Extracellular vesicles from a natural source for tailor-made nanomaterials

VES4US

[D6.5] Quality Management System (QMS)

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Authors	Giovanna L. Liguori (IGB, CNR) Annamaria Kisslinger (IEOS, CNR)

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1. EXECUTIVE SUMMARY

This document defines the Quality Management System (QMS) developed and implemented by the VES4US Consortium to ensure the quality, consistency and reliability of the project results and deliverables. The QMS facilitates the Work Packages management and coordination, monitors the processes and activities in compliance to the Project objectives and the Quality Standards identified with the final aim to deliver high-quality results and enhance their dissemination and exploitation. The VES4US QMS describes for all the Consortium members how Quality is managed and maintained throughout the project lifecycle. Great attention is paid on standardization and uniformity of procedures, as well as on the needs of researchers to guarantee reliability and reproducibility of the results together to creativity and innovation development.

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2. INTRODUCTION

The VES4US Consortium is a highly interdisciplinary and interconnected network that involves 10 teams from different entities, covering different disciplines related to research and innovation in a joint effort to develop a platform for the efficient production of extracellular vesicles (EVs) from a natural source, and their use as safe and efficient tailor-made nanocarriers in the fields of nanomedicine, cosmetics and nutraceutics. Due to their high level of heterogeneity, specific issues arise when working with EVs, which need to be addressed to assure reliability and reproducibility of scientific data as well as the possibility of manufacturing at large scale. The main aim of Work Package 6 (WP6) is to develop a Project Management System and a Quality Management System (QMS) as core aspect to meet the objectives that are set out in a timely fashion, to deliver high quality outcomes and to ensure their adequate dissemination and/or exploitation. In particular, the Task 6.2 of the WP6 consists on the development of a QMS compatible to UNI EN ISO 9001:2015 standards for the management of procedures, experimental activities and data.

The present report constitutes the VES4US QMS (Deliverable 6.5) and provides guidance and templates material for the definition and achievement of quality requirements, the standardization, validation and uniformity of experimental procedures and the reproducibility of the results.

3. QUALITY POLICY (VISION, MISSION, VALUES)

The VES4US Consortium has deployed a **QMS** based on the ISO 9001:2015 standard and on Good Research Practice principles. This system comprises both the mission, vision and values and the quality objectives themselves.

The **vision** that inspires the FET-Open VES4US project is the following:

To address the emerging issues and challenges of our fast-changing world, we need to go beyond what is known and widely accepted or adopted and let us inspire by new and visionary thoughts that can open promising paths towards radically new possibilities. Time has come to promote, sustain and enrich a creative, multidisciplinary and synergistic environment in which pioneer projects can arise, new technologies can be created and outstanding objectives can be achieved.

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VES4US aims at generating a broad range of radically new high-value products in the fields of nutrition, cosmetics and health sciences based on natural source-derived extracellular vesicles (EVs), which could be used as new generation vehicles for specific molecular delivery. The breakthrough which is required to achieve this ambitious goal is the development of a pipeline approach enabling the production and functionalisation of EVs on a large scale.

Innovation research requires even higher quality standards to guarantee standardization of the procedures, reliability and reproducibility of the results. The set-up of a dynamic, customised, research-oriented Quality and Project Management System constitute a precious support for scientific projects without creativity and innovation detriment.

The **mission** of the VES4US Consortium is the following:

- to develop a radically new platform for the efficient production and functionalisation of EVs obtained from a renewable source, and their exploitation as tailor-made delivery systems for several applications, from nanomedicine to nutraceutics.
- to set-up a Quality and Project Management System that support high-risk and multidisciplinary research projects in all their phases and promote achievement of project objectives, as well as production and exploitation of high-quality results.

The VES4US Consortium aims to foster the following **values:**

- Research Integrity
- Creativity and Innovation
- Standardization, Reproducibility and Validation
- Interdisciplinarity and Interconnection
- Shared leadership
- Transparency and Communication
- Personal and Organization Empowerment
- Respect and Inclusion
- Curiosity and Open-mind Attitude
- Enthusiasm and Cooperation

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4. ORGANIZATION

The VES4US consortium is a well-balanced group made up by 5 research centres and universities and 1 consultancy firm from 6 different European countries. The group is led by the National Research Council of Italy. The other partners are: The Institute of Technology Sligo (Ireland), the Swiss Federal Institute of Technology (Switzerland), University of Ljubljana (Slovenia), Max Planck Institute for Polymer Research (Germany) and ZABALA Innovation Consulting (Spain). The geographical distribution of the Partners is shown in Figure 1.

Figure 1. Distribution of the Partners of the Consortium

The VES4US project is composed by 7 WPs, all strictly interconnected. WP6 and 7 are transversal WPs that support the entire project execution, as shown in Figure 2.

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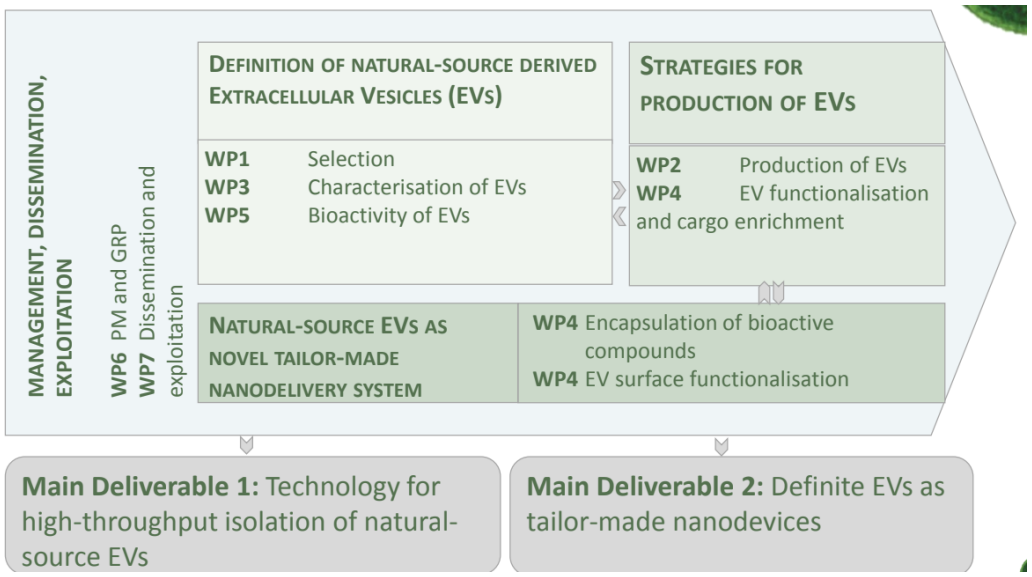

Figure 2. Structure in WPs of the VES4US project

The organizational structure of the VES4US Consortium is fully described in the project Consortium Agreement (CA) in the Section 6 “Governance Structure”. The following figure identifies the governance bodies and the interrelations among them.

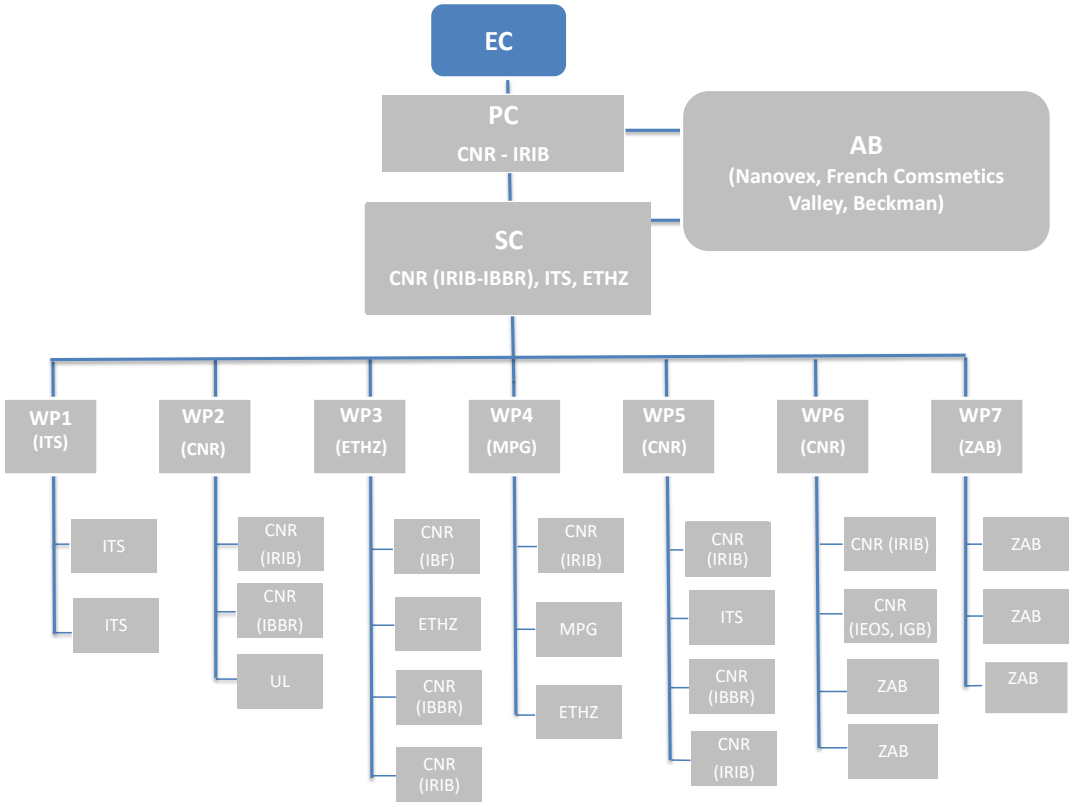

Figure 3. Organizational structure of the VES4US Consortium

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The Project and Quality Management structure is made up of the Project Coordinator (PC), the Steering Committee (SC), the Quality Managers (QMs), WP Leaders (WPLs) and Task Leaders (TLs)

The PC is Dr. Antonella Bongiovanni (CNR, IRIB) who is responsible for the technical, legal, financial and administrative management of the project, acting as the intermediary between the Partners and the European Commission (EC).

The SC (ITS, ETHZ, CNR-IRIB and -IBBR) is responsible for the technical management of the project, including project timeline, quality assurance and risk management.

The PC together with SC cooperates for ensuring that project deliverables comply with the planned activities and they are correctly and timely communicated.

The QMs (CNR-IEOS and IGB) are responsible of the development and improvement of the QMS of the project. QMs are in charge of the set-up and implementation of customised quality tools and template useful for the standardization of procedures and the performance of the overall project and monitor the application of QMS during project execution.

WPLs are responsible for the overall management and coordination at WP level and the achievement of the defined results. The WPLs report the decisions to the PC.

TLs are responsible for the execution and overall coordination of the tasks assigned to them and report to the WPLs.

Tasks participants (TPs) are responsible of performing their own activities according to the GA and the QMS, under the supervision of their own TL.

The Consortium has set up an Advisory Board (AB) composed of relevant industries from three different sectors for driving the VES4US innovation for future market up-take and an academic leader in EV field. The AB will be the organ through which these organizations will be approached for their advice and feedback on the exploitation and interpretation of results (see Section 6.6 of the CA).

The structure has to be enough to provide effective project coordination, capable to elaborate the financial, legal and administrative part of the coordination, as fully described in Section 6.1 of the CA. Each participant is fully committed to a continual improvement of both its own skills, competence and activities as well as of the overall project performance, each one in agreement and respect to its own role.

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All the details referred to the representation in meetings, how to and when convening the meetings, notice of the meeting, management of the agenda and the minutes, and voting rules are described in the Section 6.2 and 6.3 of the CA.

5. SHARED LEADERSHIP

The staff members are the **key pieces** of the QMS. People who assume responsibilities also take on leadership and their competences are based on the education and training they have received and the experience they have acquired.

The PC and the SC encourage all staff to be leaders in their own area of responsibility:

- by encouraging the active involvement of each member and teamwork;
- by supporting general commitment and continuous professional development;
- by sustaining development of both personal and organizational empowerment;
- by promoting internal communication, project-monitoring meetings and system reviews;
- by developing the policy on quality and its objectives.

6. TRAINING

To offer the professionals involved in the VES4US Consortium a work environment that helps them to face challenges, the project foresees several opportunities, incentives and training that will facilitate creativity, interdisciplinarity and the development of innovative technologies. The Consortium established continuous and integrated training actions at all levels of its structure to guarantee the development of research competencies as well as of organizational, management, interpersonal and communication skills.

The final goal is the enhancement of the career prospects of researchers and the cross-fertilisation of ideas and skills. Training is viewed henceforth both in terms of typical practical hands-on activities as well as any such action which could contribute toward the transdisciplinary development of the personnel involved in the project and the better functioning of research teams, as described in detail by the Training Plan (Deliverable 6.2).

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7. QUALITY MANAGEMENT SYSTEM (QMS)

This section describes the approach the organization uses for managing quality throughout the project's life cycle.

Scope

The VES4US QMS aims to support the project ensuring that:

- Research activities are performed efficiently and effectively, regularly documented and reported
- Deliverables are prepared to meet agreed-upon standards and requirements
- Non-conformities are identified and appropriate corrective actions are taken

VES4US QMS pays great attention to respect the needs of researchers and guarantee creativity and innovation development. It focuses on standardization and uniformity of procedures, but at the same time aims to be very light, dynamic, customised and research-oriented.

Processes

VES4US consortium has developed and implemented the QMS which is continuously updated and improved. Quality Management involves planning, doing, checking, and acting to improve project quality standards. Quality Management can be divided into three process groups: Quality Planning (QP), Quality Assurance (QA) and Quality Control (QC):

- Quality Plan applies to project research processes and project deliverables.
- Quality Assurance (QA) monitors and verifies that the processes for the management and production of the deliverables are executed and are effective.
- Quality Control (QC) monitors and verifies that project deliverables meet defined quality standards

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The processes and outcomes identified in the three phases are reported in Figure 4.

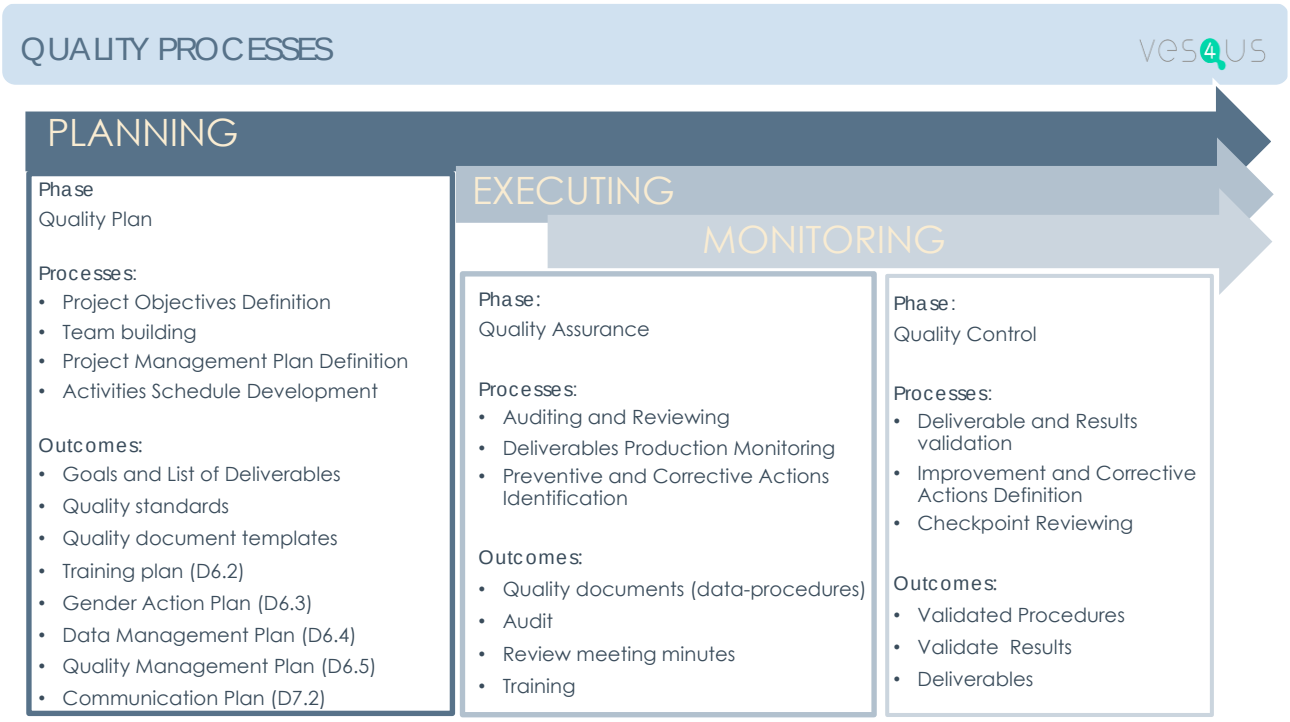

Figure 4. Schematic representation of QP, QA and QC processes and outcomes

8. QUALITY PLANNING (QP)

QP identifies the project objectives, the quality standards, the tools and documents for monitoring of the project processes and project performance and the monitoring plan for the project activities.

Project Objectives

The aim of VES4US project is to develop a radically new platform for the efficient production and functionalisation of EVs, which will enable for their exploitation as tailor-made products in the fields of nanomedicine, cosmetics and nutraceutics. A core aspect of the project is to focus on EVs from an identified natural source, which could constitute a more economically viable and sustainable source of EVs. This will allow the development of natural nanocarriers with unprecedented abilities for drug delivery in specific tissues such as brain, lung, skin, dendritic or tumor cells. The implementation of a customised and research-oriented Quality and Project management System will support the project in all its phases to promote

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achievement of project objectives, production and exploitation of high-quality results. The specific project deliverables and milestones are listed and described in the amended GA.

Quality Standards:

- Standardization and sharing of templates for data recording, work instructions and procedures
- Identification and sharing of standard operating procedures for key activities in the project
- Completion of Task activities according to the GANTT in the Grant Agreement (GA)
- Strict research collaboration inside the different Tasks and WPs as foreseen by GA
- Production of the deliverables and milestones in time according to the GA
- Interdisciplinary training according to the Training Plan (D6.2)
- Gender equality as described in the Gender Action Plan (D6.3)
- Findable, accessible, interoperable and reusable (FAIR) outputs as ensured in the Data Management Plan (D6.4)
- Dissemination and communication activities according to the Communication Plan (D7.2)
- Production of exploitable results

Quality Monitoring:

- Scientific Activities Reports
- Technical Meetings
- Internal Review Meetings
- Audits and Checklists
- Deliverable validation
- Communication and dissemination reports
- Internal Data archiving
- Exploitation Analysis and Reports
- Financial Reports

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Monitoring Plan:

According to the CA, both face-to-face and virtual meetings will be organised to review and evaluate progress with respect to the objectives and findings of the WPs. When needed specific meetings will be organised to focus on potential problems and to adopt alternative strategies in cases of unexpected pitfalls. The methodological approaches selected for the activities within the WPs will be reviewed during the meetings and harmonised where necessary.

Annual Internal Review meetings will be organised with all the participants to the projects, whereas review meetings with the EC will take place around months 14 and 37 of the project. Moreover, the AB will meet the VES4US Partners once per year.

An official agenda (where relevant) and meeting minutes shall be produced for all meetings and circulated to all Partners.

The PC (CNR-IRIB), together with the SC (ITS, ETHZ, CNR-IRIB and -IBBR) and WPLs will cooperate for ensuring that project deliverables comply with the planned activities, that they are correctly and timely communicated and that innovation thus produced is effectively translated into deliverables.

As described in the GA (article 6.4.2), the project coordinator (CNR-IRIB) takes care of collecting, reviewing and submitting reports, other deliverables and specific requested documents to the EC.

A special effort will be made to tailor the outcomes of the project in terms of relevant stakeholders (society and researchers in the different disciplines) and their future potential translation into marketable commodities or strategies (AB).

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9. QUALITY ASSURANCE (QA)

Scope

QA focuses on systematic activities and processes implemented within the QMS to provide confidence that the outcomes of the projects will fulfil the expected requirements. The goal of QA is to assure that any activity is performed well and once only, so to minimize waste of time, money and resources. QA is fundamental for all the WPs in VES4US project and should be implemented by all Partners while developing their tasks.

At this aim, VES4US Consortium shall:

- ensure that all policies, procedures, relevant regulations and codes of practice are effective and match the needs of the project;
- maintain conformity to set policies, procedures, regulations and codes of practice without significant deviations.
- regularly monitor and measure the quality of procedures and expected outcomes in view to ensure high quality standards, best value and continuous improvement.

Control of Quality records

To address these points the Consortium developed Quality documents (listed in the Section 11 of the present document and collected in the QMS Annexes), for a rigorous data documentation so as to prevent misuse, misinterpretation or confusion by secondary users, to facilitate understanding and reusing data and to assure reliability and reproducibility of the results. The Quality records have to be maintained by the Consortium and may be available when necessary. All Quality records shall be stored and kept confidential.

Internal Quality Audit

To assure that Quality documents are correctly used and project Quality is in fact being met and has been achieved, Internal Audits are performed by the QMs. The audits might consist in the examination of a representative sample of documentation and/or outcomes produced by each Partner or the collection of checklists filled in by project participants, according to their role, on the use of Quality documents and procedures and the deliverables production. Following the Audits, corrective, preventive and improvement actions will be

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defined by the QMs of the Project, approved by the PC and the SC and then performed. The result of the Internal Audit will be distributed to all Partners.

9. QUALITY CONTROL (QC)

QC refers to the operational techniques, procedures and methods that are used to determine that final products comply with the defined Quality Standards foreseen in the GA and outlined earlier in this document (Section 8). This may be done in regularly scheduled project status meetings or as necessary throughout the project lifecycle and at the end of any task activities, by taking advantage of the Quality templates and documents developed by the VES4US Consortium (see Section 11 and QMS Annexes).

QC of single SOPs, deliverables and milestones will be performed, according to the means of verification listed in the amended GA. More in detail, the TL in charge of the deliverable/milestone will perform the first document check. Document deliverable will be validated, in terms of quality, by the WPL to which the deliverable is belonging. If needed, the deliverable is forwarded to all Partners for additional comments and suggestions. PC and SC are in charge of the final QC of all the outcomes of the projects and its overall performance. PC is responsible for submission of the deliverable to the EC and to the distribution of the final version to all Consortium.

10. CONCLUSIONS

This document provides a description for all Partners involved in the VES4US project of the approach and methodologies that have been implemented within the project to ensure that Quality is considered as part of all the results produced. A great effort has been performed to define Quality tools and templates specifically suitable for such interdisciplinary and innovative research activities and to continually improve these tools collecting feedbacks by scientists performing the activities. The outcome is an agreed QMS with a light, dynamic, customised and research-oriented structure that might be an operating model for quality management of high interdisciplinary and innovation research projects

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11. LIST OF ANNEXES

Quality and Project Management Templates

1. Lab Notebook Template
2. SOP for Scientific Activities Template
3. SOP for Project Management and Support Activities Template
4. Deliverable Template
5. Meeting Agenda and Minute Template
6. Timesheet Template

Quality Assurance and Quality Control Templates

7. Lab Notebook Template Checklist
8. SOP Template Checklist
9. SOP Checklist
10. Deliverable Checklist
11. Audit Template

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