SCIENCE-BASED RISK GOVERNANCE
OF NANO-TECHNOLOGY

RISK GONE

Report on the RG framework and decision trees

DELIVERABLE 2.3

Due date of Deliverable:	30.06.2022
Actual Submission Date:	31.07.2023
Responsible partner:	UNIVE, Italy
Report Author(s):	Panagiotis Isigonis, UNIVE
Reviewed by:	Ineke Malsch, MALSCH; Ivana Vinković Vrček, IMI; Dalila Antunes, FS; Mihaela Roxana Cimpan, UiB; Maria Dusinska, Eleonora Longhin, NILU
Nature:	R (Document, report)
Dissemination Level:	PU = Public

Call:	H2020-NMBP-13-2018
Topic:	Risk Governance of nanotechnology
Project Type:	Research & Innovation Action (RIA)
Name of Lead Beneficiary:	NILU, Norway
Project Start Date:	1 January 2019
Project Duration:	56-Months

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

Document History

Version	Date	Authors/ who took action	Comment	Modifications made by
0.1	04-11-2021	Panagiotis Isigonis (UNIVE)	Draft structure of the deliverable sent to WP2 partners	Panagiotis Isigonis (UNIVE)
0.2	08-12-2021	Panagiotis Isigonis (UNIVE)	First Draft sent to WP2 partners	Panagiotis Isigonis (UNIVE)
0.3	26-05-2023	Panagiotis Isigonis (UNIVE)	Second Draft sent to Project Management Board, Advisory Board Members and WP2 partners	Panagiotis Isigonis (UNIVE), Ineke Malsch, (MALSCH), Ivana Vinković Vrček (IMI), Dalila Antunes (FS), Mihaela Roxana Cimpan (UiB)
0.4	27-07-2023	Panagiotis Isigonis (UNIVE)	Third draft	Panagiotis Isigonis (UNIVE)
0.5	30-07-2023	Maria Dusinska (NILU)	Internal review	Eleonora Longhin, PMO (NILU)
1.0	31-07-2023	Eleonora Longhin, PMO (NILU)	Submitted to Commission	

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

Abstract

This deliverable contains the information on the vision of the RiskGONE Consortium for a holistic Risk Governance (RG) framework and describes in detail the incorporation of guidance and guidelines within the framework, through the design and implementation of decision trees, for assisting stakeholders in structuring their assessment of nanomaterials and nano enabled products.

Tailored information on the topic have been published in Isigonis et al. [1] by the RiskGONE Consortium. The publication reviews the state-of-the-art, lists the identified challenges and opportunities for improvement and describes how the consortium aims to tackle the issues. In this deliverable, the decision trees are presented in full detail. The decision trees have been developed by the Consortium in various forms, based on cross-work package collaboration and aligned with the development of the RG guidelines. These guidelines have been translated into functional tools that are easy to use and update, for guiding users and stakeholders through the various steps of the RG processes.

The implementation of the framework within the RiskGONE Cloud Platform is expected to be included in Deliverable 2.5, titled “The final version of RiskGONE Database and Cloud Platform”.

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

Table of Contents

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

List of Abbreviations

AOP - Adverse Outcome Pathway

BMDL - Benchmark Dose Level

CBA - Cost Benefit Analysis

CBC - Choice-Based Conjoint

CEN-TS - European Committee for Standardisation - Technical Specification

CSS - Chemicals strategy for sustainability

DEB - Dynamic Energy Budget

DG – Directorate General

EAB - External Advisory Board

EIA - Ethical Impact Assessment

ENMs – Engineered Nanomaterials

ERA - European Research Area

EURL ECVAM – European Union Reference Laboratory for alternatives to animal testing / European Centre for the Validation of Alternative Methods

FAIR - Findable, Accessible, Interoperable and Reusable

LCA - Life Cycle Assessment

MOS - Margin of Safety

NEP - Nano-Enabled Products

NOAEL - No Observed Adverse Effect Level

NMs - Nanomaterials

OECD - Organisation for Economic Co-operation and Development

PEC - Predicted Environmental Concentration

PNEC - Predicted No Effect Concentration

POD - Point Of Departure.

RG - Risk Governance

RGC - Risk Governance Council

RRI - Responsible Research and Innovation

SbD - Safe-by-Design

SSbD - Safe- and Sustainable by-Design

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

TGs - Test Guidelines

TRL - Technology Readiness Level

SOP - Standard Operating Procedure

SWOT - Strengths, Weaknesses, Opportunities and Threats

WoE - Weight of Evidence

WTP- Willingness to Pay

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

1. Introduction

During the last decade, several attempts have been made to create a framework tailored to the risk governance (RG) of nanomaterials (NMs). Notable developments include the Nano Risk Framework [2], the ISO 31000:2018 Risk Management framework for new technologies [3], the risk governance framework of IRGC for NMs with specific guidelines on governance of emerging risks [4], [5], the iNTeg-Risk project Emerging Risk Management Framework (ERMF) [6] and the frameworks developed by EU funded projects such as NanoTEST [7], MARINA [8], SUN [9], NANoReg [10], NANoReg2 [11], caLIBRAte [12] and NanoMILE [13]. Most of these approaches contain similar elements that form the main pillars of RG for NMs, such as 'risk pre-assessment', 'risk concern/safety assessment', 'risk evaluation', 'risk management and decision making', while they are complemented by continuous supporting processes such as 'risk communication' and 'monitoring', as identified by Isigonis *et al.* [14]. The most important characteristics of these frameworks have been analysed in relation to their suitability for RG of NMs, their advantages and disadvantages, their acceptability, legal basis and broad applicability, enabling identification of knowledge gaps that need to be filled, as summarised in **Table 1**. [1]

Table 1: Characteristics of risk governance frameworks developed or adapted for NMs during the last decade

FRAMEWORK	Advantages	Limitations	Data needs	Stakeholder acceptance	Applicability to third countries	Steps needed to bring to widespread acceptability / interoperability / utility for RGC
Nano Risk Framework	Nano specificity. Result of industry-NGO dialogue, practical, transparent and flexible	Not widely accepted among NGO community, simplistic under conditions	Qualitative and normative, data are not handled	Unknown	Not country-specific	Update and expansion
ISO 31000:2018	Standardisation and wide applicability, legal basis	Not nano specific, adjustments needed	Qualitative and normative, data are not handled	Partial	Global	Nano specificity
IRGC	Introduced by neutral party with good reputation, widely known. Wide applicability	Not nano specific, generic risk governance concept, no legal status of the organisation, not applied in a comprehensive tool	Qualitative and normative, data are not handled	Partial	Not country-specific	Nano specificity, integration in a comprehensive online web-tool as a decision supporting system
iNTeg-Risk ERMF	Nano specificity. Expansion of emerging risk management framework to NMs, elaboration	Not applied in a comprehensive tool	Qualitative and normative, data are not handled	Unknown	EU-centric	Expansion to cover all stages of risk governance, integration in a comprehensive online web-tool

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

	of IRGC framework					
NanoTEST	*Nano specificity. Development of tools, Testing strategy (in vitro, in silico) and high throughput methods*	*Limited to hazard and risk assessment*	*High*	*Partial*	*Not country-specific*	*Integration in a comprehensive online web-tool as a decision supporting system for risk governance of NMs*
MARINA	*Nano specificity. First generation, nano-specific and applied framework.*	*Focus only on risk assessment strategies and risk management toolbox*	*High*	*Unknown*	*EU-centric*	*Expansion to cover all stages of risk governance, integration in a comprehensive online web-tool*
SUN	*Nano specificity. Covers regulatory risk assessment functionalities. Framework supported by modular decision support system, online access. Tiered approach, tested.*	*Data intensive*	*Tier 1: limited, Tier 2: high*	*Partial*	*EU-centric, possibly extendable*	*Expansion to integrate further modules, include guidance*
NANoREG 1	*Nano specificity. Applicability of EU regulatory frameworks to NMs, practical guidance for regulatory and industry bodies. Covers strategies for REACH implementation. Supported by NANoREG Toolbox*	*Not applied in a comprehensive tool*	*Medium*	*Partial*	*EU-centric (adapts REACH), possibly extendable*	*Integration in a comprehensive online web-tool as a decision supporting system for risk governance of NMs, including examples of case studies and user-friendly search system for basic user queries*
NANoREG 2	*Nano specificity. Defines SbD concept for NMs. Covers grouping concepts within regulatory frameworks.* *Provides new approaches of grouping NMs.*	*Not applied in a comprehensive tool*	*Medium*	*Partial*	*EU-centric, possibly extendable*	*Integration in a comprehensive online web-tool as a decision supporting system for risk governance of NMs, including examples of case studies and user-friendly search*

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

	Safe innovation approach					*system for basic user queries*
caLIBRAte	*Nano specificity. Supported by the nano-risk governance portal, business innovation centric, elaboration of ERMF framework*	*Not applied in a comprehensive tool*	*High, depending on tool selection*	*Unknown*	*EU-centric, possibly extendable*	*Integration in a comprehensive online web-tool as a decision supporting system*
NanoMILE / NanoCommons	*Nano specificity. Predictive models, Risk Assessment Tools for the Virtual Screening of NMs through the Enalos Cloud Platform*	*Lacking guidance, life cycle considerations*	*High*	*Unknown*	*Non country specific*	*Available as a cloud platform and integrated as a tool in the NanoCommons research infrastructure; will be packaged as standalone software, more case studies to be included, range of NMs and endpoints extended in NanoCommons and NanoSolveIT projects*

A straight-forward methodology has been adopted here for the assessment of the relevant existing frameworks, by combining elements of gap analysis and SWOT (strengths, weaknesses, opportunities and threats) analysis. In the first phase, the frameworks have been analysed to distinguish their main advantages and disadvantages, in terms of their suitability for adoption and expansion within a general setting for the RG of NMs. Advantageous characteristics present in the various frameworks have been identified, such as nano specificity, incorporation of Safe- and Sustainable by-Design (SSbD) elements for NMs, wide applicability, presence of guidance, comprehensive applied tools etc. In addition, the most important drawbacks of each effort have also been identified, such as the lack of guidance, lack of nano specificity and applicability in comprehensive tools, the (over)simplicity of some frameworks, the focus on a limited set of RG processes etc. The second phase of analysis focused on identifying the level of data intensity that is required for the application of each framework (e.g., qualitative vs quantitative assessments, low/medium/high data intensity) and specific characteristics related to the stakeholder acceptance, in terms of regulatory compliance, and the applicability of the frameworks in low- and middle-income countries. It is worth noting at this stage that none of the proposed frameworks has complete regulatory acceptance/adoption so far, which together with the legal basis are two rather important characteristics in the effort to establish frameworks and standards suitable for RG of NMs overall. The last phase of the analysis performed herein considered possible improvements and steps that would allow widespread acceptability and possible utility of each analysed framework by stakeholders. This step identified a number of options such as expansion to cover a larger number of RG processes, integration in web tools or decision support systems, provision of extensive guidance and others. All in all, this analysis allowed extraction of the important characteristics from each framework for further utilization within the design of the RG framework that has been developed by the RiskGONE Consortium.

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

The proposed framework aims to incorporate valuable existing information and the new developments into one structure. The existing RG frameworks have specific drawbacks, as analysed and summarised in Table 1, and include fragmented resources based on the background and the scope of their development, therefore it is considered sensible to collect all the important elements under one umbrella, i.e., within the envisioned holistic RG framework.

To support innovation, a strong focus of recent research has been driven towards establishing procedures that would allow the integration of the SSbD concept into NMs development and commercialisation at the outset, therefore aiming to couple the RG processes with regulatory and business needs and embedding RG concepts into the underlying frameworks [15]–[18].

The integration of SbD together with concepts of 'Quality-by-Design' and 'Sustainability-by-Design' for NMs has been envisioned in related frameworks [19], [20]. To achieve such an operationalisation of SSbD and related concepts, scientific and regulatory needs are mapped in parallel with innovation management needs that together with prevention-based and safer-innovation approaches have to be incorporated within the emerging RG frameworks. Achievement of such a holistic, operational and transparent framework, acceptable to and trusted by all stakeholders is the ultimate goal of RG research.

Despite the undoubted progress in the field, consensus on the safe development and handling of nanotechnology among the various stakeholder groups is still considered as a great challenge [21]. Therefore, the three H2020-funded research projects, funded under the call NMBP-13-2008 (Gov4Nano [22], NANORIGO [23] and RiskGONE [24]), aimed to support the translation of research advances into regulation and industrial practice, and to integrate research, development and innovation (R&D&I) processes in nanotechnology in a holistic way. These projects aim to design and implement a broadly accepted among stakeholders, scientifically-based RG framework for NMs by filling identified gaps of the existing efforts [25] (see Table 1 above for some of the key information gaps identified in terms of broad applicability, stakeholder acceptability and legal basis). Furthermore, the projects aim to support the framework through a dedicated web platform and allow modular expansion possibilities to accommodate the future needs of NMs industries, regulators and the general public. This approach is expected to enable a continuous incorporation of the evolving state of the science to facilitates responsive re-thinking of nanosafety governance to address these future needs. In addition, in close cooperation with all consortia, three H2020-funded research projects (NanoCommons [26], NanoInformaTIX [27] and NanoSolveIT [28]) are developing models which can make predictions based on prior experimental inputs, utilising only knowledge of NM structure and composition, enabling NMs developers to screen NMs *in silico* before actually producing them, thus ensuring that the properties of concern are reduced or eliminated, which would make the NMs SSbD [29].

2. RiskGONE RG framework and decision trees

RiskGONE RG framework

Responsible and sustainable nanotechnology innovation requires the development and implementation of widely agreed strategies and tools for prevention, assessment, communication and management of risks and impacts, across materials and product life cycles. It should also reflect contiguous concerns, such as the circular economy, critical raw materials, the water and waste framework directives [30], [31] and guidance in food and feed chains [32], ultimately leading to the development of a holistic RG framework for nanotechnologies and NMs [25]. Within the RiskGONE project, a modular RG framework has been envisioned, based on the state-of-the-art in the nanotechnology sector, the incorporation of risk/benefit ratio and ethical assessments [33] and the efforts to couple the notions of life cycle thinking,

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

prevention-based RG, SSbD, safe innovation governance, contiguous frameworks and open data initiatives with the existing four main pillars of the RG process, as shown in **Figure 1**.

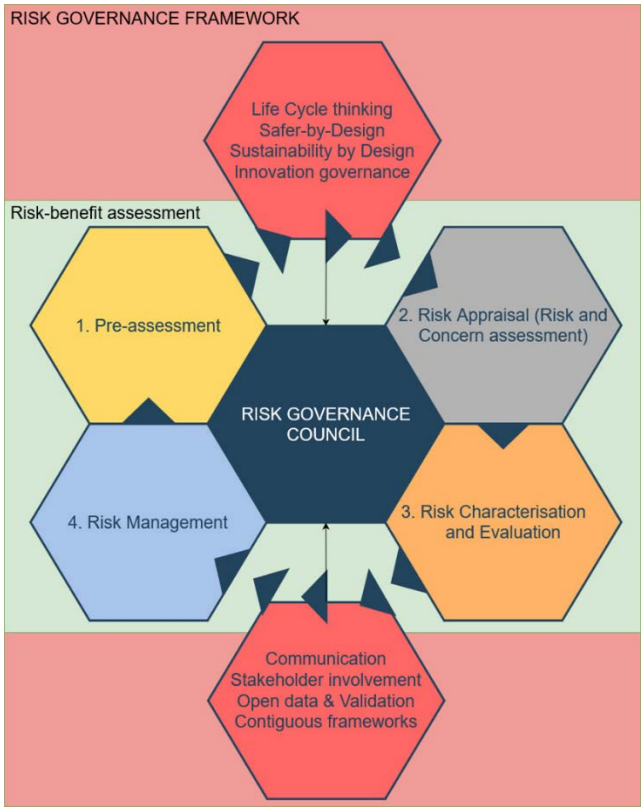

Figure 1: Schematic illustration of the holistic and implementable RiskGONE universal nanotechnologies RG framework [1]

The principal components of RG frameworks, such as risk pre-assessment, risk appraisal, risk evaluation and risk management have been described extensively in various previous studies [4], [14]. They are accepted by the scientific community as important steps in chemical and material assessment and are used in the most recent research regarding RG processes for NMs. Our study uses the pre-existing principal components as the basis of the envisioned RG framework and focuses on the development and incorporation of specific elements that are currently missing and are considered essential towards the establishment of science-based RG of NMs, as also seen in Table 1. These elements include the following:

- Promotion of the incorporation of the SSbD concept, alongside the Sustainability by design and Quality by Design concepts, within assessment frameworks and their operationalisation through comprehensive tools, which are currently in their infancy or missing completely. This effort is meant both to help innovation governance, to support responsible research and innovation with practical and operational tools and to enhance predictive actions and measures covering the life cycle of NMs or even precede their realization via *in silico* screening.
- Guidance and standardization documents, for enhancing the regulatory compliance and acceptance of the developed framework and the incorporated tools.
- Strengthening of the scientific efforts towards open data and global data availability, through the development of open databases and repositories supporting FAIR data and promoting the FAIRification processes.
- Utilization of RG tools (both existing and those to be developed) and incorporation of decision trees that will guide the users (covering regulators, industry and the public) in the use of the cloud platform (thus the applied framework) and the redirection to available resources for the needs of each stakeholder group. Resources will include guidance documents, standardization

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

documents, public summaries, internet resources (databases, information portals), communication tools and scientific tools.

The RG frameworks developed so far have not been designed with exclusive consideration of how they would be operationalised, i.e., outlining how the framework would support the work of stakeholders such as regulators, industry, society and other groups. The foundation of the RG activities, based on the RiskGONE consortium vision, should be based on various key steps for creating a strong formal framework: i) using FAIR (Findable, Accessible, Interoperable and Reusable [34]) scientific data; ii) making use of OECD / EURL ECVAM (European Union Reference Laboratory for alternatives to animal testing / European Centre for the Validation of Alternative Methods) validated datasets and nanoinformatics tools; iii) enabling the operationality of the tools for aligning the RG practices through accessible cloud platforms; and iv) aligning with open data initiatives and supporting the validation processes for data and models.

The vision is thus to design a framework for supporting stakeholders through the early adoption of scientific advances and emerging data and their translation via functional tools, all within a transparent, guided decision scheme considering the needs and expectations of the various stakeholders. The RG framework is available as an interoperable cloud platform with a user-friendly interface and operationalised via a set of decision trees implemented into a modular decision support tool providing instruments, guidance and guidelines for different aspects of the RG of NMs, such as:

- Characterisation, Fate, and Dosimetry of NMs
- Human Hazard Assessment
- Environmental Hazard/Effect Assessment
- Exposure Assessment
- Risk Assessment
- Life Cycle Analysis
- Economic Assessment
- Ethical Impact Assessment

Tools are categorized based on their suitability for use in the different RG processes and their reliability to support them. Specific assessment has been done in previous projects, such as within the H2020 caLIBRAte [12] project where the evaluation of the relevance of tools for horizon scanning, environmental risk assessment and human health risk assessment has been performed. These results have been complemented with new tools, especially those developed within the RiskGONE, NANORIGO and Gov4Nano governance projects, as well as NanoSolveIT, NanoCommons and NanoInformaTIX nanoinformatics projects [26]–[28]. Multiple tools covering the multiple stages of RG processes therefore they are expected to be proposed to the users in the various modular yet integrated segments of the decision trees that will be used to guide the users to appropriate resources [14].

The decision trees have been designed and implemented, to provide scientific and regulatory support via reinforced decision-making tools for relevant stakeholders, including industry, regulators, insurance companies, NGOs and the general public. The decision trees have been complemented by relevant toolboxes and guidance materials, to support stakeholders in the RG processes. The required, critical properties of nanoforms would be predicted (calculated) with the implemented nanoinformatics tools that have been developed by the collaborating projects (NanoSolveIT, NanoCommons and NanoInformaTIX). The framework is expected to support regulatory decision-making as well as business management needs, through the adoption of best practices, the promotion of Responsible Research and Innovation (RRI) [35]–[37] and the exploration of frameworks for Responsible Innovation [38] for integration with the proposed RG framework to align policy-making with research practices. Extension to other relevant advanced materials and emerging technologies is also envisaged along with leveraging of best practice from contiguous disciplines.

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

Implementation of RiskGONE RG framework into the RiskGONE Cloud Platform

The implementation of the RiskGONE framework, and the decision trees that are presented in detail in the following sections, into the RiskGONE Cloud platform is available online at http://www.enaloscloud.novamechanics.com/riskgone.html.

Within the RiskGONE Cloud platform, dedicated sections for the RG framework phases have been produced and the decision trees have been made available in a modular format, at all the sections that are considered relevant. The user in this way has an easy-to-use and navigate platform, which provides organised access to the different topics, based on the needs of stakeholders.

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

Decision trees and guidance for users

The decision trees and the guidance for users of the RiskGONE Cloud platform has been organised in various levels in order to allow a modular representation of the results and outputs of the research project towards the various types of stakeholders. In this sense, three main levels have been identified:

1. Level 1 – Expected experience level of the user;
2. Level 2 – Specific topics of interest related to the RG framework of nanomaterials;
3. Level 3 – Contiguous topics of interest.

Level 1 – Novice vs Experienced user

In the first RiskGONE decision tree, users are guided through some introductory topics, based on their knowledge and experience to allow an easier navigation of the contents of the RiskGONE Cloud platform and the scientific outputs of the RiskGONE project. The experience level decision tree is presented below in Table 2.

Table 2: Decision tree based on user experience level

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Are you an experienced user?	Yes/No	Binary	Yes	1A-1D	The aim is to guide the different types of users to find the most appropriate information they might be looking for within the Risk Governance Cloud Platform.
				No	2	
1A	Looking for information on TGs?	Yes/No	Binary	Yes	TGs →	Link to TGs page [To be defined]
				No	1B	
1B	Looking for the library of tools?	Yes/No	Binary	Yes	Library →	Link to library of tools page [To be defined]
				No	1C	
1C	Looking for Risk Governance guidelines?	Yes/No	Binary	Yes	Guidelines →	Link to guidelines page [To be defined]

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

				No	1D	
1D	Looking for data sources and databases?	Yes/No	Binary	Yes	Data →	Link to eNanoMapper and data pages [To be defined]
				No	2	
2	Are you familiar with the most recent regulatory definitions of NMs?	Yes/No	Binary	Yes	3	
				No	NMs →	Link to page with definitions and regulatory info (chapter 1.3, D3.1)
3	Is the assessment of your nanomaterial split into distinctive stages related to the risk governance process?	Yes/No	Binary	Yes	3A-3D	
				No	RiskGONE RG framework →	Link to RG framework page
3A	Looking for support to perform the pre-assessment phase?	Yes/No	Binary	Yes	RG framework ph. 1 →	Link to pre-assessment info page
				No	3B	
3B	Looking for support to perform the risk appraisal phase?	Yes/No	Binary	Yes	RG framework ph. 2 →	Link to risk appraisal info page
				No	3C	

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

3C	Looking for support to perform the risk characterisation and evaluation phase?	Yes/No	Binary	Yes	RG framework ph. 3 →	Link to risk characterisation and evaluation info page
				No	3D	
3D	Looking for support to perform the risk management phase?	Yes/No	Binary	Yes	RG framework ph. 4 →	Link to risk management info page
				No	4	
4	Please return to the main menu and restart your navigation of the RiskGONE Cloud platform				→	Return to main page

The experience level decision tree is illustrated at Figure 2 below.

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

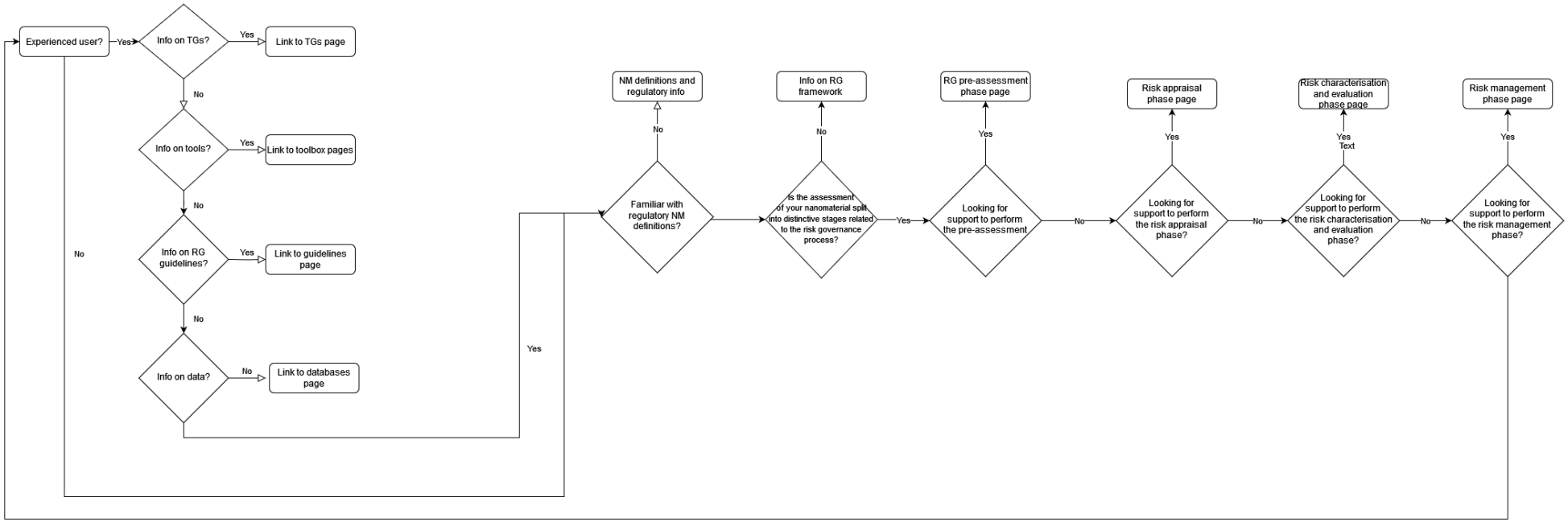

Figure 2: The illustrated version of the experience level decision tree

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

Level 2 – RiskGONE guidelines

2.1 Characterisation, Fate, and Dosimetry of NMs

Specific guidelines have been produced for the Characterisation, Fate, and Dosimetry of NMs and are described in the series of Deliverables of WP4, namely D4.2 to D4.9. The Characterisation, Fate, and Dosimetry of NMs decision tree is presented below in Table 3.

Table 3: Characterisation, Fate, and Dosimetry of NMs Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Are you familiar with the main characterisation parameters for NMs?	Yes/No	Binary	Yes	2	Continue assessment
				No	→	Read chapter 6.1 of RiskGONE D3.1
2	Are you familiar with characterisation methods & their applicability to different NMs types?	Yes/No	Binary	Yes	3	
				No	→	Read chapter 6.2 of RiskGONE D3.1
3	Looking for information on NMs characterisation in biological and environmental fluids?	Yes/No	Binary	Yes	→	Read chapter 6.3 of RiskGONE D3.1
				No	4	
4	Looking for information on NMs dose metrics?	Yes/No	Binary	Yes	→	Read chapter 6.4 of RiskGONE D3.1
				No	4A	
4A	Have you checked the RiskGONE in-vitro dosimetry tool?	Yes/No	Binary	Yes	5	
				No	→	Link to http://www.enaloscloud.novamechanics.com/riskgone/InVitroDosimetry/
5	Looking for information on minimum requirements for nanomaterials characterisation?	Yes/No	Binary	Yes	→	Read chapter 6.5 of RiskGONE D3.1
				No	6	
6	Looking for the guidance document on hydrodynamic diameter and size distribution determination?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.2
				No	7	

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

7	Looking for the guidance document on the dispersibility of ENMs?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.3
				No	8	
8	Looking for the guidance document on the determination of ENMs endotoxins content?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.4
				No	9	
9	Looking for the guidance document on zeta potential determination?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.5
				No	10	
10	Looking for the guidance document on particle counting?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.6
				No	11	
11	Looking for the guidance document on effective density?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.7
				No	12	
12	Looking for the Report on the applicability of OECD TGs for determination of the environmental fate of ENMs?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.8
				No	13	
13	Looking for the Harmonised SOP for the resuspension of ENMs in biological media and in vitro dosimetry?	Yes/No	Binary	Yes	→	Link to RiskGONE D4.9
				No		Return to main menu

The Characterisation, Fate, and Dosimetry of NMs decision tree is illustrated at Figure 3 below.

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

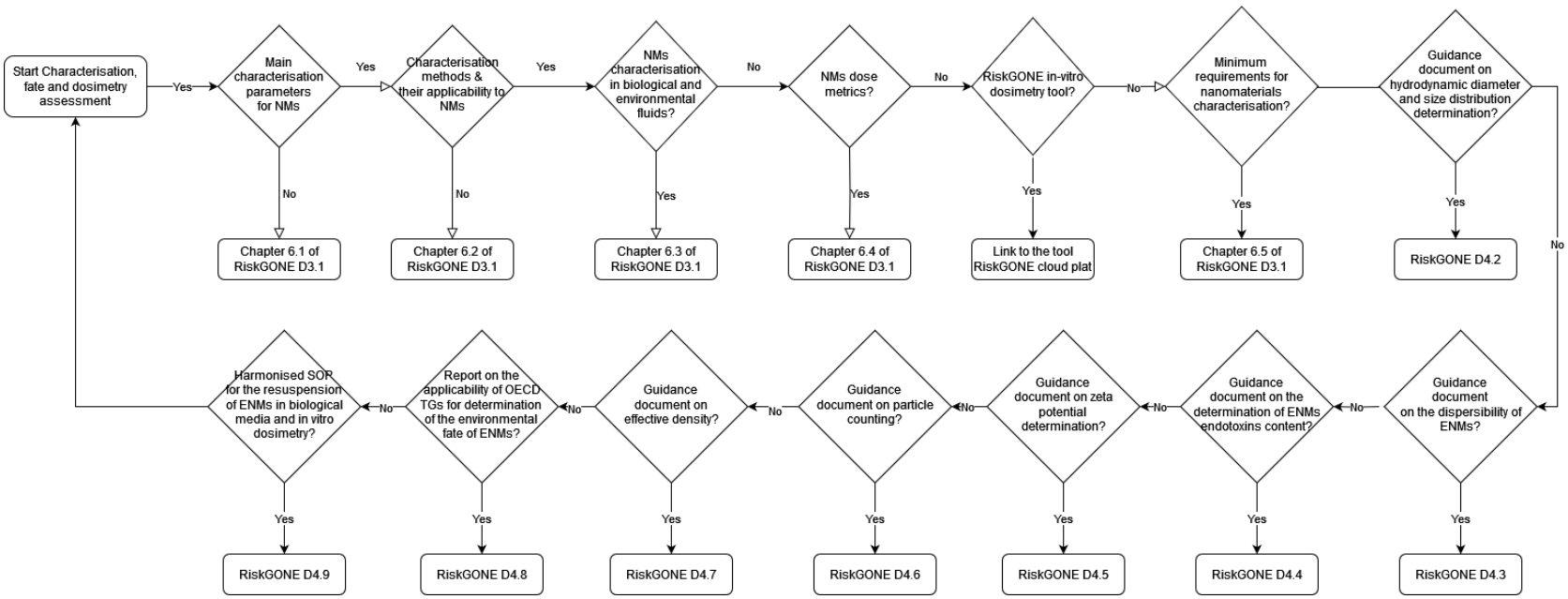

Figure 3: The illustrated version of the Characterisation, Fate, and Dosimetry of NMs decision tree

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

2.2 Human Hazard Assessment

Specific guidelines have been produced for the Human Hazard Assessment and are described in the series of Deliverables of WP5, namely D5.1 to D5.5. The Human Hazard decision tree is presented below in Table 4.

Table 4: Human Hazard Assessment Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Are you familiar with the human hazard assessment of NMs?	Yes/No	Binary	Yes	2	Continue assessment
				No	→	Read chapter 7.1 of RiskGONE D3.1
2	Looking for the Report on the final harmonised SOPs used to propose amendments to the existing OECD TGs?	Yes/No	Binary	Yes	→	Link to RiskGONE D5.1
				No	3	
3	Looking for the Report on the harmonised SOPs on high throughput approaches for hazard assessment of ENMs?	Yes/No	Binary	Yes	→	Link to RiskGONE D5.2
				No	4	
4	Looking for the Report on nano-specific sex differences to direct future hazard assessment approaches?	Yes/No	Binary	Yes	→	Link to RiskGONE D5.3
				No	5	
5	Looking for the Report on the proof of concept evaluation of SOPs for innovative *in vitro* models and mechanistically relevant assays for nanosafety human hazard assessment?	Yes/No	Binary	Yes	→	Link to RiskGONE D5.4
				No	6	
6	Looking for the Report on the expert meeting AOP draft review?	Yes/No	Binary	Yes	→	Link to RiskGONE D5.5
				No		Return to main menu

The Human Hazard Assessment decision tree is illustrated at Figure 4 below.

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

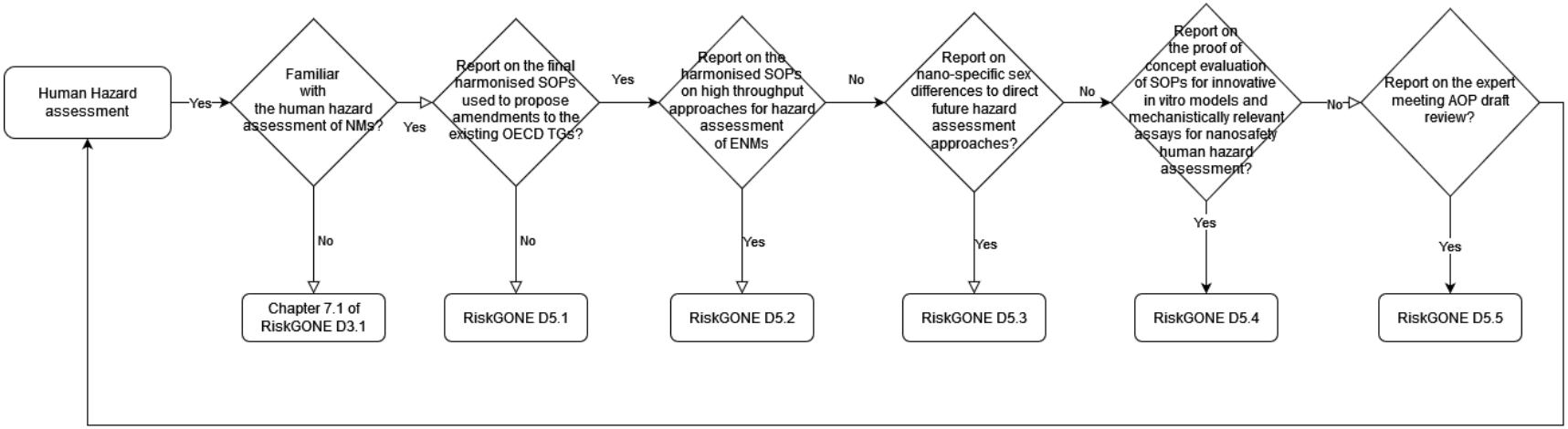

Figure 4: The illustrated version of the Human Hazard Assessment decision tree

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

2.3 Environmental Hazard/Effect Assessment

Specific guidelines have been produced for the Environmental Hazard/Effect Assessment of NMs and are described in the series of Deliverables of WP6, namely D6.1 to D6.6. The Environmental Hazard/Effect Assessment decision tree is presented below in Table 5.

Table 5: Environmental Hazard/Effect Assessment Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Are you familiar with the environmental hazard characterisation of NMs?	Yes/No	Binary	Yes	2	Continue assessment
				No	→	Read chapter 7.2 of RiskGONE D3.1
2	Looking for the Report on the final harmonised SOPs used to propose amendments to the existing OECD TGs?	Yes/No	Binary	Yes	→	Link to RiskGONE D6.1
				No	3	
3	Looking for the Report on pre-validated high throughput (in vitro) and miniaturised (in vivo) methods for ecotoxicity testing?	Yes/No	Binary	Yes	→	Link to RiskGONE D6.2
				No	4	
4	Looking for the Documented protocols, data capture, and meta data templates for revised OECD tests, and pre-validated alternative test methods?	Yes/No	Binary	Yes	→	Link to RiskGONE D6.3
				No	5	
5	Looking for the Report on feedback on an initial draft of DEBbased AOP for chronic ecotoxicity to ENMs?	Yes/No	Binary	Yes	→	Link to RiskGONE D6.4
				No	6	
6	Looking for the Report on DEB-based AOP for chronic ecotoxicity to ENMs, and extension to multigenerational effects?	Yes/No	Binary	Yes	→	Link to RiskGONE D6.5
				No	7	

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

7	Looking for the Report on nano-specific gender differences to direct future ERA approaches?	Yes/No	Binary	Yes	→	Link to RiskGONE D6.6
				No		Return to main menu

The Environmental Hazard Assessment decision tree is illustrated at Figure 5 below.

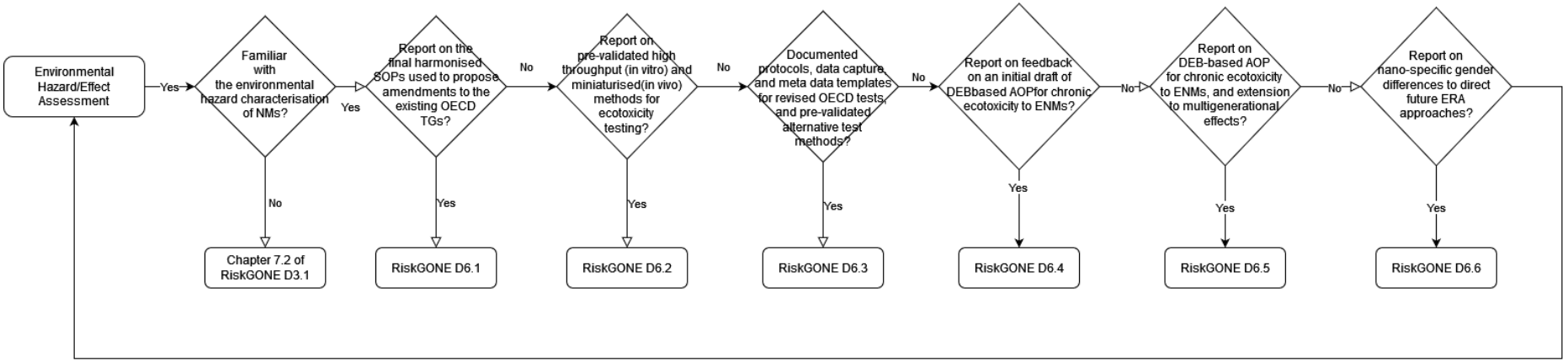

Figure 5: The illustrated version of the Environmental Hazard Assessment decision tree

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

2.4 Exposure Assessment

Even though the RiskGONE project did not produce specific guidelines for Exposure Assessment of nanomaterials, relevant resources and materials have been collected in the Exposure Assessment decision tree, which is presented below in Table 6.

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Are you familiar with the exposure assessment as part of the risk assessment process?	Yes/No	Binary	Yes	2	
				No	→	Link to NanoCommons Risk assessment page https://nanocommons.github.io/user-handbook/risk-assessment/
2	Have you checked the NanoSolveIT exposure models?	Yes/No	Binary	Yes	3	
				No	→	Link to NanoSolveIT exposure models https://cloud.nanosolveit.eu/services/exposure-models/
3	Have you checked the exposure models available at the NanoRisk Governance portal?	Yes/No	Binary	Yes		Return to main menu
				No	→	Link to tools page of NanoRisk Governance portal http://nanoriskgov.eu/library.html

Table 6: Exposure Assessment Decision tree

The Exposure Assessment decision tree is illustrated at Figure 6 below.

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

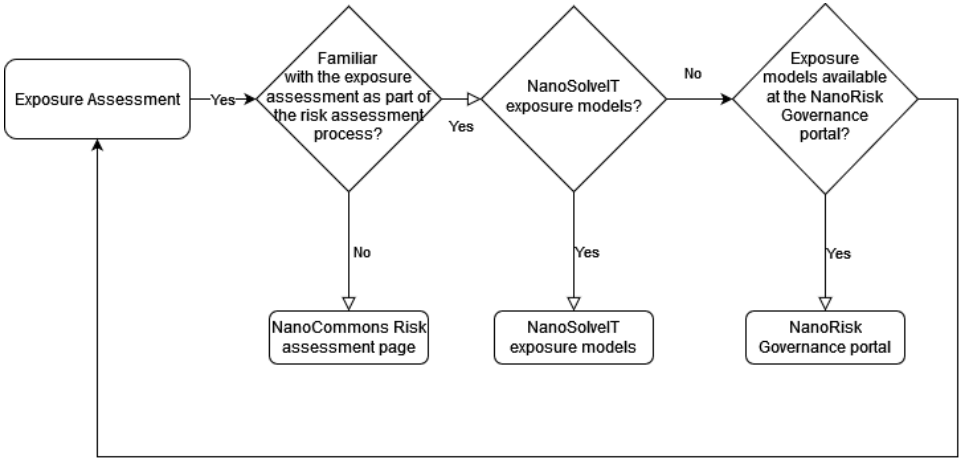

Figure 6: The illustrated version of the Exposure Assessment decision tree

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

2.5 Risk Assessment

Specific guidelines have been produced for the Risk Assessment of nanomaterials and are described in Deliverable 3.1, titled "Draft guidelines for risk assessment". The Risk Assessment decision tree is presented below in Table 7.

Table 7: Risk Assessment Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Looking for an Overview of industrial sectors utilising nanomaterials & their current regulations?	Yes/No	Binary	Yes	→	Link to chapter 1.2 of RiskGONE D3.1
				No	2	
2	Looking for an overview of Common features of Risk Assessment across industrial sectors?	Yes/No	Binary	Yes	→	Link to chapter 1.4 of RiskGONE D3.1
				No	3	
3	Looking for an overview of Safety considerations for nanomaterials?	Yes/No	Binary	Yes	→	Link to chapter 2 of RiskGONE D3.1
				No	4	
4	Looking for an overview of Data quality considerations for nanomaterials Risk Assessment?	Yes/No	Binary	Yes	→	Link to chapter 3 of RiskGONE D3.1
				No	5	
5	Looking for an overview of Physico-Chemical Characterisation of nanomaterials?	Yes/No	Binary	Yes	→	Link to chapter 6 of RiskGONE D3.1 and suggestion to go to Decision tree 2.1 (Physico-Chemical Characterisation of nanomaterials)
				No	6	
6	Looking for an overview of Hazard characterisation of NMs?	Yes/No	Binary	Yes	→	Link to chapter 7 of RiskGONE D3.1 and suggestion to go to Decision trees 2.2 (Human Hazard Assessment) and 2.3 (Environmental Hazard/Effect Assessment)
				No	7	
7	Looking for an overview on Risk Assessment guidelines?	Yes/No	Binary	Yes	→	Link to chapter 8 of RiskGONE D3.1
				No	7A-7E	
7A	Looking for information on the Toxicological point of departure (POD)?	Yes/No	Binary	Yes	→	Link to chapter 8.1 of RiskGONE D3.1

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

				No	7B	
7B	Looking for information on BMDL or NOAEL?	Yes/No	Binary	Yes	→	Link to chapter 8.2 of RiskGONE D3.1
				No	7C	
7C	Looking for information on PEC and PNEC?	Yes/No	Binary	Yes	→	Link to chapter 8.3 of RiskGONE D3.1
				No	7D	
7D	Looking for information on Non-threshold and Threshold effects - the Margin of Safety (MoS)?	Yes/No	Binary	Yes	→	Link to chapter 8.4 of RiskGONE D3.1
				No	7E	
7E	Looking for information on the Calculation of the margin of safety?	Yes/No	Binary	Yes	→	Link to chapter 8.5 of RiskGONE D3.1
				No		Return to main menu

BMDL-benchmark dose level; MOS- Margin of safety; NOAEL- No Observed Adverse Effect Level; PEC-Predicted environmental concentration; PNEC- Predicted no effect concentration; POD-Point of departure.

The Risk Assessment decision tree is illustrated at Figure 7 below.

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

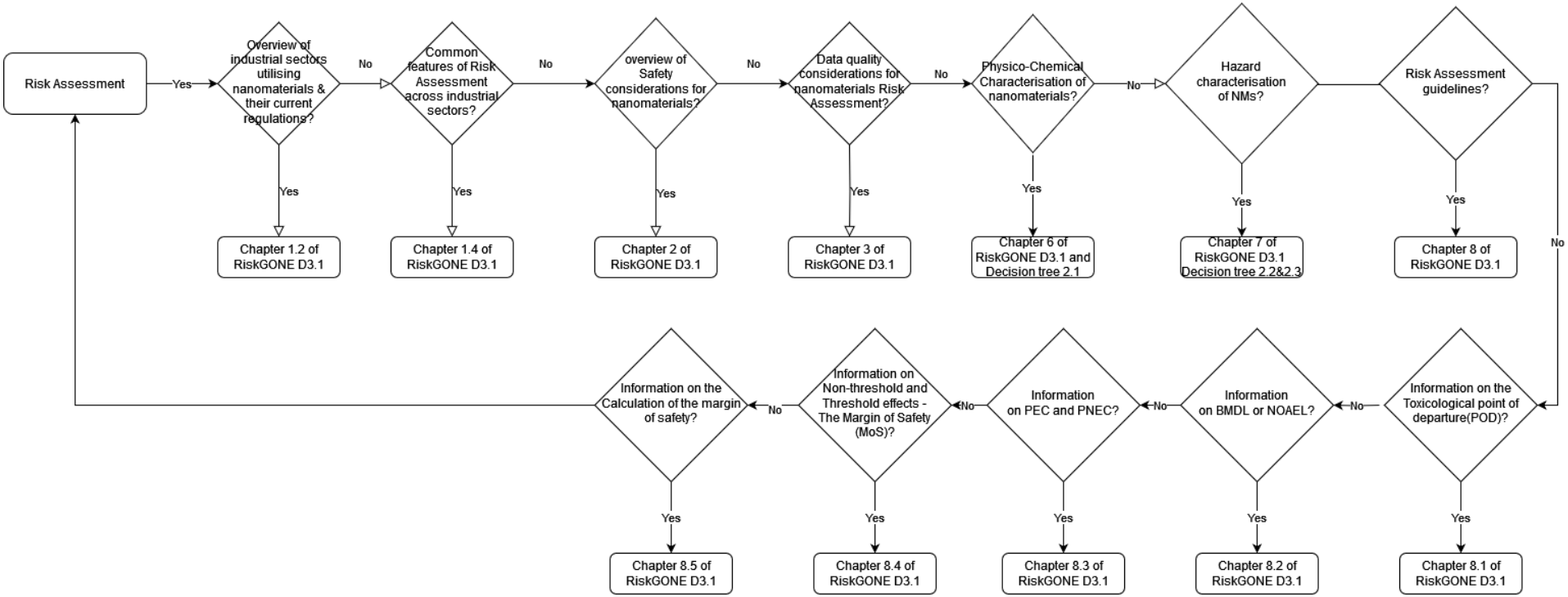

Figure 7: The illustrated version of the Risk Assessment decision tree

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

2.6 Life Cycle Assessment

Specific guidelines have been produced for the Life Cycle Assessment of nanomaterials and are described in Deliverable 3.2, titled "Draft guidelines regarding the quantification of lifecycle environmental and human health risk indicators". The LCA decision tree is presented below in Table 8.

Table 8: Life Cycle Analysis decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Are you familiar with CEN-TS-17276:2018 document?	Yes/No	Binary	Yes	2	Continue assessment
				No	→	Link to CEN-TS-17276:2018 document
2	Do you have LCA competences?	Yes/No	Binary	Yes	3	
				No	→	Suggest performing Qualitative screening analysis, chapter 3.1 of RiskGONE D3.2
3	Is the TRL of developed technology >=5	Yes/No	Binary	Yes	→	Suggest performing Comparative LCA, chapter 3.3 of RiskGONE D3.2
				No	4	
4	Available LCA study from literature?	Yes/No	Binary	Yes	5	Suggest performing Screening LCA study, chapter 3.2 of RiskGONE D3.2
				No	5	Suggest performing Qualitative screening analysis, chapter 3.1 of RiskGONE D3.2
Starting LCA assessment						
5	Familiar with basic LCA concepts?	Yes/No	Binary	Yes	6	
				No	→	Read chapter 1 of RiskGONE D3.2
6	Clearly defined system boundaries?	Yes/No	Binary	Yes	7	
				No	→	Read chapter 2.1 of RiskGONE D3.2
7	Clearly defined functional units?	Yes/No	Binary	Yes	8	
				No	→	Read chapter 2.1 of RiskGONED3.2
8	Is the material properly characterised (apart from chemical constitution)?	Yes/No	Binary	Yes	9	
				No	→	Collect info on size and shape, dissolution and dispersion properties, surface properties, information on coating (if applied), information on the

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

						potential for agglomeration and aggregation. Suggestion to go to Decision tree 2.1 (Physico-Chemical Characterisation of nanomaterials)
9	Identified sources of ENM and NEP release along the life cycle stages considered?	Yes/No	Binary	Yes	10	
				No	→	Read chapter 2.2 of RiskGONE D3.2
10	Ecotoxicity and human toxicity impacts included in the assessment?	Yes/No	Binary	Yes	→	Read chapter 2.2 of RiskGONE D3.2
				No	11	
11	Familiar with the management of uncertainty in LCA?	Yes/No	Binary	Yes	End of assessment	
				No	→	Read chapter 2.4 of RiskGONE D3.2

The LCA decision tree is illustrated at Figure 8 and Figure 9 below.

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

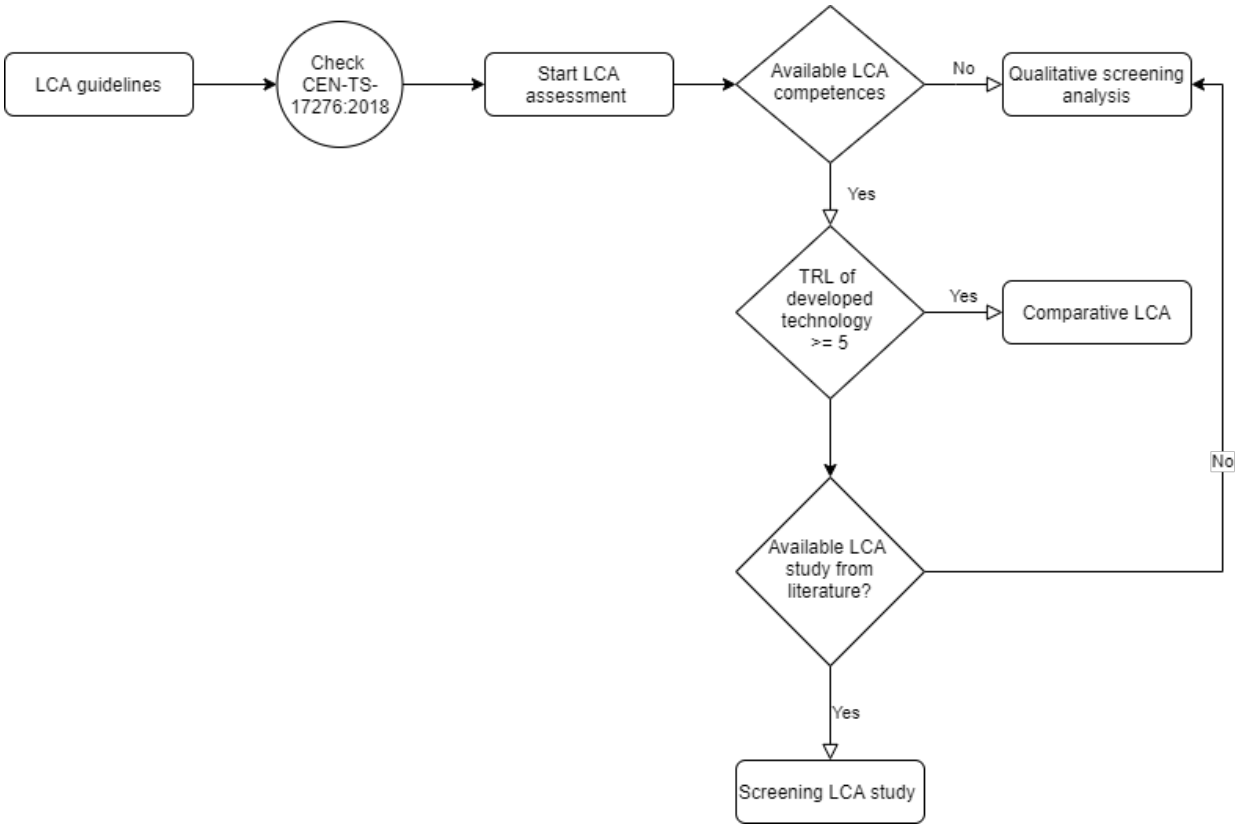

Figure 8: The illustrated version of the 1st step of LCA assessment decision tree.

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

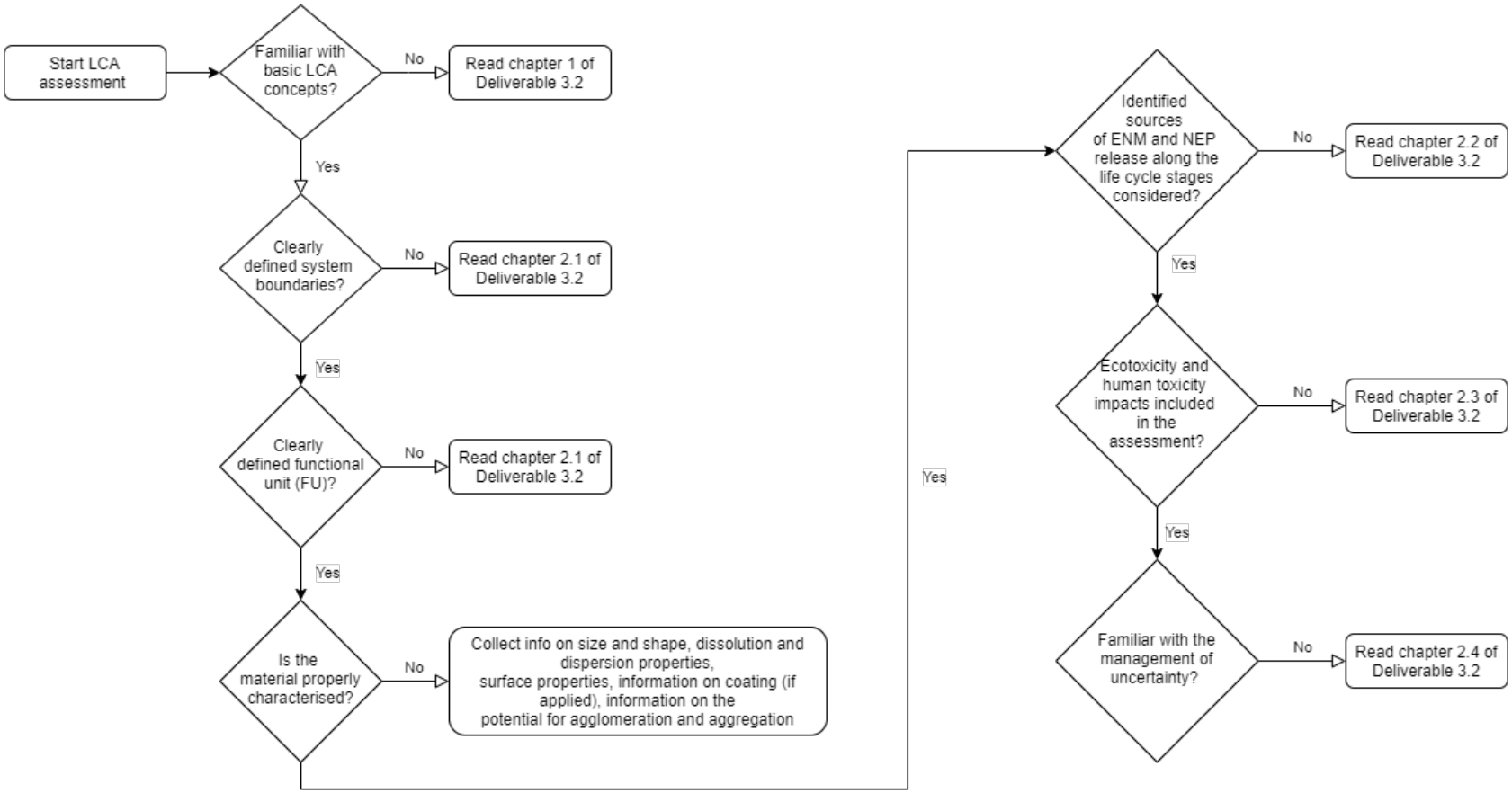

Figure 9: The illustrated version of the 2nd step of LCA assessment decision tree.

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

2.7 Economic Assessment

Specific guidelines have been produced for the Economic Assessment of nanomaterials and are described in Deliverable 3.3, titled "Draft guidelines regarding the quantification of macro-economic benefits". The Economic Assessment decision tree is presented below in Table 9.

Table 9: Economic Assessment Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
0	Have you read RiskGONE D3.3?	Yes/No	Binary	Yes	1	
				No	→	Link to RiskGONE D3.3
1	Does the assessment concern the production of a specific ENM product or product group?	Yes/No	Binary	Yes	1A	Continue assessment
				No	2	
1A	Establish WTP using CBC			Yes	1B	
1B	Identify producer surplus, consumer surplus and deadweight loss			Yes	1C	
1C	Is a broader perspective on cost and benefits desired?	Yes/No	Binary	Yes	1D	
				No	→	Perform Assessment using WTP
1D	Perform (relative) CBA			Yes	→	Perform Assessment using WTP and CBA
2	Does the assessment concern the utilisation of a specific ENM product or product group?	Yes/No	Binary	Yes	2A	
				No	3	
2A	Do specific data allow for a more accurate attribution of costs and benefits to ENMs?			Yes	→	Use regression and other techniques to inform a (relative) CBA (Assessment using detailed CBA)
				No	→	Perform (relative) CBA using broad assumptions (Assessment using simple CBA)
3	Reconsider the scope of the study	Yes/No	Binary	Yes	1	Restart the assessment
				No	→	No economic assessment

WTP- Willingness to Pay; CBA- Cost Benefit Analysis; CBC- Choice-Based Conjoint.

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

The economic assessment decision tree is illustrated in Figure 10 below.

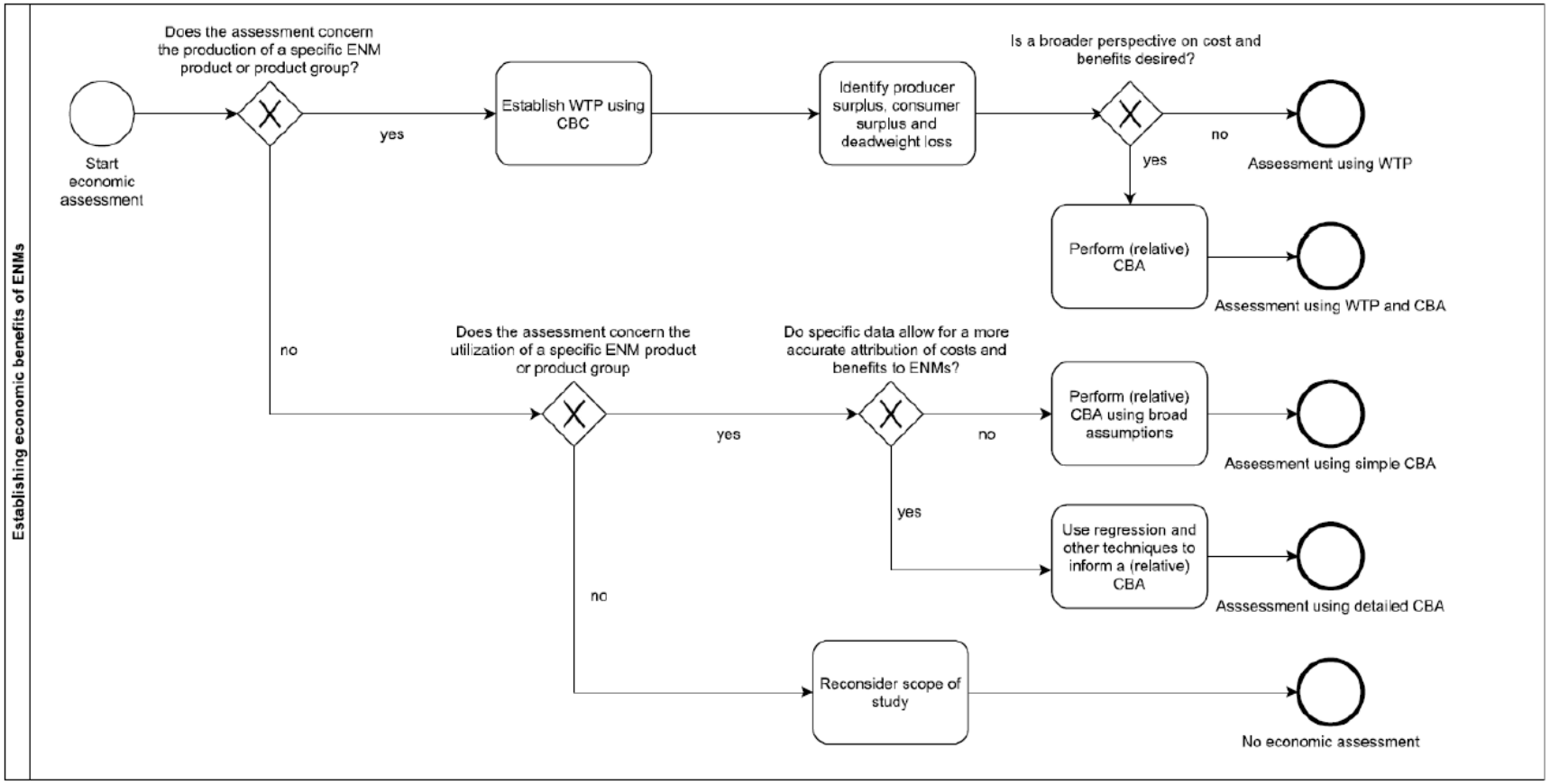

Figure 10: The illustrated version of the economic assessment decision tree.

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

2.8 Ethical Impact Assessment

Specific guidelines have been produced for the Ethical Impact Assessment (EIA) of nanomaterials and are described in Deliverable 3.6, titled "Draft guidelines on Identification of regulatory and ethical risk thresholds". The EIA decision trees are split into 6 distinct steps, as presented below in Table 10.

Table 10: Ethical Impact Assessment steps

Step	Action	Risk Governance Framework stage
1	Screening Ethical Impacts	Risk pre-appraisal stage
2	Drafting EIA plan	Risk pre-appraisal stage
3	Identifying ethical impacts	Risk perception and concern assessment
4	Evaluating the ethical impacts	Evaluating risks
5	Formulating and implementing remedial actions	Risk management
6	Reviewing and auditing the EIA	Monitoring and feedback

The following decision tree guides the user to the selection of the appropriate resource:

Table 11: Ethical Impact Assessment Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Have you read the guidelines for performing EIA assessment?	Yes/No	Binary	Yes	2	
				No	1A →	Link to RiskGONE D3.6
2	Have you performed step 1 of EIA "screen ethical impacts"?	Yes/No	Binary	Yes	3	
				No	2A →	Link to screening ethical impacts page
3	Have you performed step 2 of EIA "drafting EIA plan"?	Yes/No	Binary	Yes	4	
				No	3A →	Link to Drafting EIA plan page
4	Have you performed step 3 of EIA "Identifying ethical impacts"?	Yes/No	Binary	Yes	5	
				No	4A →	Link to Identifying ethical impacts page
5	Have you performed step 4 of EIA "Evaluating the ethical impacts"?	Yes/No	Binary	Yes	6	
				No	5A →	Link to Evaluating the ethical impacts page

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

6	Have you performed step 5 of EIA "Formulating and implementing remedial actions"?	Yes/No	Binary	Yes	7	
				No	6A →	Link to Formulating and implementing remedial actions page
7	Have you performed step 6 of EIA "Reviewing and auditing the EIA"?	Yes/No	Binary	Yes	End	Go to summary page
				No	7A →	Link to Reviewing and auditing the EIA page

The EIA decision tree is illustrated at Figure 11 below.

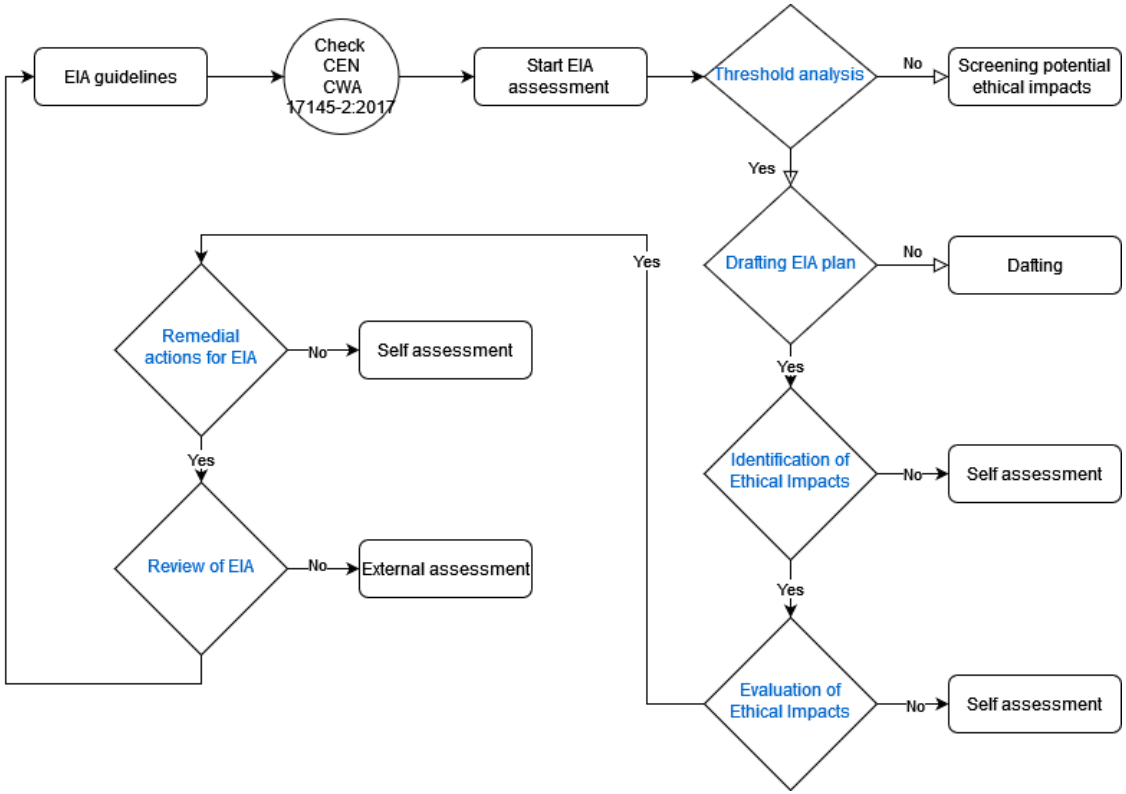

Figure 11: The illustrated version of the EIA decision tree.

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

Level 3 – Contiguous topics

3.1 Risk Governance phases

Specific guidelines have been produced for the Risk Governance phases and are described in dedicated pages of the RiskGONE Cloud platform. The Risk Governance phases decision tree is presented below in Table 12.

Table 12: Risk Governance phases Decision Tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Is the assessment of your nanomaterial split into distinctive stages related to the risk governance process?	Yes/No	Binary	Yes	1A-1D	
				No	RiskGONE RG framework →	Link to RG framework page
1A	Looking for support to perform the pre-assessment phase?	Yes/No	Binary	Yes	RG framework ph. 1 →	Link to pre-assessment info page
				No	1B	
1B	Looking for support to perform the risk appraisal phase?	Yes/No	Binary	Yes	RG framework ph. 2 →	Link to risk appraisal info page
				No	1C	
1C	Looking for support to perform the risk characterisation and evaluation phase?	Yes/No	Binary	Yes	RG framework ph. 3 →	Link to risk characterisation and evaluation info page
				No	1D	
1D	Looking for support to perform the risk management phase?	Yes/No	Binary	Yes	RG framework ph. 4 →	Link to risk management info page
				No	2	
2	Please return to the main menu and restart your navigation of the RiskGONE Cloud platform	Yes/No	Binary	Yes	→	Return to main page
				No	→	Exit

The Risk Governance phases decision tree is illustrated at Figure 12 below.

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

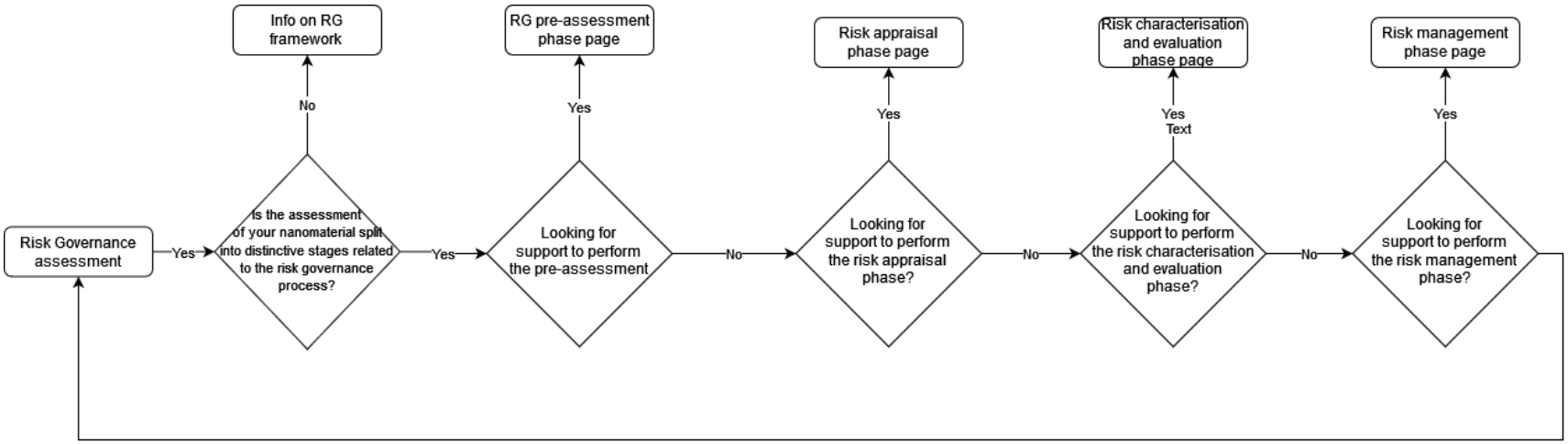

Figure 12: The illustrated version of the Risk Governance phases decision tree

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

3.2 SSbD, new methodologies and general innovation governance

Materials have been gathered related to SSbD, new methodologies and innovation governance of nanomaterials. The SSbD, new methodologies and general innovation governance decision tree is presented below in Table 13.

Table 13: SSbD, new methodologies and general innovation governance Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Looking for an introduction to Safe and Sustainable by Design framework and principles?	Yes/No	Binary	Yes	→	Link to RiskGONE SSbD page, NanoCommons SSbD page (https://nanocommons.github.io/user-handbook/SSbD/) and chapter 1.5 of D3.1
				No	2	
2	Looking for an introduction to New Approach Methodologies?	Yes/No	Binary	Yes	→	Read chapter 4 of RiskGONE D3.1
				No	3	
3	Looking for information on extrapolation from *in vitro* to *in vivo*, and from in silico to humans?	Yes/No	Binary	Yes	→	Read chapter 5 of RiskGONE D3.1
				No	4	
4	Looking for information on nanoinformatics models and services?	Yes/No	Binary	Yes	4A-4B	
				No	5	
4A	Are you familiar with the NanoSolveIT nanoinformatics tools?	Yes/No	Binary	Yes	4B	
				No	→	Link to NanoSolveIT Cloud platform https://cloud.nanosolveit.eu/services/
4B	Are you familiar with the NanoCommons nanoinformatics tools?	Yes/No	Binary	Yes	5	
				No	→	Link to NanoCommons nanoinformatics page https://nanocommons.github.io/user-handbook/nanoinformatics/
5	Have you checked the available platforms at the NanoRisk Governance portal?	Yes/No	Binary	Yes		Return to main menu

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

				No	→	Link to NanoRisk Governance portal platforms page http://nanoriskgov.eu/platforms.html

The SSbD, new methodologies and general innovation governance decision tree is illustrated at Figure 13 below.

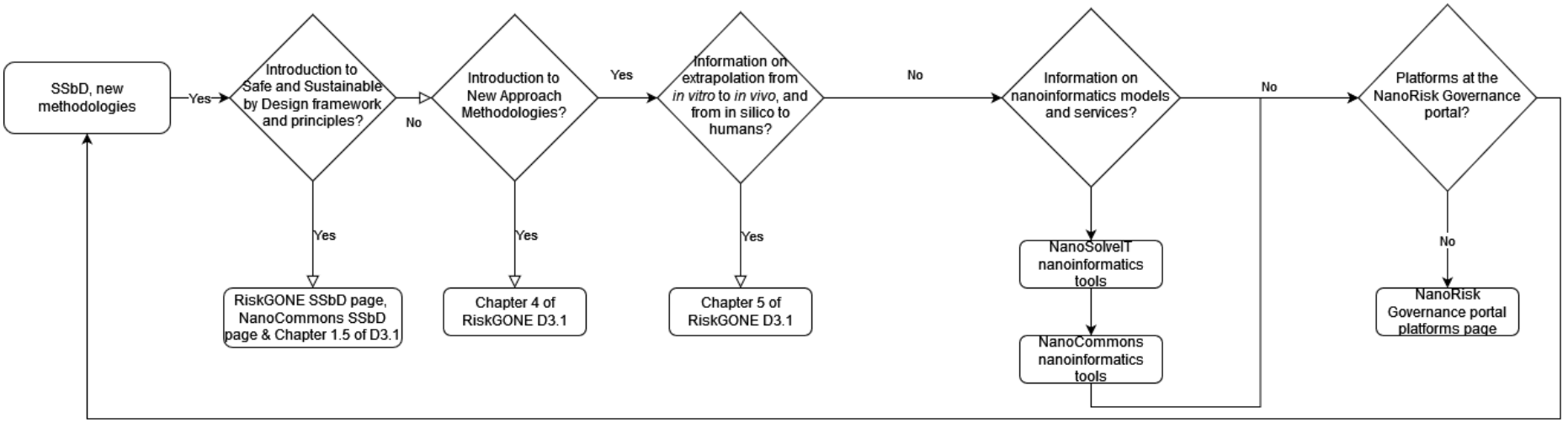

Figure 13: The illustrated version of the SSbD, new methodologies and general innovation governance decision tree

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

3.3 Technical guidance and standardisation

Materials have been gathered related to Technical guidance and standardisation for nanomaterials. The Technical guidance and standardisation decision tree is presented below in Table 14.

Table 14: Technical guidance and standardisation Decision tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Have you visited the RiskGONE TGs and guidelines dedicated page?	Yes/No	Binary	Yes	2	
				No	→	Link to TG – Guidelines page
2	Have you visited the NanoCommons NanoRisk Governance handbook page?	Yes/No	Binary	Yes	3	
				No	→	Link to NanoCommons NanoRisk Governance page https://nanocommons.github.io/user-handbook/NanoGovernance/
3	Have you visited the Guidance page of the NanoRisk Governance portal?	Yes/No	Binary	Yes	4	
				No	→	Link to Guidance page of NanoRisk Governance portal http://nanoriskgov.eu/guidance.html
4	Have you checked the RiskGONE training materials?	Yes/No	Binary	Yes		Return to main menu
				No	→	Link to RiskGONE training page

The Technical guidance and standardisation decision tree is illustrated at Figure 14 below.

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

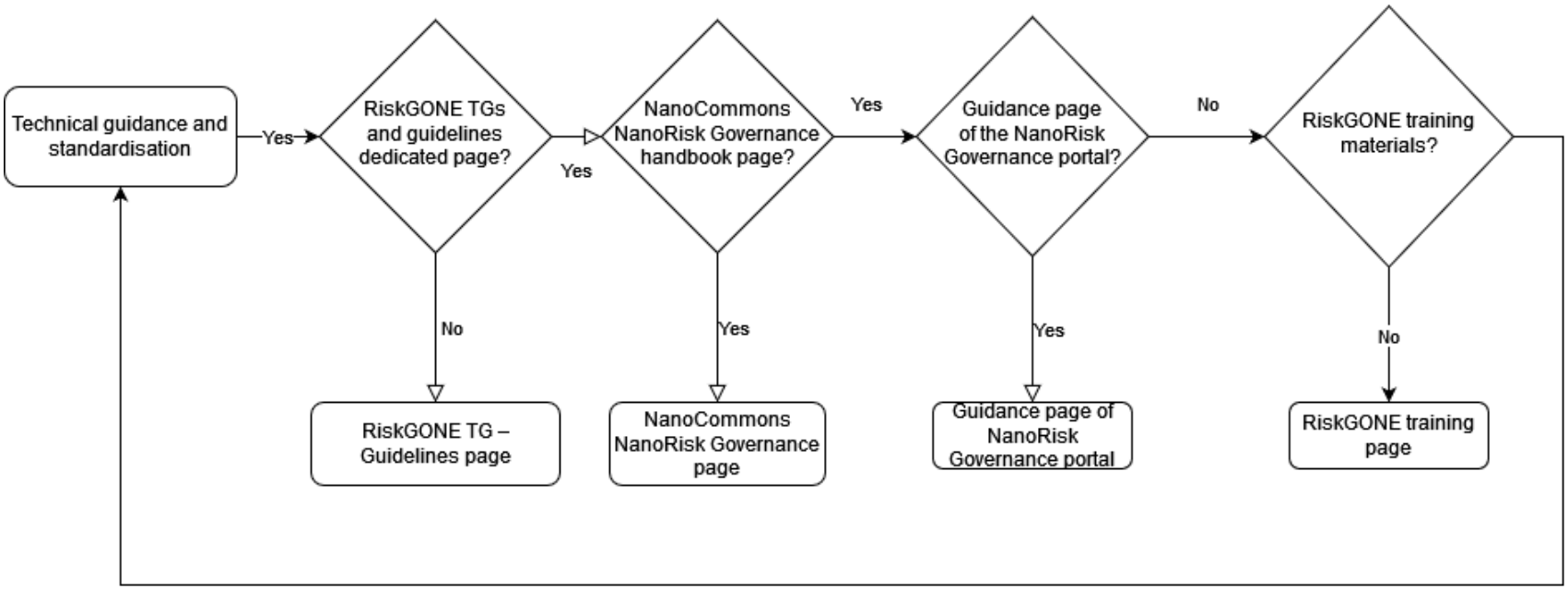

Figure 14: The illustrated version of the Technical guidance and standardisation decision tree

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

3.4 Data quality, Open data and FAIR principles

Materials have been gathered related to Data quality, Open data and FAIR principles. The Data quality, Open data and FAIR principles decision tree is presented below in Table 15.

Table 15: Data quality, Open data and FAIR principles Decision Tree

Question #	Question text	Answer	Type	If	Jump to	Guidance
1	Looking for an introduction to data quality and Weight of evidence (WoE) methodologies?	Yes/No	Binary	Yes	→	Read chapters 3.1 and 3.2 of RiskGONE D3.1
				No	2	
2	Looking for information on data quality characteristics?	Yes/No	Binary	Yes	→	Read chapter 3.3 of RiskGONE D3.1
				No	3	
3	Looking for information on Data quality assessment schemes?	Yes/No	Binary	Yes	→	Read chapter 3.4 of RiskGONE D3.1
				No	4	
4	Looking for information on Data Entry Templates?	Yes/No	Binary	Yes	4A	
				No	5	
4A	Would you like to access the RiskGONE data templates?	Yes/No	Binary	Yes	→	Link to eNanoMapper data entry templates of RiskGONE
				No	→ and then 5	Read chapter 3.5 of RiskGONE D3.1
5	Looking for information on quality in Metrology?	Yes/No	Binary	Yes	→	Read chapter 3.6 of RiskGONE D3.1
				No	6	
6	Looking for information on scientific approaches for data quality assessment?	Yes/No	Binary	Yes	→	Read chapter 3.7 of RiskGONE D3.1
				No	7	

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

7	Looking for information on Open Data and Data management?	Yes/No	Binary	Yes	→	Link to NanoCommons Data Management page https://nanocommons.github.io/user-handbook/data-management/
				No	8	
8	Looking for information on FAIR principles and FAIRification?	Yes/No	Binary	Yes	→	Link to NanoCommons FAIRification page https://nanocommons.github.io/user-handbook/FAIRification/
				No	9	
9	Have you checked the data info page of the NanoRisk Governance Portal?	Yes/No	Binary	Yes		Return to main menu
				No	→	http://nanoriskgov.eu/data.html

The Data quality, Open data and FAIR principles decision tree is illustrated at Figure 15 below.

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

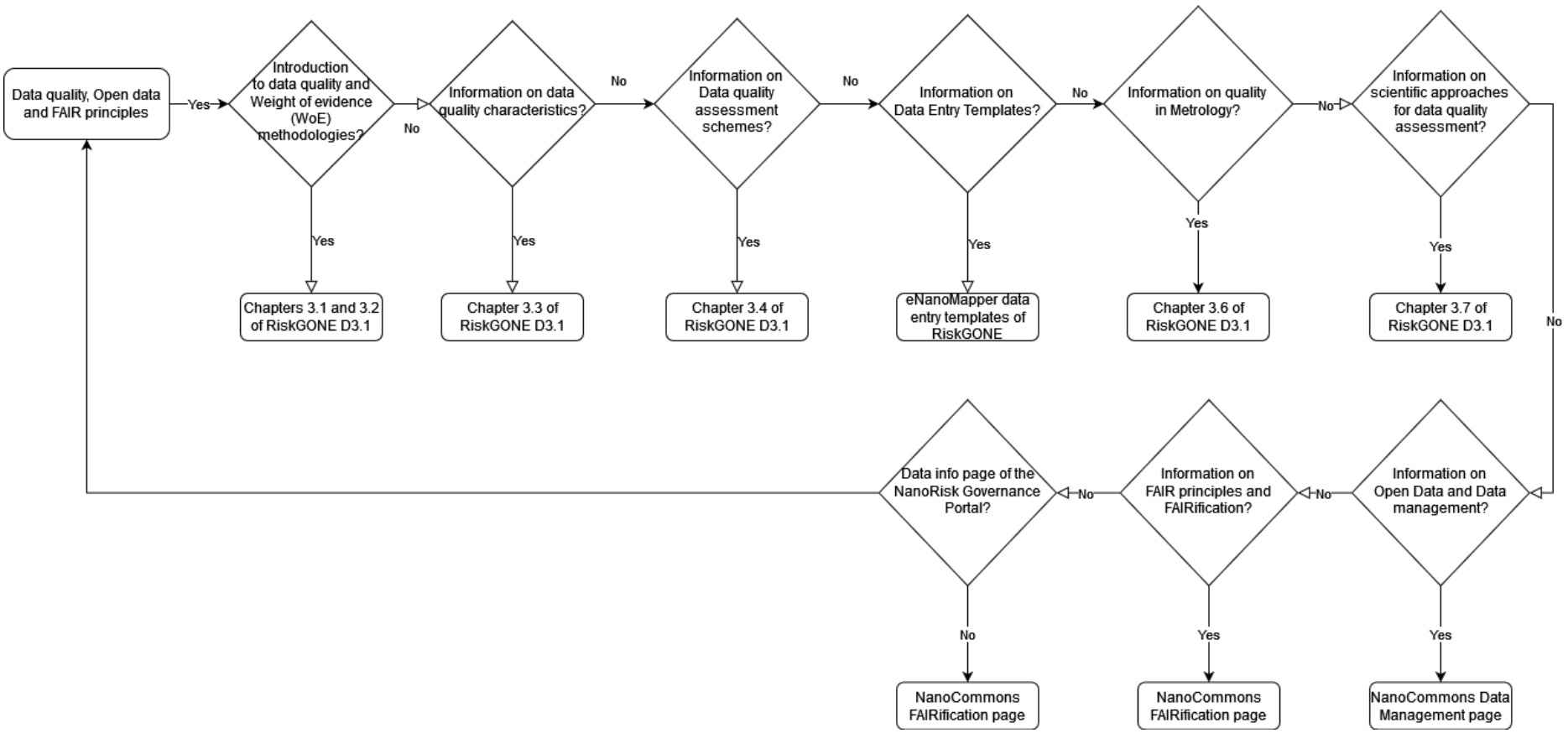

Figure 15: The illustrated version of the Data quality, Open data and FAIR principles decision tree

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

Feedback by the RGC

Following the changes in the European regulatory landscape such as the establishment by DG Environment of the High-Level roundtable, and the ongoing plan for the implementation of the 2020 Chemicals strategy for sustainability (CSS), there has been less interest from stakeholders for the Risk Governance Council (RGC) than originally anticipated. This has required refocusing of the activities related to the RGC, to allow emphasis on the areas that will achieve maximum benefit and to reflect the changed external landscape, that have been made official through the amendment of the RiskGONE project in 2022. In this view, the feedback by the Risk governance pre-council/committee (EAB members), as described in the original proposal, has not been materialised since the RGC implementation has been re-evaluated and considered out of scope.

3. Conclusions

Deliverable 2.3 includes the description of the modular and easy-to-use decision trees, which have been developed by the RiskGONE consortium for complementing and operationalising the RiskGONE RG framework and its IT implementation into the RiskGONE Cloud platform. The decision trees provide easy navigation to the different aspects of the governance of NMs and the various scientific outputs of the RiskGONE project, such as: Characterisation, fate, and dosimetry of NMs, Human hazard and environmental hazard assessment, Risk Assessment, Economic assessment, Ethical and LCA assessment and more, as described in Chapter 2. The decision trees are complemented by toolboxes and other materials, as part of the overall architecture of the RiskGONE Cloud Platform, which is described in D2.5.

4. Deviations

The RiskGONE Consortium envisioned a specific structure and role for the RGC, under the auspices of the Agencies of the European Commission. The decision trees and the RG framework, including the various tools, guidance and guidelines, were originally planned to be transferred to the RGC, which would act as a science-based governance body for ENMs safety and would provide responsible 2-way communication with stakeholders and civil society. Following the updates on the European regulatory landscape and the subsequent amendments of the project as described above, the scope and content of D2.3 had to be updated and changed to fit the needs of various different types of stakeholders, which led to a deviation in the foreseen delivery date of the deliverable. To minimize the impact of this deviation, WP2 partners have re-evaluated the content of the guiding schemes and adapted to include information that was not foreseen before. Nevertheless, the successful implementation of the decision trees within the RiskGONE Cloud platform has been completed, therefore it is considered that the overall quality of the scientific output of the project has not been influenced by the delay.

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

5. References

[1] P. Isigonis *et al.*, 'Risk Governance of Emerging Technologies Demonstrated in Terms of its Applicability to Nanomaterials', *Small*, vol. 16, no. 36, p. 2003303, Sep. 2020, doi: 10.1002/smll.202003303.

[2] Environmental Defense Fund and DuPont, 'Nano Risk Framework', Washington, 2007.

[3] ISO organisation and R. M. ISO/TC 262, 'ISO 31000:2018, Risk management — Guidelines', 2018.

[4] IRGC, 'Introduction to the IRGC Risk Governance Framework, revised version', 2017, doi: 10.5075/EPFL-IRGC-233739.

[5] O. Renn, A. Klinke, and M. van Asselt, 'Coping with Complexity, Uncertainty and Ambiguity in Risk Governance: A Synthesis', *AMBIO*, vol. 40, no. 2, pp. 231–246, Mar. 2011, doi: 10.1007/s13280-010-0134-0.

[6] A. Jovanovic *et al.*, 'Managing emerging technology-related risks', no. CWA 16649, 2013.

[7] 'NanoTEST FP7 Project'. http://www.nanotest-fp7.eu/

[8] 'MARINA FP7 Project'. https://cordis.europa.eu/project/id/263215

[9] 'SUN FP7 Project'. http://www.sun-fp7.eu/

[10] 'NANoREG FP7 Project'. http://www.nanoreg.eu/

[11] 'NANoREG2 H2020 Project'. http://www.nanoreg2.eu/

[12] 'caLIBRAte H2020 Project'. http://www.nanocalibrate.eu

[13] 'NanoMILE FP7 Project'. http://www.nanomile.eu-vri.eu

[14] P. Isigonis *et al.*, 'Risk Governance of Nanomaterials: Review of Criteria and Tools for Risk Communication, Evaluation, and Mitigation', *Nanomaterials*, vol. 9, no. 5, p. 696, May 2019, doi: 10.3390/nano9050696.

[15] E. Semenzin *et al.*, 'Guiding the development of sustainable nano-enabled products for the conservation of works of art: proposal for a framework implementing the Safe by Design concept', *Environmental Science and Pollution Research*, vol. 26, no. 25, pp. 26146–26158, Sep. 2019, doi: 10.1007/s11356-019-05819-2.

[16] A. Kraegeloh, B. Suarez-Merino, T. Sluijters, and C. Micheletti, 'Implementation of Safe-by-Design for Nanomaterial Development and Safe Innovation: Why We Need a Comprehensive Approach.', *Nanomaterials*, vol. 8, no. 4, p. 239, Apr. 2018, doi: 10.3390/nano8040239.

[17] A. Sips, C. Noorlander, H. Lehmann, and K. Höhener, 'NANoREG Safe-by-Design (SbD) Concept to be used for the first ProSafe Call and EU US CoR', 2015.

[18] R. Hjorth, L. van Hove, and F. Wickson, 'What can nanosafety learn from drug development? The feasibility of "safety by design"', *Nanotoxicology*, vol. 11, no. 3. Taylor and Francis Ltd, pp. 305–312, Mar. 16, 2017. doi: 10.1080/17435390.2017.1299891.

[19] K. Savolainen *et al.*, *Nanosafety in Europe 2015-2025: Towards Safe and Sustainable Nanomaterials and Nanotechnology Innovations*. 2013. doi: 10.13140/2.1.3084.8969.

[20] C. W. Babbitt and E. A. Moore, 'Sustainable nanomaterials by design', *Nature Nanotechnology*, vol. 13, no. 8, pp. 621–623, Aug. 2018, doi: 10.1038/s41565-018-0235-7.

[21] A. D. Maynard and R. J. Aitken, '"Safe handling of nanotechnology" ten years on', *Nature Nanotechnology*, vol. 11, no. 12, pp. 998–1000, Dec. 2016, doi: 10.1038/nnano.2016.270.

[22] 'Gov4NANO H2020 Project'. http://www.gov4nano.eu

[23] 'NANORIGO H2020 Project'. http://www.nanorigo.eu

[24] 'RiskGONE H2020 Project'. http://www.riskgone.eu/

[25] J. J. Scott-Fordsmand *et al.*, 'We need governance of Nanotechnology now: developing a sustainable system for European society', 2020, doi: Submitted for publication.

[26] 'NanoCommons H2020 Project'. http://www.nanocommons.eu/

[27] 'NanoInformaTIX H2020 Project'. http://www.nanoinformatix.eu/

[28] 'NanoSolveIT H2020 Project'. http://www.nanosolveit.eu/

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

[29] D. D. Varsou *et al.*, 'A safe-by-design tool for functionalised nanomaterials through the Enalos Nanoinformatics Cloud platform', *Nanoscale Advances*, vol. 1, no. 2, pp. 706–718, 2019, doi: 10.1039/c8na00142a.
[30] EU, 'Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy', 2000.
[31] EU, 'Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives', 2008.
[32] A. Hardy *et al.*, 'Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health', Wiley-Blackwell Publishing Ltd, Jul. 2018. doi: 10.2903/j.efsa.2018.5327.
[33] I. Malsch, P. Isigonis, and M. Dusinska, 'Embedding Ethical Impact Assessment in Nanosafety Decision Support', 2019, doi: Manuscript submitted for publication.
[34] M. D. Wilkinson *et al.*, 'The FAIR Guiding Principles for scientific data management and stewardship', *Scientific Data*, vol. 3, no. 1, p. 160018, Dec. 2016, doi: 10.1038/sdata.2016.18.
[35] R. Owen, P. Macnaghten, and J. Stilgoe, 'Responsible research and innovation: From science in society to science for society, with society', *Science and Public Policy*, vol. 39, no. 6, pp. 751–760, Dec. 2012, doi: 10.1093/scipol/scs093.
[36] A. Grunwald, 'Responsible Research and Innovation: An Emerging Issue in Research Policy Rooted in the Debate on Nanotechnology', 2014, pp. 191–205. doi: 10.1007/978-94-017-9103-8_12.
[37] I. Mahapatra, J. R. A. Clark, P. J. Dobson, R. Owen, I. Lynch, and J. R. Lead, 'Expert perspectives on potential environmental risks from nanomedicines and adequacy of the current guideline on environmental risk assessment', *Environmental Science: Nano*, vol. 5, no. 8, pp. 1873–1889, 2018, doi: 10.1039/c8en00053k.
[38] J. Stilgoe, R. Owen, and P. Macnaghten, 'Developing a framework for responsible innovation', *Research Policy*, vol. 42, no. 9, pp. 1568–1580, Nov. 2013, doi: 10.1016/J.RESPOL.2013.05.008.
[39] T. Gebel *et al.*, 'Manufactured nanomaterials: categorization and approaches to hazard assessment', *Archives of Toxicology*, vol. 88, no. 12. Springer Verlag, pp. 2191–2211, Nov. 29, 2014. doi: 10.1007/s00204-014-1383-7.
[40] K. Donaldson and C. A. Poland, 'Nanotoxicity: Challenging the myth of nano-specific toxicity', *Current Opinion in Biotechnology*, vol. 24, no. 4. Elsevier Current Trends, pp. 724–734, Aug. 01, 2013. doi: 10.1016/j.copbio.2013.05.003.
[41] A. E. Nel *et al.*, 'Where Are We Heading in Nanotechnology Environmental Health and Safety and Materials Characterization?', *ACS Nano*, vol. 9, no. 6. American Chemical Society, pp. 5627–5630, Jun. 23, 2015. doi: 10.1021/acsnano.5b03496.
[42] M. Riediker *et al.*, 'Particle toxicology and health - Where are we?', *Particle and Fibre Toxicology*, vol. 16, no. 1. BioMed Central Ltd., Apr. 23, 2019. doi: 10.1186/s12989-019-0302-8.
[43] B. C. Steimle, J. L. Fenton, and R. E. Schaak, 'Rational construction of a scalable heterostructured nanorod megalibrary', *Science*, vol. 367, no. 6476, pp. 418–424, Jan. 2020, doi: 10.1126/science.aaz1172.
[44] L.-J. A. Ellis, E. Valsami-Jones, and I. Lynch, ' Exposure medium and particle ageing moderate the toxicological effects of nanomaterials to Daphnia magna over multiple generations: a case for standard test review? ', *Environmental Science: Nano*, 2020, doi: 10.1039/d0en00049c.
[45] L. Armand *et al.*, 'Long-term exposure of A549 cells to titanium dioxide nanoparticles induces DNA damage and sensitizes cells towards genotoxic agents', *Nanotoxicology*, vol. 10, no. 7, pp. 913–923, Aug. 2016, doi: 10.3109/17435390.2016.1141338.

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

www.riskgone.eu | riskgone@nilu.no

VENICE, 31 07 2023

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