environment qualification should be done only using its technical data. We suggest to address this requirements engineering problem by allowing the definition of an integrated environment profile merging three components: "building", "instrumentation" and "requirements".

Environment monitoring should allow to trace use and to give immediate feedback to practitioners via a dashboard, but also to collect data for further audits. We propose to address monitoring platform implementation issues by the use of service-oriented architectures, particularly to sustain environment changes (building, requirements, instrumentation).

There is not much research on global approaches of requirements engineering (from conception to audit) targeting normed environments. It is this lack that we aim at tackling and in this thesis we validate the first steps of our proposition.

Acknowledgment

This work is funded by the Nocosium company under a French "Convention Industrielle de Formation par la REcherche (CIFRE)" Doctoral Convention.

References

[1] Intermittent Preventive Treatment in Infants, "WHO Policy recommendation on Intermittent Preventive Treatment during infancy with sulphadoxine-pyrimethamine (SP-IPTi) for Plasmodium falciparum malaria control in Africa," World Health Organization, WHO Policy Recommendation, Mar 2010.

[2] T. Hoet, "Le concept de l'asepsie progressive et son impact sur le comportement dans le bloc opératoire," *Inter Bloc*, pp. 24–27, 1994.

[3] International Organization for Standardization, "Cleanrooms and associated controlled environments — Part 1: Classification of air cleanliness," International Organization for Standardization, ISO 14644-1, 1999.

[4] Agence Française de Sécurité Sanitaire des Produits de Santé, "Bonnes Pratiques de Préparation," Ministère du travail, de l'emploi et de la santé, Tech. Rep., Dec 2007.

[5] ——, "Bonnes Pratiques de Fabrication," Ministère du travail, de l'emploi et de la santé, Fascicule spécial 2011/8 bis, Jul 2011.

[6] Direction de l'Hospitalisation et de l'Organisation des Soins, "Bonnes Pratiques de Pharmacie Hospitalière," Ministère de l'Emploi et de la Solidarité – Ministère délégué à la santé, Tech. Rep., Jun 2001.

[7] Agence Française de NORmalisation, "Établissements de santé - Zones à environnement maîtrisé - Exigences relatives à la maîtrise de la contamination aéroportée," Agence Française de NORmalisation, Tech. Rep. NF S90-351, Apr 2013.

[8] International Organization for Standardization, "Cleanrooms and associated controlled environments — Part 4: Design, construction and start-up," International Organization for Standardization, ISO 14644-4, 2001.

[9] P. Zave, "Classification of research efforts in requirements engineering," *ACM Comput. Surv.*, 1997.

[10] A. Gelibert, S. Jean, and D. Genon-Catalot, "Plateforme Ouverte de Supervision et de Traçabilité pour les Environnements Confinés," in *Actes de la conférence MajecSTIC 2012*, Oct 2012.

[11] D. C. Schmidt, "Model-Driven Engineering," *IEEE Computer*, vol. 39, no. 2, Feb 2006.

[12] MoDRE Workshop. [retrieved: Jan 8, 2014]. [Online]. Available: http://cserg0.site.uottawa.ca/modre2013

[13] J. Bezivin, F. Jouault, and P. Valduriez, "On the need for Megamodels," in *Conference on Object-Oriented Programming Systems, Languages, and Applications*, 2004.

[14] European Parliament and Council, "Directive 2007/47/EC," European Union, Directive 2007/47/CE, Sep 2007.

[15] Food US, "Drug Administration, 21 CFR Part 11 Electronic Records," *Electronic Signatures (Final Rule)*, 1997.

[16] A. van Lamsweerde, A. Dardenne, B. Delcourt, and F. Dubisy, "The KAOS Project: Knowledge Acquisition in Automated Specification of Software," in *AAAI Spring Symp. Series*, ser. Track: "Design of Composite Systems". Stanford University, Mar 1991, pp. 59–62.

[17] N. Sannier, B. Baudry, and T. Nguyen, "Formalizing standards and regulations variability in longlife projects. a challenge for model-driven engineering," in *Proceedings of the Model-Driven Requirements Engineering workshop (MoDRE'11) at RE'11*, Trento, Italy, Aug 2011.

[18] R. Panesar-Walawege, "Using Model-Driven Engineering to Support the Certification of Safety-Critical Systems," Ph.D. dissertation, University of Oslo, Jul 2012.