The final version of RiskGONE Database and Cloud Platform

DELIVERABLE 2.5

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Abstract

This deliverable describes and demonstrates the final version of the RiskGONE Database and the RiskGONE Cloud Platform, as they can be found online at https://search.data.enanomapper.net/projects/riskgone and http://www.enaloscloud.novamechanics.com/riskgone.html respectively.

The RiskGONE Cloud Platform serves as a comprehensive solution for the management and governance of Engineered Nanomaterials (ENMs). Powered by Enalos Cloud Platform (developed by NovaM), the deliverable includes short descriptions of the following section: the key technical components, features, potential use-cases of the system and demonstration of representative RiskGONE services.

The RiskGONE - eNanoMapper database is operational at https://search.data.enanomapper.net/projects/riskgone. The user guide was developed for web browser and programmatic access. The database includes FP7 NANoREG, ENPRA, MARINA, NanoTEST, Nanogenotox, H2020 Nanoreg2, caLIBRAte, GRACIOUS and RiskGONE WP4 and WP5 data. Access is granted to partners requesting access; web-based access and access for developers (API key and OAuth2) has been also provided.

In order to promote harmonization of data entry templates, while still allowing flexibility to adapt to different experiment details, IDEA developed an online Data Template Wizard, with ready-to-use Excel data entry templates and integrated ontology lookup. The *in vitro* assay templates follow the recommended layout provided by WP5 partners. Existing data entry templates for physicochemical and ecotoxicity studies are also included and have been further adapted through WP4 and WP6 collaboration and included into the Template Wizard.

The Template Wizard is being used by several H2020 projects. New data templates have been developed by RiskGONE and already reused by several other H2020 nanosafety, advanced materials and microplastic projects by developing their own templates for different types of assays. A collaborative publication on Template Wizard has been accepted for publication in Nature Protocols (led by IDEA and NILU).

Bioschemas and schema.org annotation has been implemented in the eNanoMapper database and the datasets can be found at Google Dataset. For reusability, first domain-specific maturity indicators need to be developed that formalize downstream us needs. These indicators specify what characteristics data should have to be useful to some use case, risk governance in particular. The NSDRA indicators have been implemented in the Template Validator, an online tool integrated in the Nanosafety Data Interface, allowing to convert filled in data templates into machine readable format.

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 814425.

List of Abbreviations

AB - Alamar blue

API – application programming interface

CFE – Colony Forming Efficiency assay

COMET assay - Single-cell gel electrophoresis (comet) assay

D - Deliverable

DB – Database

DLS - Dynamic Light Scattering

ELS - Electrophoretic Light Scattering

ENM – Engineered nanomaterial

ERM - European Registry of Materials

FAIR - principles of findability, accessibility, interoperability, and reusability

FF - Force-Field

HPRT - hypoxanthine phosphorybosyl transferase, mammalian cell HPRT gene mutation assay

IAM - Identity and Access Management

IDEA - Ideacosult Limited Liability Company, RiskGONE partner

JSON - JavaScript Object Notation

LCA – Life Cycle Assessment

M – RiskGONE project month

NILU - Norsk Institutt for Luftforskning, RiskGONE coordinator

NovaM – Novamechanics Ltd.

NPs - Nanoparticles

NSDRA - NanoSafety Data Reusability Assessment

NTA - Nanoparticle Tracking Analysis

OAuth2 - Open Authorization

OECD - Organisation for Economic Co-operation and Development

RDF - Resource Description Framework

RG – Risk Governance

SQL - Structured query language

SSbD - Safe-and-Sustainable-by-Design

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TEM - Transmission Electron Microscopy

TGs - Test Guidelines

UI - User Interface

UM - Maastricht University (Dutch: Universiteit Maastricht), RiskGONE partner

UNIVE - Ca' Foscari University of Venice

VCM - Volumetric Centrifugation Method

WP – Work Package

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1. Technical & Scientific progress

This deliverable reports on the results of Tasks T2.2 (Risk governance framework and decision trees), T2.3 (Database and data curation) and T2.4 (Implementation of the risk governance decision support tool), as they have been combined and integrated within the RiskGONE Cloud Platform.

1.1. RiskGONE database

RiskGONE - eNanoMapper database

As described in D2.2 data curation encompasses all the activities that are necessary throughout the process of extracting, organising, and entering data and knowledge into discrete formats within digital resources, and is central to the process of enabling data integration regardless of the size, scope or purpose of a given project.

RiskGONE - eNanoMapper database was launched at the beginning of the project at https://search.data.enanomapper.net/projects/riskgone, with content currently includes data from FP7 NANoREG , NanoTEST, MARINA, ENPRA, NanoGenotox and H2020 NANoREG2, caLIBRAte, GRACIOUS projects, as well as newly generated data from RISKGONE partners (WP4, Characterisation, *in Vitro* Dosimetry and Environmental Fate, and WP5, Human Hazard Assessment). The RiskGONE data is maintained in a dedicated eNanoMapper database instance for the RiskGONE project, accessible only by project partners. Access was granted to 49 people from 18 RiskGONE partner organisations.

The RiskGONE – enanoMapper database is part of the Nanosafety Data Interface (Jeliazkova et. al., 2021) https://search.data.enanomapper.net/ , integrates a number of project specific (nano)material safety databases, implemented as eNanoMapper database instances. Click on the project icon launches a login page (Figure 1).

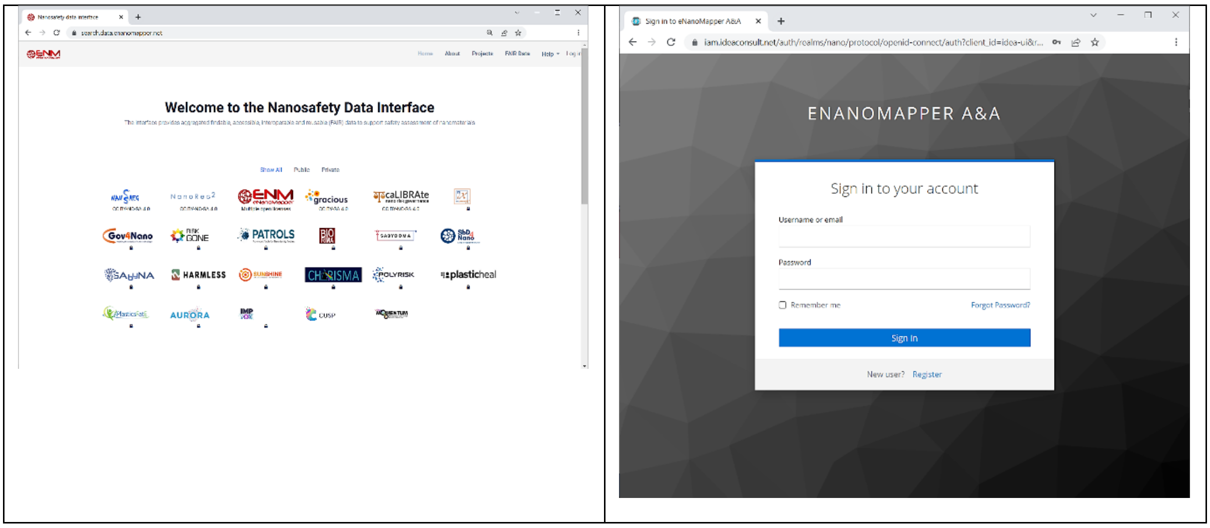

Figure 1. The Nanosafety Data interface login page have been updated, there is now single login page for all projects including RiskGONE. The RiskGONE – eNanoMapper database is a dedicated eNanoMapper database instance, accessible only to project partners.

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On successful login, the RiskGONE starting page appears (Figure 2). If login is not successful, or the user does not have rights to access RiskGONE database, an error message appears at the bottom right.

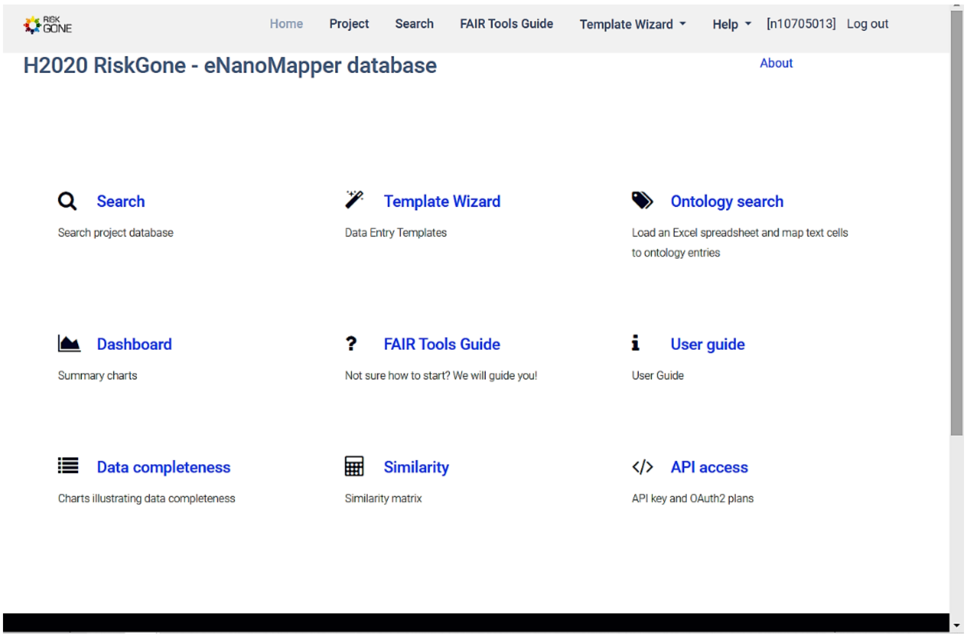

Figure 2. RiskGONE – eNanoMapper database starting page, providing entry points to different functionalities (e.g., Search, Dashboard, Template Wizard, etc) The API access links provides information for programmatic access, useful for integration with the RiskGONE cloud platform.

Material identifiers

D2.2 describes the engineered nanomaterials (ENMs) identifiers defined by the European Registry of Materials Identifiers (ERM identifiers, Figure 3) introduced by the NanoCommons project and were adopted by H2020 RiskGONE, NanoSolveIT, NanoFASE, caLIBRAte, SbD4Nano, POLYRISK, HARMLESS and SABYDOMA projects. The ERM identifiers are maintained at https://github.com/NanoCommons/identifiers.

A document defining ERM identifiers for RiskGONE materials was prepared by UM and is available at NILU server ("Nanomaterial identifiers and Guidance on using these identifiers in RiskGONE research output" https://nilu365.sharepoint.com/:w:/r/sites/Project-RiskGONE/_layouts/15/doc2.aspx?sourcedoc=%7B0285F765-13EB-4437-9600-5066C3C1315F%7D&file=Nanomaterial%20identifiers%20and%20Guidance%20on%20using%20these%20identifiers%20in%20RiskGONE%20research%20output_v1.4.docx&action=edit&mobileredirect=true&wdPreviousSession=c870707a-1359-4735-b760-634fb0b7616b&wdOrigin=TEAMS-ELECTRON.teams.undefined). The data include material composition and basic physicochemical properties from data sheets. This information was entered into Material composition template (10.5281/zenodo.7751340) and imported into RiskGONE eNanoMapper database using the eNanoMapper FAIRification workflow (Kochev et. al., 2020).

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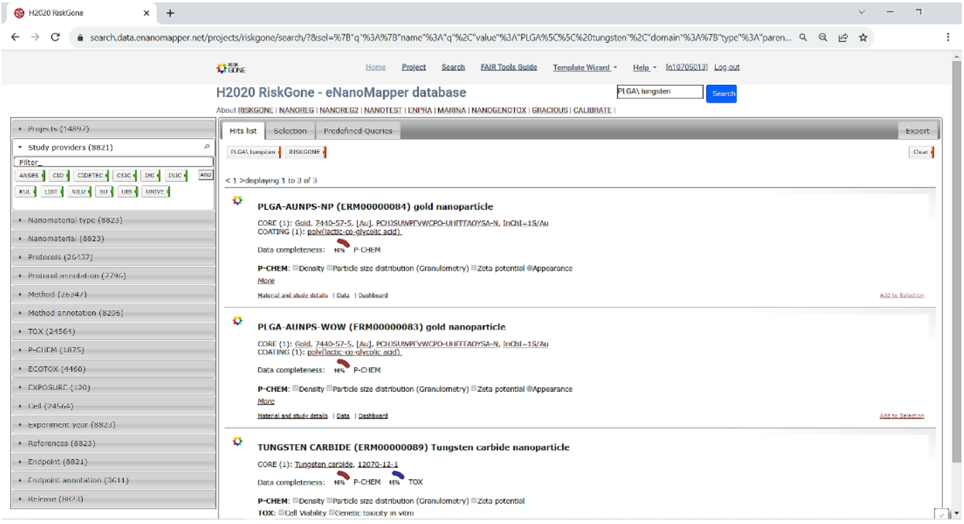

Figure 3. RiskGONE database search page, showing materials using ERM identifiers, e.g., ERM00000089 for Tungsten Carbide

Data entry workflow tools

Within RiskGONE and together with other projects IDEA developed a Template Wizard to easily compile the required metadata to accompany data and align it to existing community standards and databases, thereby streamlining several aspects of FAIR. These templates have been implemented as an online tool, thereby enabling re-use of the downloadable meta(data) capture templates by the research community.

The data entry templates were collaboratively created with active involvement from WP4, WP5 and WP6 partners who provided data. Once the layout and content were agreed, the templates were integrated into the Template Wizard, which is an online tool allowing sharing and downloading of dynamically customizable templates. The tool is designed to be user-friendly, attractive to data providers and to improve awareness and re-use of existing templates by new projects and when adding new (or extended) end-points. The online template validator allows self-evaluation of the template (to ensure mapping to the data schema and machine-readability of the captured data) and transformation by the open-source parser into a machine-readable format (e.g., json or rdf) compliant with the FAIR principles.

Templates for physicochemical characterization, hazard assessment (cell viability, genotoxicity, environmental organism dose response tests etc.) are available. RiskGONE partners have provided layout specifications for physicochemical characterization of NMs size via particle size analysis by Transmission Electron Microscopy (TEM), Dynamic Light Scattering (DLS) and Nanoparticle Tracking Analysis (NTA), zeta potential by Electrophoretic Light Scattering (ELS) and effective density by Volumetric Centrifugation Method (VCM), assessment of endotoxin contamination of NMs, assays for hazard assessment including genotoxicity tests (Comet assay, micronucleus and HPRT tests) cytotoxicity assays such as the Colony Forming Efficiency (CFE) assay, Alamar blue (AB) cell viability assay and bio-impedance, and ecotoxicity assays including Daphnia immobilization (OECD TG 202) and Daphnia reproduction (OECD TG 211).

The Template Wizard can be used independently of the eNanoMapper database, enabling data producers to create FAIR data resources for upload to any repository. The harmonized templates aim to

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make data presentation, interlaboratory comparisons, and meta-analyses more reliable and to streamline the evaluation and regulation process.

The over a decade of experience in nanosafety data collection was utilized by RiskGONE together with other ongoing projects. All this collaborative effort in co-creation of template wizard was described in the paper *Template Wizard: co-creation of data collection templates for safety assessment of (nano)materials* by Jeliazkova et al. which is now accepted for publishing in Nature Protocols journal. All steps how the RiskGONE templates for data collections were co-created is described in D2.2 and illustrated in Figures 4-6.

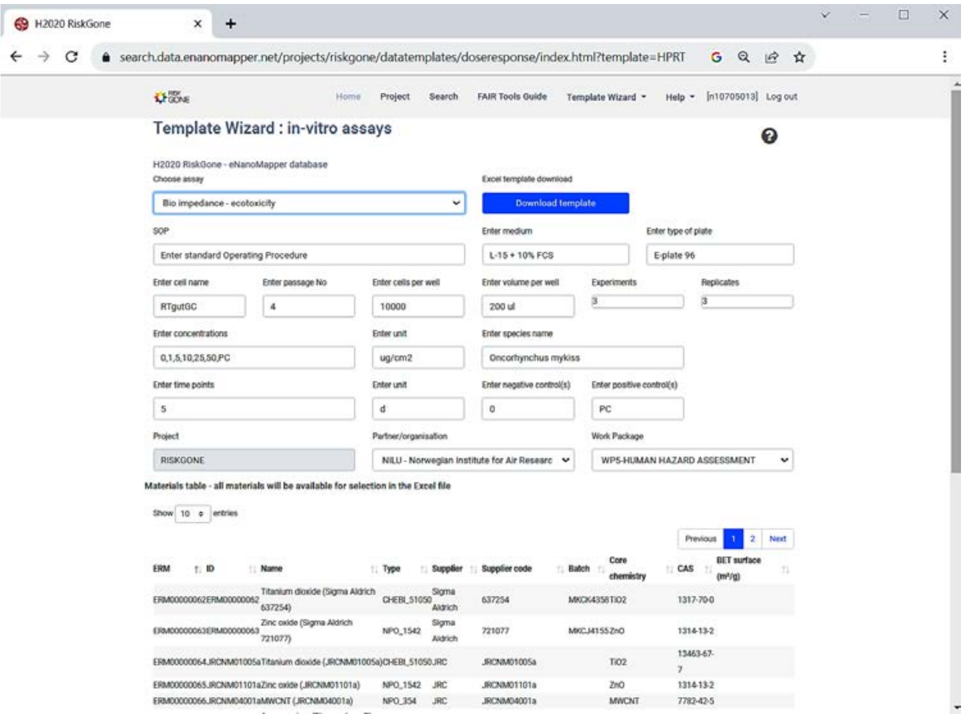

Figure 4. RiskGONE – eNanoMapper database Template Wizard, showing Bioimpedance (ecotoxicity) download page. At the bottom RiskGONE materials with ERM (and other) identifiers are also shown.

To facilitate access to the growing number of templates, the Template Wizard gallery page was redesigned as an interactive table, in which users can search for templates by type or category or free text. For example, Figure 5 shows the available templates, filtered by the text "riskgone".

The individual templates are accessed by clicking on the link in the first column (Template Wizard link).

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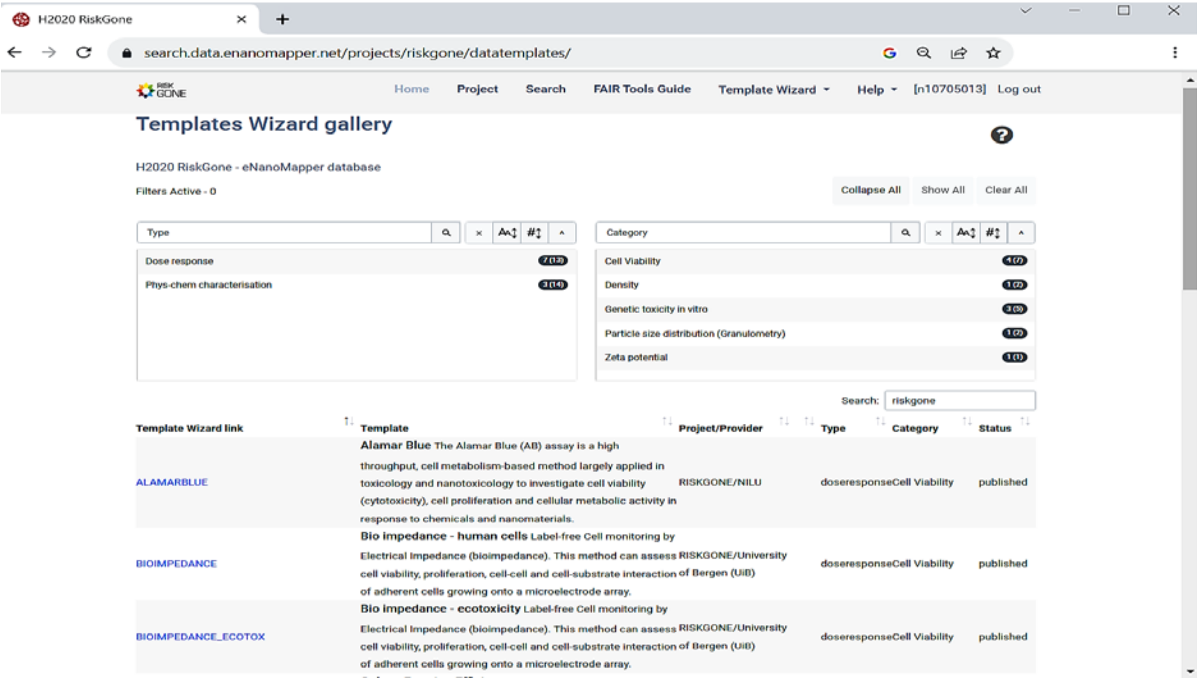

Figure 5. RiskGONE – eNanoMapper database Template Wizard gallery, listing 10 templates, developed by RiskGONE

The question mark at the top right of the Template Wizard gallery page leads to a help page on the Template Wizard.

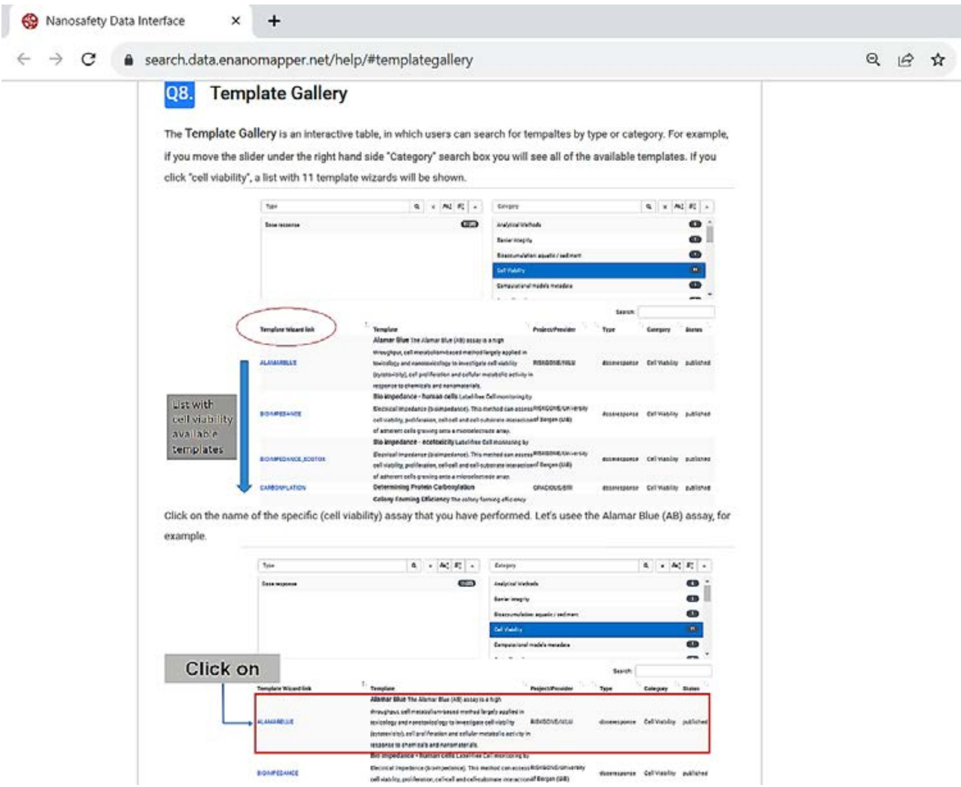

Figure 6. The Template Wizard help page.

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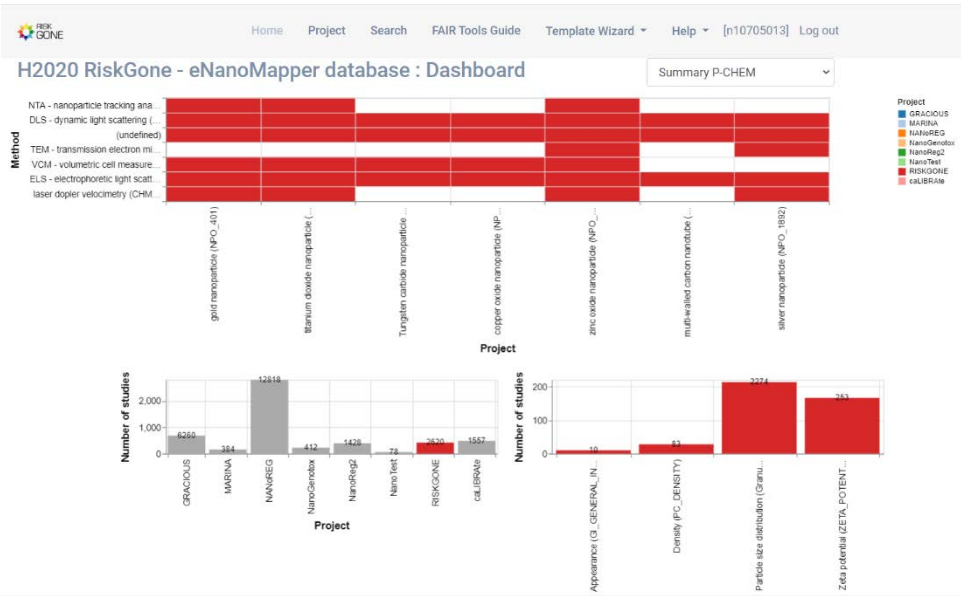
While the customized data entry templates downloaded from the Template Wizard can be directly submitted to an arbitrary data repository with the intention of human (re)use, the main reason for developing the approach described here is the ability to convert the templates to machine readable formats, enabling data indexing and therefore query and broader findability, generating automatic ontology or schema annotations (for example, using the NanoSafety Data Reusability Assessment (NSDRA) tool at https://nsdra.org/ which compiles domain-specific FAIR data minimal requirement and maturity indicators from several sources and assess template compliance with these indicators) and ultimately data analysis.

Data content

The WP4-6 data were imported into RiskGONE eNanoMapper database using the eNanoMapper FAIRification workflow. A summary of the data is available at https://search.data.enanomapper.net/projects/riskgone/dashboard/ (Figure 7 and Figure 8); full data can be queried and retrieved via https://search.data.enanomapper.net/projects/riskgone/search.



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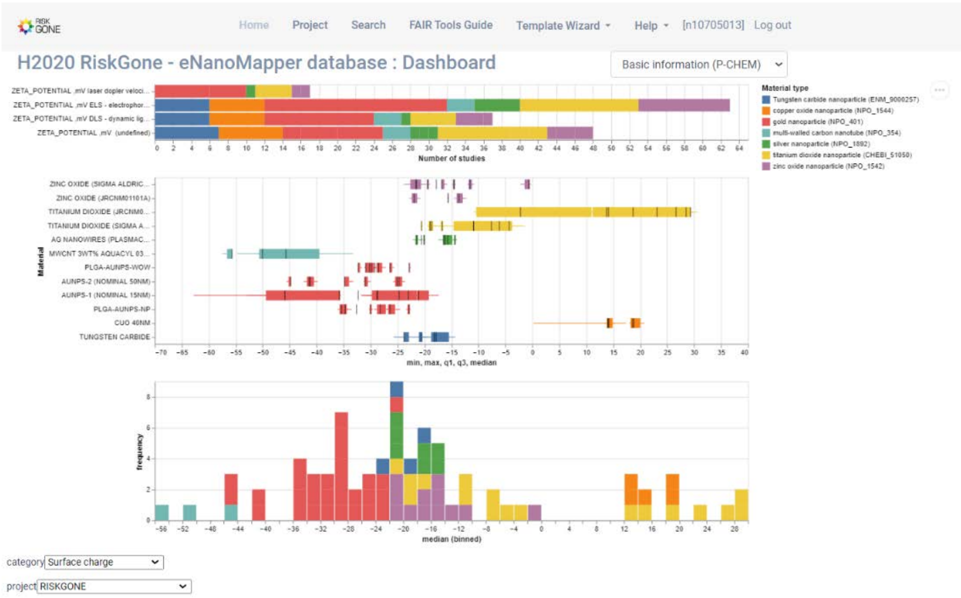

Figure 7. RiskGONE – eNanoMapper database physicochemical characterisation overview (top) and surface charge distributions of RiskGONE materials (bottom) available at https://search.data.enanomapper.net/projects/riskgone/dashboard/ .

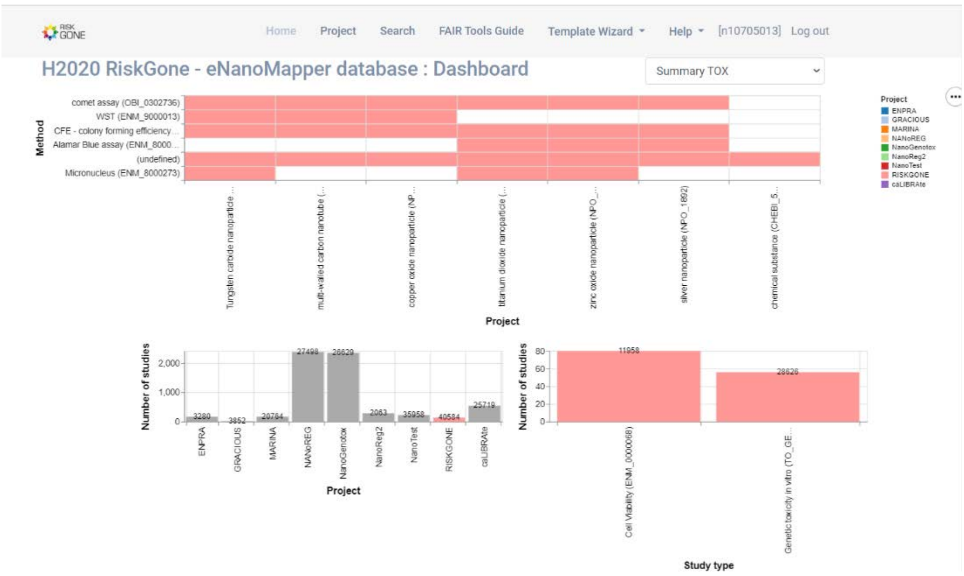

Figure 8. RiskGONE – eNanoMapper database in-vitro data overview, available at https://search.data.enanomapper.net/projects/riskgone/dashboard/.

Jupyter notebooks to support data analysis and data retrieval are available in a private GitHub repository (Figure 9).

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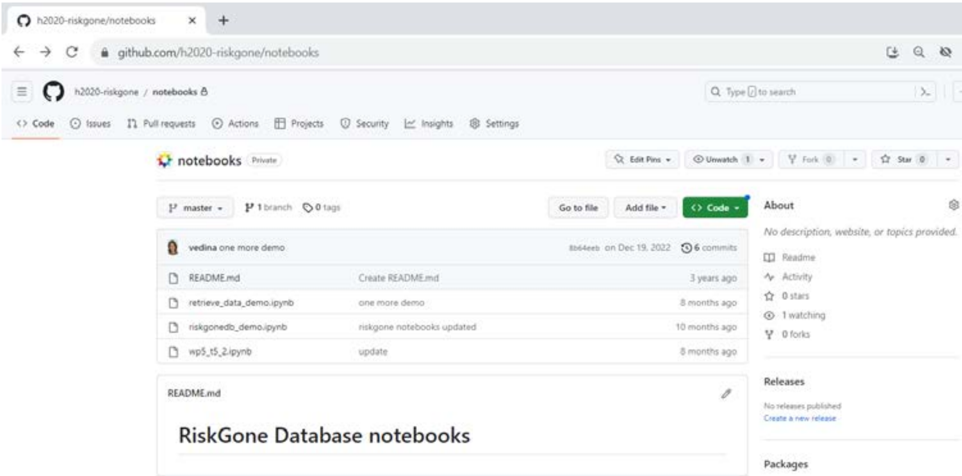

Figure 9. Jupyter notebooks to demonstrate programmatic data retrieval for data analysis at https://github.com/h2020-riskgone/notebooks.

Summary of the data generated by RiskGONE partners and imported into the RiskGONE eNanoMapper database so far are provided on Figure 10. Full data can be queried and retrieved via https://search.data.enanomapper.net/projects/riskgone/search and the corresponding API endpoints.

Figure 10. RiskGONE – eNanoMapper database interactive overview, available at https://search.data.enanomapper.net/projects/riskgone/dashboard/. Material ERM identifiers and ontology annotation of material and method types are shown, as retrieved from the database.

Data usage and FAIRness

- While data can be queried, retrieved and viewed through a web browser, programmatic access is necessary to support modelling and link to the RG Cloud platform. The RiskGONE eNanoMapper database can be programmatically accessed via an API. Standard Authentication mechanisms as API key and OAuth2 are provided with detailed explanation in D2.2 and online help at RiskGONE database and eNanoMapper API portal pages (Figure 11).

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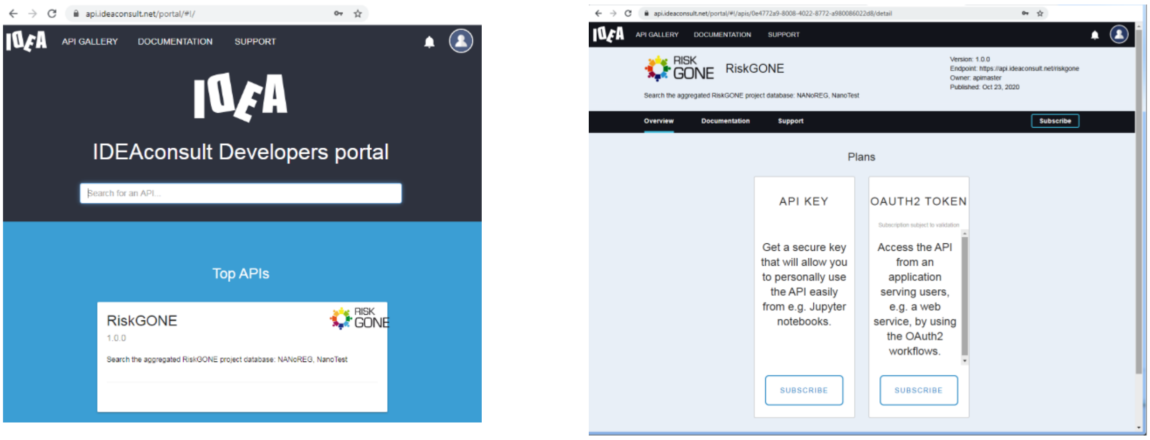

Figure 11. RiskGONE – eNanoMapper database API access portal at api.ideaconsult.net with interactive OpenAPI3 documentation and access plans

Data usage, FAIRness and utility for risk assessment and governance

The RiskGONE database has been developed for containing data on human and environmental health and safety of ENMs, that can be used for performing various activities under the RG framework that is being developed in T2.2. RG activities include risk assessment and management, risk benefit assessment, human and ecotoxicological hazard assessment among others. All these activities will be supported by the related models and tools, as identified in WP2-WP3-WP4-WP5-WP6 of the project. In this view, the objective of the database development in T2.3 is to provide the users of the RG framework and the related models/tools with reliable datasets which can be used for performing RG of ENMs. Scenario building has been performed under T2.5, where the case studies for the demonstration of the RG framework have been formed by the project consortium. The database integrates existing datasets with data that are collected during the project duration, as part of the work in the experimental WPs (WP3-WP6).

1.2. RiskGONE Cloud Platform

The RiskGONE Cloud Platform (http://www.enaloscloud.novamechanics.com/riskgone.html, Figure 12) addresses the need for a user-friendly interface that can produce in few steps property calculations for ENMs through web-services. The RiskGONE Cloud Platform hosts all the scientific outputs of the RiskGONE project, organized in various categories and sections, that allows easy navigation to all interested stakeholders. The RiskGONE services are briefly described below. The RiskGONE Cloud platform includes the following sections (Figure 13):

- Services: A collection of services and tools developed by the RiskGONE partners.
- Decision trees: List of the various decision trees and links to the respective pages.
- TGs – Guidelines: A collection of information from the experimental work packages of the project, as well as guidelines for risk-benefit assessment, including socio-economic assessment, ethics, LCA and more.
- Project Deliverables: List of RiskGONE deliverables.

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- Data and DBs: Access to the RiskGONE eNanoMapper instance and other relevant databases.
- Regulatory information: An overview of nanosafety definitions and regulatory information.
- RG framework overview / Library of tools: An overview of the RiskGONE risk governance framework and Library of relevant tools.
- Safe-and-Sustainable-by-Design (SSbD): An overview of the state-of-the-art of scientific literature and information on Safe-and-Sustainable-by-Design (SSbD).

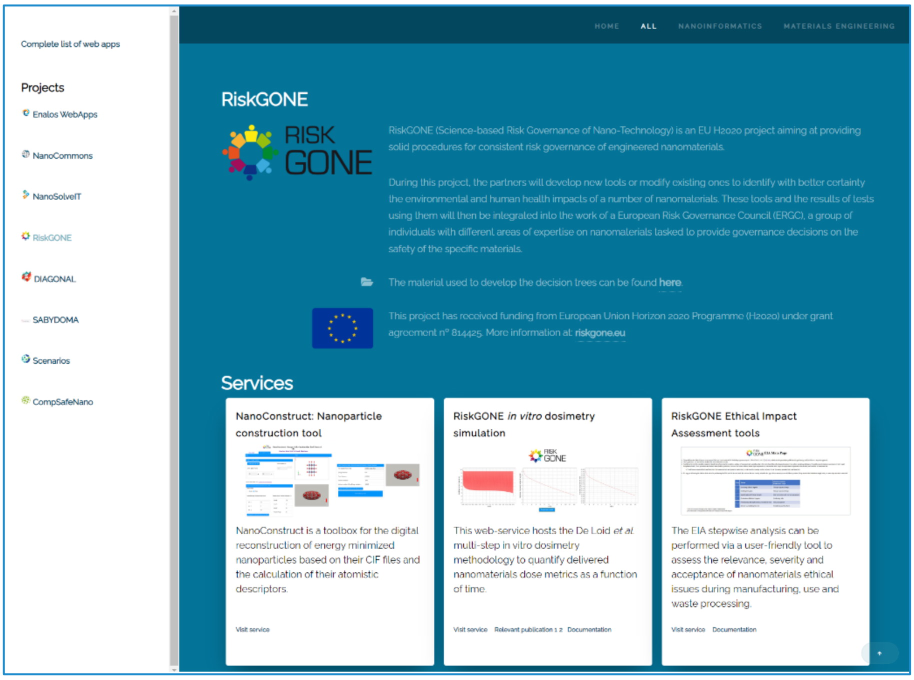

Figure 12: Screenshot of the RiskGONE platform (http://enaloscloud.novamechanics.com/riskgone/).

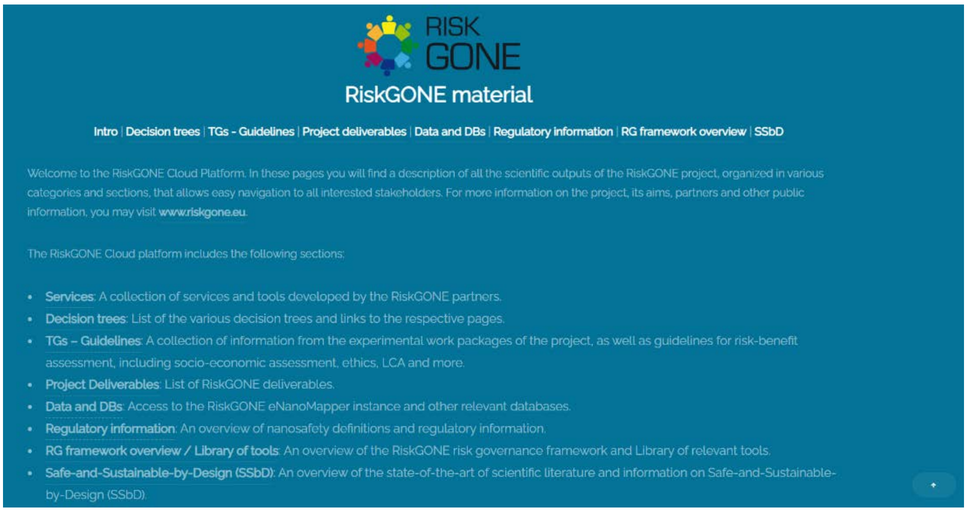

Figure 13: Screenshot of the RiskGONE Cloud Platform material page. Stakeholders can browse the different pages and access the RiskGONE material.

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Technical Details on RiskGONE Cloud Platform powered by Enalos Cloud Platform

The RiskGONE Cloud Platform serves as a comprehensive solution for the management and governance of ENMs. Powered by Enalos Cloud Platform (developed by NovaM), this section explores the key technical components, features, and potential use-cases of the system.

Architecture Overview

The RiskGONE Cloud Platform, powered by Enalos Cloud Platform, is constructed around a modern, modular architecture that prioritizes both robust functionality and user-centric design. The architecture has been thoughtfully planned to incorporate four critical elements: Wildfly Application Server, Keycloak Server, MySQL Database Management System, and Docker Images. Each of these components plays a unique role in the system and is specifically designed to be both scalable and interoperable. This choice of architecture offers a number of advantages, including:

Modular Design

The modular nature of the architecture means that each component — whether it is the application server, identity management system, database, or microservices — can be developed, deployed, and maintained independently of the others. This modularity makes it easier to upgrade individual elements, fix bugs, or even replace components with minimal impact on the overall system. It also speeds up the development process, as multiple teams can work simultaneously on different modules.

Scalability

Built with scalability in mind, each component can be easily scaled up or down to match the requirements of the project at any given time. For instance, the Wildfly Application Server is well-known for its high-performance capabilities and can be horizontally scaled to accommodate an increasing number of users. Similarly, the MySQL databases can be sharded or clustered to improve read/write capabilities, and Docker images can be orchestrated via Kubernetes for better resource management.

Interoperability

Interoperability is a key feature of the RiskGONE Cloud Platform. It is designed to seamlessly integrate with other databases, tools, and external APIs, thus ensuring that the platform remains flexible and can adapt to the changing landscape of ENM governance. The use of industry-standard technologies like SQL for database management and OAuth 2.0 for identity management also makes it easier to integrate new features or connect with existing systems.

User Interaction

A primary objective of the architecture is to facilitate seamless user interaction. Wildfly provides a robust yet lightweight application server where the interaction point between the users and the system's web applications is located. By employing an intuitive User Interface (UI) and responsive design, the platform aims to offer a user-friendly experience across various devices and operating systems.

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Data Security and Management

Ensuring data security and robust management capabilities are fundamental to the architecture. The Keycloak Server manages Identity and Access Management (IAM), implementing multiple layers of security protocols to ensure that only authorized personnel can access sensitive information. The use of MySQL ensures data integrity while also offering robust backup and recovery options. Docker images add an additional layer of security by isolating applications into containers, thus minimizing the risks associated with unauthorized data access.

By harmoniously integrating these features into a unified architectural framework, the RiskGONE Cloud Platform achieves its primary objectives of scalability, robustness, and ease of use, while also ensuring stringent data security and management protocols.

Key Components

The RiskGONE Cloud Platform as an Enalos Cloud Platform instance is built around four cornerstone technologies – Wildfly Application Server, Keycloak Server, MySQL Database Management System, and Docker Images. Each component plays an instrumental role in ensuring the platform's performance, security, and flexibility. Here we focus on the Wildfly Application Server to provide an in-depth understanding of its functionalities and importance in user interaction.

Wildfly Application Server

Role and Functionalities. The Wildfly Application Server acts as the backbone of the RiskGONE Cloud Platform, serving as the primary node that bridges the gap between end-users and the platform's diverse web applications. It is configured to manage the execution environment for the Java applications that make up the web services. Key functionalities include:

- **Resource Allocation**: Wildfly dynamically allocates system resources like memory and CPU cycles for running applications, ensuring optimal performance.
- **Request Handling**: It handles all incoming HTTP and HTTPS requests and directs them to the appropriate web application for processing.
- **Session Management**: Wildfly oversees user sessions, ensuring a seamless user experience by maintaining state information as users interact with various applications.

Importance in User Interaction. The Wildfly Application Server plays a pivotal role in shaping the user experience on the RiskGONE Cloud Platform for several reasons:

- **Speed and Efficiency**: Designed for high-performance computing, Wildfly ensures quick load times for applications and rapid data retrieval, making the user experience fast and efficient.
- **Security**: It incorporates various security protocols like SSL/TLS for encrypted connections and integrates with the Keycloak Server for robust Identity and Access Management, thus securing user interactions.
- **Seamlessness**: Its ability to maintain state information across different web applications ensures that users have a seamless experience, free from the inconvenience of repeated logins or data entries. (no user login needed or data entries)
- **Resource Optimization**: By dynamically allocating resources, it ensures that applications run smoothly even under high user load, thus maintaining a consistent and responsive user experience.

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Docker Images

Role and Functionalities.

Docker Images form a critical component in the RiskGONE Cloud Platform's architecture. They enable a microservices-based approach that is instrumental in achieving modular development and deployment. Here are some of the functionalities Docker Images bring to the platform:

- **Isolation**: Each Docker image provides an isolated environment for running applications, meaning that each microservice is completely self-contained. This enables developers to build, update, and scale each service independently of the others.
- **Portability**: Docker images encapsulate all of the dependencies an application needs to run. This ensures that applications behave consistently across different development, staging, and production environments.
- **Resource Efficiency**: Docker enables efficient use of system resources as multiple containers can share the same OS kernel, unlike traditional virtual machines that require their own operating system.
- **Service Orchestration**: Through orchestration tools like Kubernetes or Docker Swarm, Docker Images can be automatically deployed, scaled, and managed. This is essential for maintaining system reliability and scalability.

Security Features.

Docker Images are configured to offer robust security features that protect the integrity of the platform and its data:

- **Container Isolation**: Docker provides a high degree of isolation between containers, ensuring that applications running in different containers cannot interfere with each other. This is particularly important for multi-tenant environments and for isolating potentially vulnerable services.
- **Immutable Infrastructure**: Once a Docker image is built, it does not change, meaning that there is a strong guarantee of consistency across different deployment environments. This immutability reduces the risk of unauthorized changes or security vulnerabilities.
- **Secure Communication**: Docker can be configured to enforce secure, encrypted communications between containers and between containers and external services, further reducing the surface area for potential attacks.
- **Access Control**: Through integration with the platform's Identity and Access Management system (provided by Keycloak), Docker containers can have fine-grained access control policies, ensuring that only authorized personnel can interact with each service.

Advantages and Features

The RiskGONE Cloud Platform offers a comprehensive set of advantages and features that set it apart as a robust, secure, and user-friendly system. Each advantage serves as a cornerstone for building a system that meets the demands of modern ENM governance and data management. The following subsections detail these advantages:

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Modularity

Easy Updates. Modularity allows for individual components to be updated independently, without causing disruptions to other parts of the system. This ensures that new features or security patches can be rolled out smoothly, without affecting the system's overall performance.

System Modifications. Modular architecture also facilitates system modifications. Whether it is a minor change to a single module or a major overhaul involving several components, the modular approach ensures that the impact is localized, thereby reducing system downtime and potential bugs.

Scalability

Scaling of Services. The platform is designed to scale both vertically and horizontally, depending on the needs of the project. Services can be added or expanded quickly, allowing the platform to handle increased loads efficiently.

Resource Allocation. Smart resource allocation algorithms ensure that each service uses just the resources it needs, optimizing system performance without waste. This makes it easier to scale resources down during periods of low demand, reducing operational costs.

Security

Advanced IAM. Through the integration of Keycloak Server, the platform offers advanced Identity and Access Management (IAM) features. This ensures that each user's identity is rigorously authenticated and authorized, enhancing data security.

Containerization Features. Security is also enhanced through Docker's containerization features, which isolate applications and services in a controlled environment, minimizing risks associated with unauthorized data access or system vulnerabilities.

Flexibility

Easy Addition and Removal. The platform's architecture allows for the easy addition and removal of services and functionalities. This is crucial for adapting to new requirements or for phasing out obsolete features, all without affecting the system's core functions.

Dynamic Configurations. Administrators can make dynamic changes to the configuration of services and features, adapting the platform to meet specific user needs or to comply with changing regulations.

Interoperability

Seamless Integration. Designed with interoperability in mind, the platform can seamlessly integrate with various external databases, tools, and APIs. This ensures that the platform remains adaptable and can easily fit into existing enterprise ecosystems.

Potential Use Cases

The RiskGONE Cloud Platform has been designed to cater to a wide range of applications and stakeholders, especially emphasizing the governance of ENMs. Its modular, secure, and interoperable

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nature makes it a powerful tool for academic research, industrial applications, regulatory oversight, and public awareness. Below, we detail how each of these sectors can benefit from the platform's features:

Academic Research

Comprehensive Data Repositories. The platform offers comprehensive databases, including experimental results, risk assessments, and material properties, that are crucial for academic research into ENMs. Researchers can draw upon this repository for comparative studies, meta-analysis, and new discoveries.

Research Tools. The advanced analytical tools provided by the platform facilitate simulations, data modelling, and other computational work needed for cutting-edge ENM research.

Industrial Applications

Risk Assessment. Industries that manufacture or use ENMs can utilize the RiskGONE platform for comprehensive risk assessments. It provides tools and guidelines for evaluating the safety of new materials, ensuring compliance with existing standards.

Compliance and Reporting. The platform's guidelines and decision trees make it simpler for industries to adhere to local, national, and international regulations governing ENMs, thereby streamlining the compliance and reporting process.

Regulatory Oversight

Policy Development. Policymakers can tap into the platform’s wealth of data and tools to craft more effective and evidence-based regulations governing the safe use and disposal of ENMs.

Regulatory Enforcement. With access to current and reliable data, regulatory bodies can better monitor industry practices, ensuring adherence to ENM-related safety guidelines and taking corrective actions when necessary.

Public Awareness

Educational Resource. The platform's user-friendly interface and comprehensive guidelines can serve as an excellent educational resource for the general public, enhancing awareness about the risks and benefits associated with ENMs.

Transparency. By providing open access to research data and regulatory guidelines, the RiskGONE platform helps instill public confidence in the governance processes surrounding ENMs, thus contributing to social license to operate. The RiskGONE Cloud Platform is not just a technical solution but a multifaceted platform that addresses the complex governance challenges associated with ENMs. By offering specific tools and resources for academic research, industrial applications, regulatory oversight, and public awareness, it plays a pivotal role in promoting safe and responsible use of nanomaterials.

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NanoConstruct toolbox

Computational tools have been widely used for predicting material properties in the past. Nowadays, the rapid development of computers has increased interest in these tools due to their speed and low cost compared to physical experiments. Furthermore, mixing nanomaterials with other materials to create sols, emulsions, gels, or foams can lead to improved material properties. Efficient computational screening techniques are needed to quickly discover the most promising combinations. Atomistic simulations can be used for the screening process after digitally reconstructing the systems to be investigated. However, digitally reconstructing systems containing secondary phases, such as Nanoparticles (NPs) is not a straightforward task. NanoConstruct, a toolbox hosted in the RiskGONE Cloud Platform (Figure 14) powered by the Enalos Cloud Platform (http://enaloscloud.novamechanics.com/riskgone/nanoconstruct/), has been developed to overcome this barrier. NanoConstruct uses Crystallographic Information Files available on crystallographic databases as input to geometrically reconstruct crystalline NPs, while maintaining stoichiometry by removing excess atoms on the surface. Additionally, NanoConstruct searches the OPENKIM database and selects the Force-Field (FF) that is less generic and simultaneously contains every chemical element of the NP. The option to select a different OPENKIM FF than the suggested one is also available. After the FF selection, energy minimization is applied to investigate the NP's stability, while several descriptors are calculated for subsequent Machine Learning analysis.

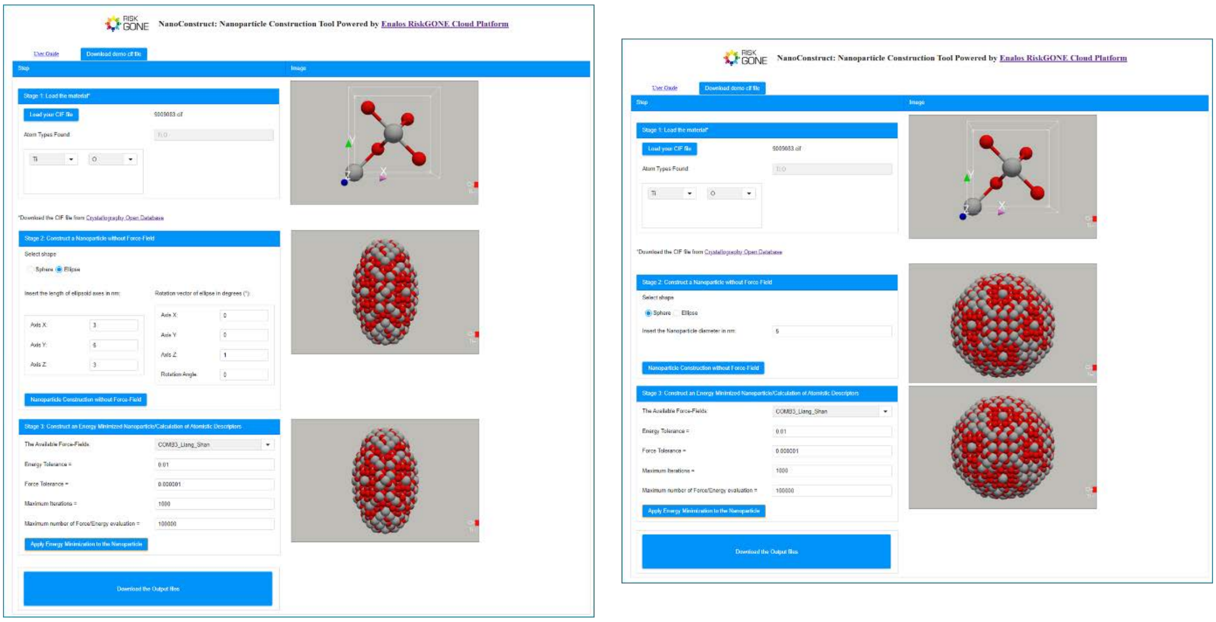

Figure 14: Screenshots of the NanoConstruct toolbox in RiskGONE Cloud Platform.

RiskGONE in vitro dosimetry simulation

ENM toxicity testing using in vitro assays requires the ENMs to be dispersed in cell culture medium and applied to multiwell cell culture plates. There are numerous techniques and protocols for dispersing ENMs in aqueous media that should be harmonized. Various endpoints are measured during in vitro testing following the exposure, commonly lasting for 24-48 h, and the dose-response relationship is commonly reported. However, the effective dose is not necessarily equal to the nominal dose, since the cells seeded in the plate wells will only react with the ENMs that reach the bottom of the plate. Therefore,

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for the correct reporting of the ENM dosage regimen, the nominal dose should be adjusted. De Loid *et al*. addressed the aforementioned issues by developing a multi-step in vitro dosimetry methodology to quantify delivered dose metrics as a function of time which consists of three interconnected parts: 1) ENM dispersion preparation; 2) ENM dispersion characterization; 3) numerical transport modelling to derive the delivered dose metrics. Our work falls into the category of the numerical transport modelling to derive dose metrics. We developed a user-friendly web-based application, termed as "*in vitro* dosimetry application" (Figure 15) designed especially for non-expert users. (Cheimarios et. al. 2022). The *in vitro* dosimetry application is based on the Distorted Grid fate and transport model and calculates the mass, number and surface area-based concentrations in the cellular microenvironment throughout the duration of the exposure. (http://www.enaloscloud.novamechanics.com/riskgone/InVitroDosimetry/)

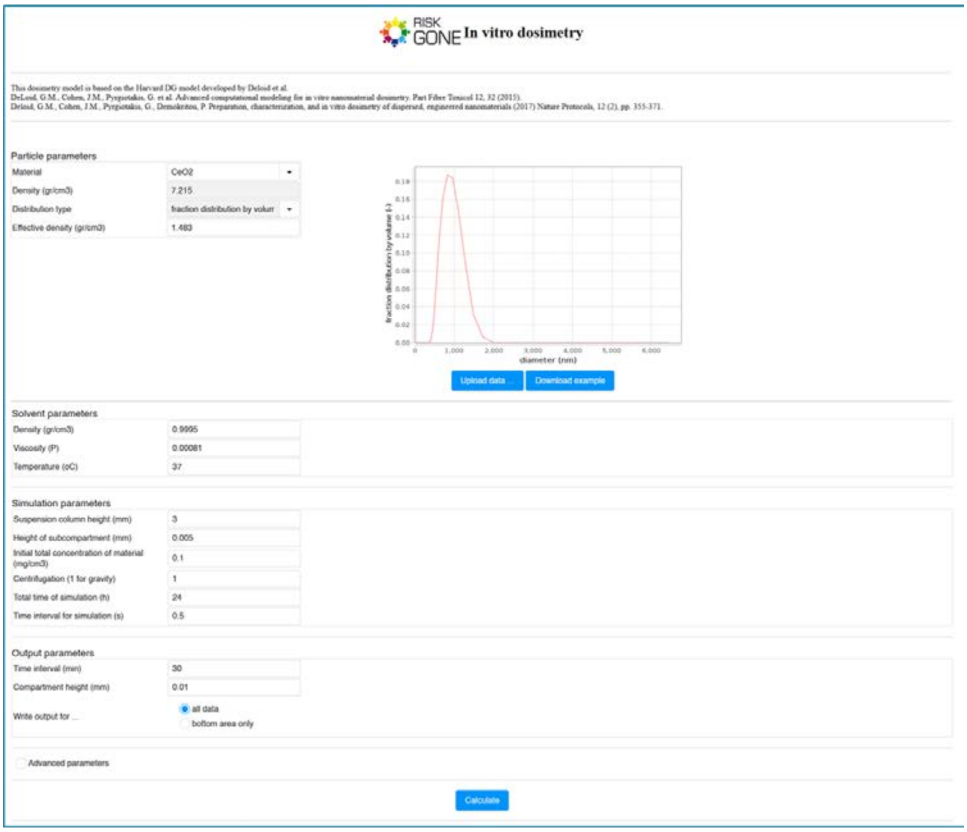

Figure 15: Screenshot of the *in vitro* dosimetry application.

2. Deviations from Description of Action

No deviations.

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3. Conclusions

Deliverable 2.5, as a software demonstrator document, reports the main functionalities and technical solutions used for the development and integration of the final version of the RiskGONE Database and the RiskGONE Cloud Platform, as they can be found online at https://search.data.enanomapper.net/projects/riskgone and http://www.enaloscloud.novamechanics.com/riskgone.html respectively.

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