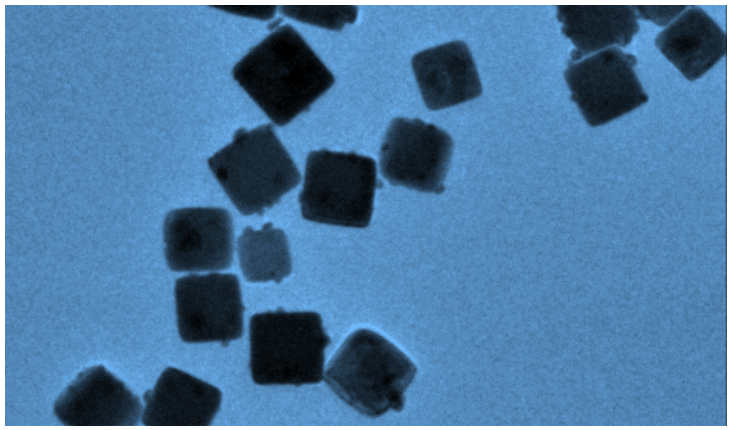


01
July 2015

Assessment and mitigation of nano-enabled product risks on human and environmental health

GUIDEnano

INSIDE THIS ISSUE

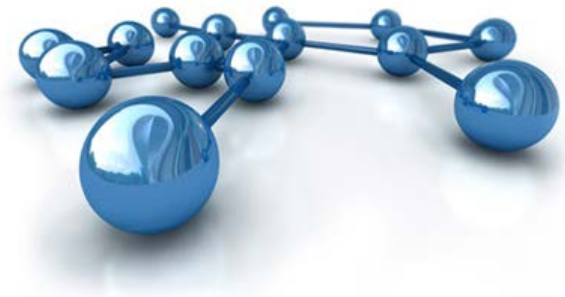
Project Presentation

The main objective of GUIDEnano is to develop innovative methodologies to evaluate and manage human and environmental health risks of nano-enabled products, considering the whole product life cycle.

A strategy to identify hot spots for release of nanomaterials (NMs) will be followed by decision trees to guide on the use of (computational) exposure models and, when necessary, design cost-effective approaches for experimental exposure assessment. These will include on-site and off-site monitoring of industrial processes, use, accelerated aging, recycling and disposal set-ups. Similarly, a tiered strategy to evaluate the environmental fate and the hazards for ecosystem and human health of NMs will be developed.

The project will consider pristine synthesized NMs, transformed NMs released during the life cycle of the product, and interactions of the NMs with other substances in their host matrices and ubiquitous pollutants. The project will also develop innovative solutions to reduce identified risks. These will include safer-by-design approaches, new technological solutions for exposure control measures, and solutions for waste minimization and treatment.

These developments will be incorporated into a web-based Guidance Tool, which will guide the nano-enabled product developers (industry) into the design and application of the most appropriate risk assessment & mitigation strategy for a specific product. This methodology will set up the basis for the certification (by an independent third party), as a risk communication tool addressed to regulators, insurance companies, and society.



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GUIDEnano

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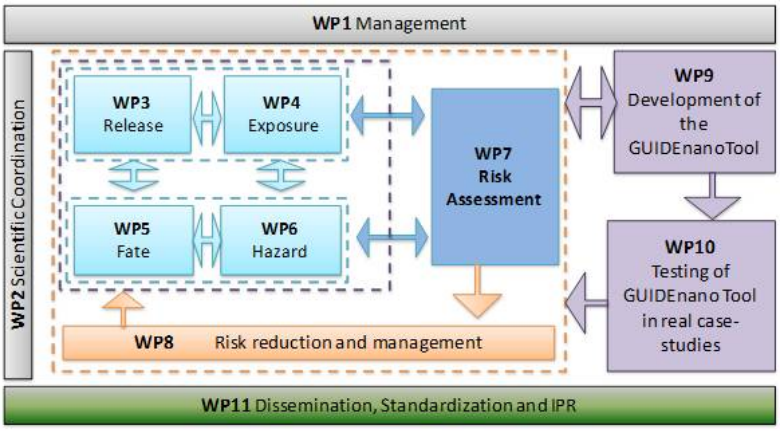
STRUCTURE BEHIND THE PROJECT

GUIDEnano is structured into 11 work packages arranged in four main blocks:

- **WP1 and WP2:** *Coordination block*
- **WPs 3-8:** *Knowledge block: subdivided into different technological building sub-blocks. It will generate the scientific input to the GUIDEnano Tool.*
- **WP9 and WP10:** *Tool development and case studies to validate the tool*
- **WP11:** *Dissemination, Standardization, and IPR block.*



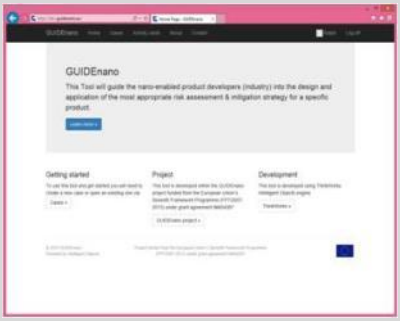
WORK PLAN

Three versions of the GUIDEnano Tool will be released during the project. GUIDEnano Tool.v1 is already developed and incorporates the release, exposure and environmental fate prediction modules.

AFTER 18 MONTHS

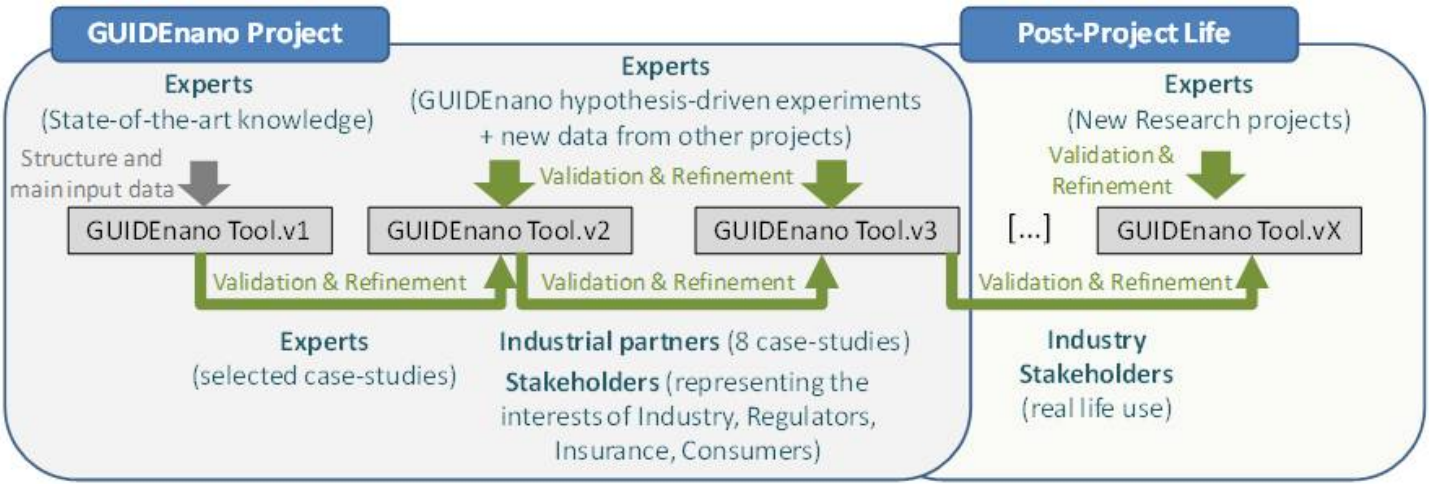
Main achievements

GUIDEnano tool v1 was released in month 18. This version enables the user to model the life cycle of a nanomaterial-enabled product, from production until disposal. V1 focuses on the material flow, identifying relevant exposure/release and hazard hotspots. Future versions 2 and 3 will incorporate hazard and risk assessment as well as a decision module to support the user in selection of appropriate risk refinement and risk mitigation activities.



GUIDEnano Tool v.2 will refine such modules and add the hazard and risk assessment ones, as well as the decision module to support the user in the selection of appropriate risk refinement and risk mitigation activities.

GUIDEnano Tool v.2 will be used by the industrial partners of the consortium to test 8 case studies, and will also be presented to different stakeholders. The feedback received as well as the results of the experiments performed during the project (and from other running projects) will be used to refine the Tool and generate GUIDEnano Tool.v3, the final product of the GUIDEnano project. We are also currently evaluating different options to ensure the sustainable hosting and exploitation of the Tool after the project ends.



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Our work progress and people

WP3

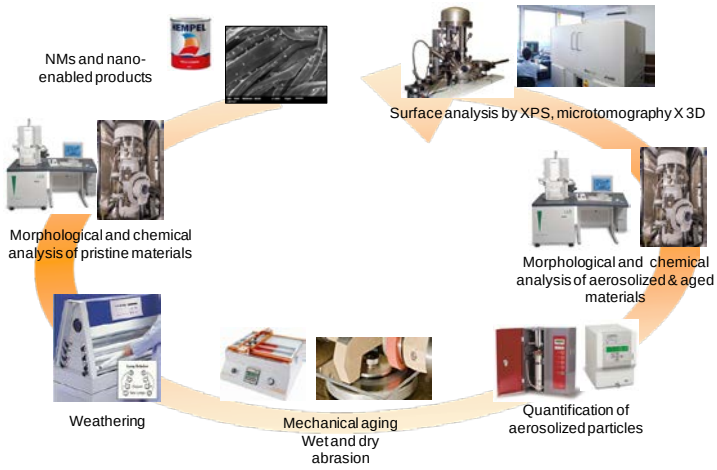
Partners:

LIFE CYCLE OF NM-ENABLED PRODUCTS

The main objective is to develop a strategy to identify and predict release into the environment of NM throughohout the life cycle of NM-enabled products.

A literature review on nanomaterials release into the environment during the entire life cycle of NM-enabled products has been conducted. As a result, a preliminary release library has been developed containing detailed information regarding release estimates, tests conducted and material characterization. Moreover, some critical research data gaps that have not been sufficiently addressed in the literature have been identified (D3.1). On this basis, a strategy to predict release into the different environmental compartments has been developed. Assumptions and uncertainty associated to these decisions are currently under discussion between WP3 and WP7. This strategy is based on a stepwise approach divided in three different levels which depends on the degree of knowledge of the release scenario. Currently, a series of experiments are being conducted to reduce key uncertainties that lead to the prediction of release.

Scheme showing the experimental settings to simulate and characterize the potential release from the nano-enabled products along their life-cycle



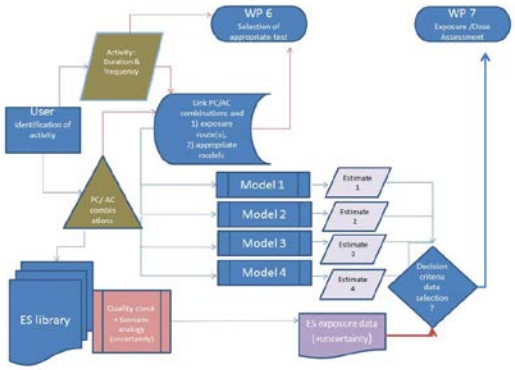
WP4

Partners:

EXPOSURE ASSESSMENT

The main objective is to develop an approach to predict worker and consumer exposure to NMs and NM-enabled products. As the GUIDEnano tool should provide a scientifically sound probabilistic risk assessment, i.e. a distribution of the risk characterization ratio, the focus of the exposure assessment is on providing distributions of exposure for relevant exposure scenarios.

Existing models that predict exposure for relevant scenarios were identified. The next step was to check their performance for nanomaterials, followed by generation of new exposure data to (re)calibrate or adjust the models. Data will also be used to complete so called Exposure Scenarios (ES) to be included in the Exposure Scenario Library. Since relatively few data exist on the effectiveness of exposure control measures, simulated workplace exposure studies will be conducted to provide quantitative information. All measurements will be conducted in close collaboration with the sister projects SUN and NanoREG.



Flow chart of information within the WP4, showing exposure assessment by model estimates, from the ES library and from measurements

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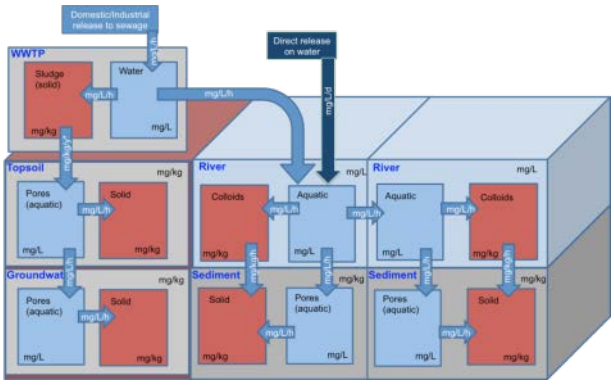
Our work progress and people

WP5

ENVIRONMENTAL FATE

The main objective of this WP is to generate strategies to understand how NMs behave in natural systems including the critical transformation reactions. Several key questions are being specifically quantitatively addressed to develop a conceptual fate model framework (Figure 1) focused on NM fate and behavior for implementation into the GUIDEnano Tool and parameterized using data already available in the literature or by obtaining experimental results when data gaps are identified.

The environmental component of the GUIDEnano Tool will contain a customizable model world, which was already established. The GUIDEnano fate model world includes fresh, estuarine and marine waters, soil, and wastewater treatment compartments (Figure 1). Each different compartment belongs to a certain class, has its own set of properties and has methods that calculate the fate of the NM objects based on their properties as well as the properties of the compartment. The experimental task of this WP includes: i) determination of the validity of the transfer factor as the key parameter in the waste water treatment plant fate model, ii) determination of the relationships between NM, soil properties and fate descriptors (k_a, k_d, k_t), iii) quantification of the migration parameters of different nZVI in the subsurface, and iv) quantification of the kinetic rates for dissolution, aggregation and sedimentation, and determination of the main components present in the environmental compartment dictating these kinetic rates. This experimental task will allow developing the world fate model for different case-studies.



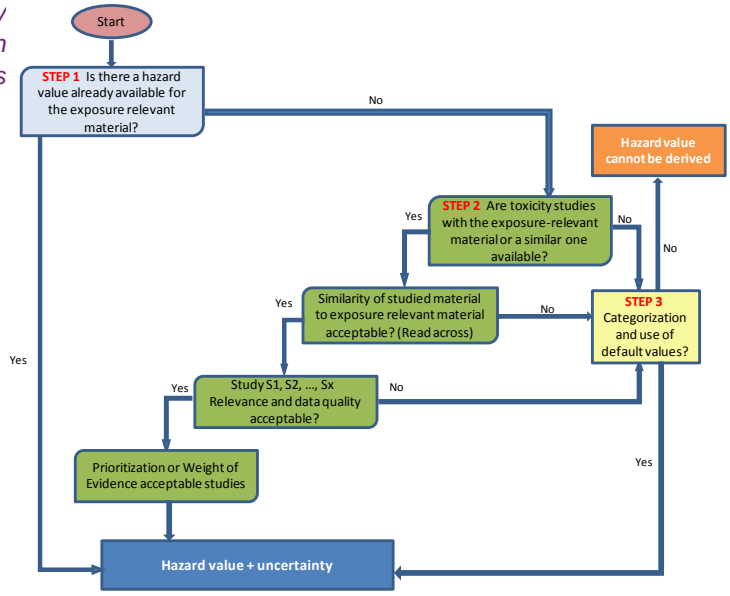
*Schematic overview of the model world approach for the first version of the tool. Units in the compartments are time-dependent mass concentrations, whereas the arrows contain units per time unit as it concerns fluxes between compartments. All compartments contain two objects: an aquatic and a solid between which there is NPs transfer. * - Application of sludge to soils in the order of a certain tonnage per year (a different unit compared to other processes that occur much faster).*

WP6

HAZARD ASSESSMENT

The main goal of this WP is to develop a strategy for predicting the ecotoxicological and human health hazard of the exposure-relevant NM forms throughout the lifecycle of NM-enabled products.

The human and eco-toxicologists worked together to develop a hazard assessment strategy that would enable the estimation of hazard values for any nanomaterial based on the available existing data, even "no data". This is framed around making both nanomaterial related read across assumptions and using normal toxicological extrapolations and assessment factors. Experimental efforts are now underway to assess and underpin the accuracy of the assumptions and extrapolations made within the initial framework, which should allow assignment of uncertainty measures to the "worst case hazard estimates".



GUIDEnano hazard assessment strategy for a human and environmental risk assessment. Note: a hazard value could be threshold, for example a PNEC-, DNEL-, or OEL-like value; or a statement, for example mutagenic/non-mutagenic

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WP7

Partners:

TNO innovation for life

INIA Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria

rivm Rijksinstituut voor Volksgezondheid en Milieu

Pinsent Masons

RISK ASSESSMENT

The main goal of this work package is to develop a strategy for risk assessment of release- and exposure-relevant NMs in NM-enabled products throughout the various product life-cycle stages. This risk assessment strategy is incorporated in the interactive web-based GUIDEnano Tool, which will guide the NM-enabled product developers (mainly industry) into the design and application of the most appropriate risk assessment and mitigation strategy for a specific product. The strategy will be evaluated with hypothetical and real case studies within the project.

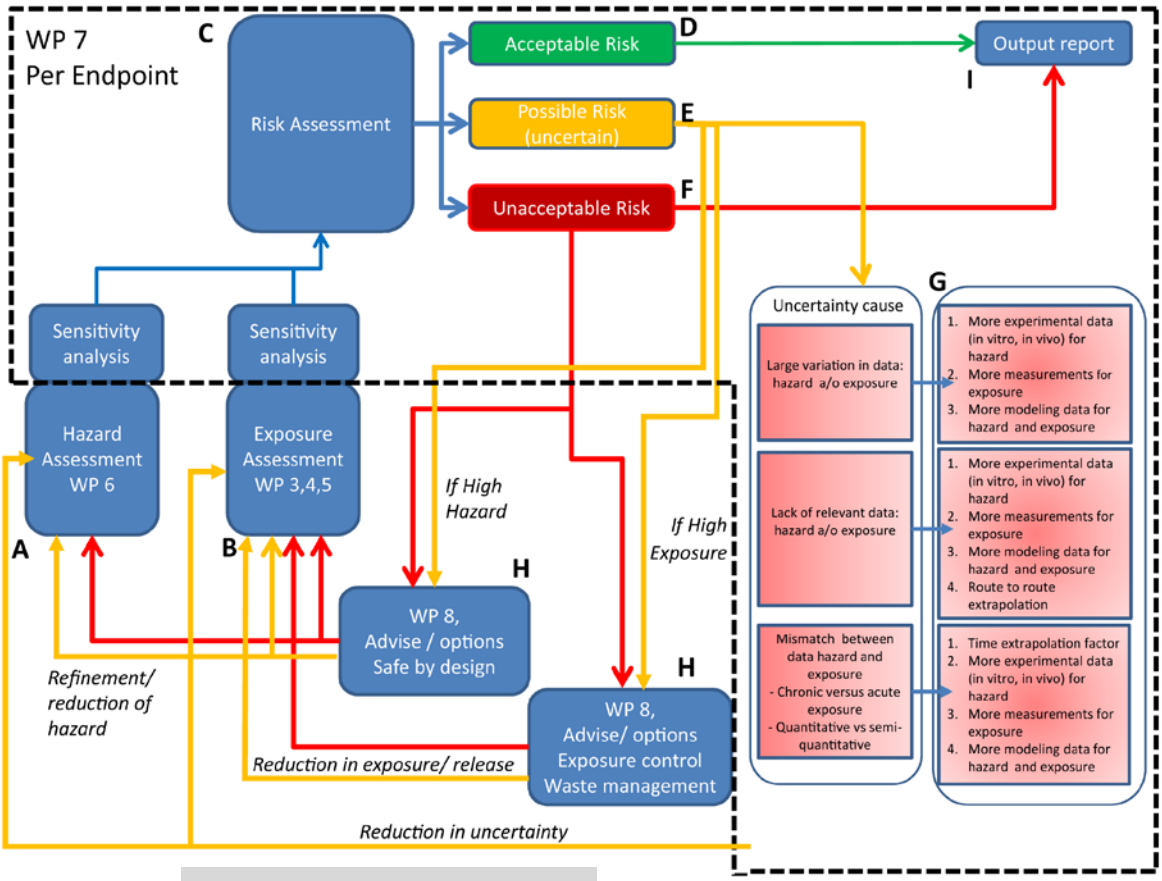
The initial decision flow for risk assessment to be incorporated in the GUIDEnano tool has been developed during several expert meetings. To develop the initial strategy to assess the risk of NMs, information on existing risk assessment methodologies was used, together with discussions with experts from inside and outside the project.

The strategy can be divided in four main elements: i) Input and information requirements (hazard and exposure assessment); ii) Risk assessment (calculation of a risk ratio and classification into three risk categories); iii) Reduction of uncertainty and Risk mitigation; iv) Output report

A suitable sensitivity analysis tool has been created by using Shiny, a web application framework for R that allows the user to manually input equations and parameter values. The results of the sensitivity analysis need to be further discussed with the individual WPs in the coming months.

The outline of the output report of the tool has been discussed. A detailed background report with all information generated by the tool together with an executive summary will be provided to the user with a summary of the risk assessment (probability of risk) together with proposed follow up actions.

A first draft approach to evaluate on the acceptability of the risk assessment process by insurance communities and other relevant stakeholders has been developed. The purpose of the exercise of obtaining feedback from industry stakeholders in relation to the GUIDEnano tool is to seek views, which will help to shape the output of the Tool dependent upon the needs of its target market.



Draft risk assessment decision flow

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GUIDEnano

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Our work progress and people

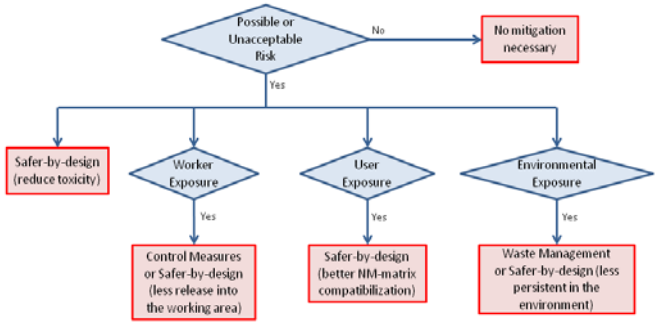
WP8

NEW TECHNOLOGIES FOR RISK REDUCTION AND RISK MANAGEMENT

The main goal of this work package is to develop the different strategies for reducing the potential risks detected in the risk assessment done by the GUIDEnano Tool. The intention is that the final user will obtain a list of risk mitigation measures that will make the whole process safe, if possible. The different risk mitigation strategies (safer-by-design, occupational exposure control and advanced waste management) will be evaluated with hypothetical and real case studies within the project.

The different risk mitigation strategies are divided in three approaches: Safer-by-design, Exposure Control and Waste management. Safer-by-design strategies do not only focus on hazard reduction, but other strategies are considered such as reduction of the release during the use phase and reduction of the environmental or occupational exposure. Occupational exposure control strategies are divided into engineered measures (e.g. fumehoods, closed systems and ventilation) and "nano-specific" personal protective equipment. Waste management strategies focus on the minimization of NM released into the environment and in assuring waste management workers safety. A series of decision trees have been developed to drive from Risk Assessment results to Risk Mitigation strategies within GUIDEnano Tool.
Furthermore, different experimental work is being developed to evaluate the efficiencies of different risk mitigation strategies when working with nanomaterials. This experimental work was designed to be as reliable as possible: i) Different NM have been designed in agreement with other WPs to evaluate different safer-by-design strategies, from less toxic materials to more perdurable nano-enabled products; ii) A protocol for a reliable efficiency evaluation of occupational exposure control measures for NM was developed, as well as the necessary setups for such evaluation; iii) The efficiencies of different strategies for NM removal from industrial waste water are being determined, and different reuse, recycling and material/energy recovery strategies are being developed together with industries in the consortium.

Draft of Risk Mitigation decision tree



WP9

DEVELOPMENT OF THE INTERACTIVE WEB-BASED GUIDEnano Tool

The main objective of this WP is to develop a web-based tool that guides end-users step by step to the relevant information for their risk assessments and for defining mitigation plans.

GUIDEnano tool v1 has been released in month 18. The main focus of version 1 is to enable expert users to:

- Add, categorize and describe the nanomaterial and all its forms before, during and after the life of the nano-enabled product under consideration
- Add and connect activities which may affect the nanomaterial form and flow at the different stages within the life cycle and may cause releases to environmental compartments
- Have an overview on nanomaterial flow amounts and rates during the entire life cycle
- Add environmental compartments and zones where released nanomaterials can end up and on which they can be transformed and/or transported
- Add processes and timeframes within zones in order to describe the release, emission,_transformation and/or transportation within a zone or between zones
- Add human and/or species (bio compartments) potentially exposed to either a concentration of nanomaterial in a zone over a period of time or direct exposure
- Have an overview of the identified hazard endpoints per bio compartment potentially exposed during the entire life cycle

The Tool is built on a modular basis which will be easy to update in the future. Later versions 2 and 3 will incorporate hazard and risk assessment as well as a decission module to support the user in selection of appropiate risk refinment and risk mititagion activites.

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GUIDE nano

CASE STUDIES

ANTIFOULING PAINTS FOR SHIPS

ZnO

ANTISLIP / PHOTOCATALYTIC CERAMIC TILES

Al_2O_3/SiO_2 - TiO_2

COATING FOR FOOD PACKAGING

Nanocelullose

ANTIMICROBIAL FABRICS

Ag

PHOTOCATALYTIC HOT BITUMINOUS MIXTURES

TiO_2

SELF-CLEANING AGENT

TiO_2 + Ag

POLYMERS FOR FUEL SYSTEM COMPONENTS

MWCNT

GROUNDWATER REMEDIATION

nFe^0

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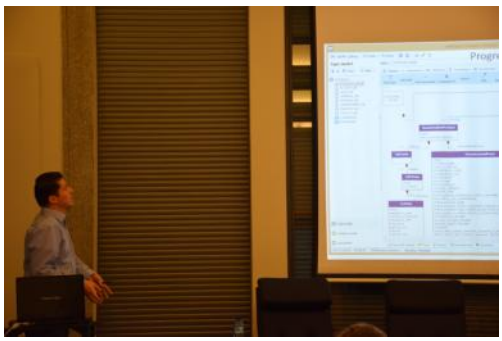
Meetings within the project

12-Month Meeting in Madrid (11/2014)

Over 50 researchers attended the 12 month meeting that took place at the facilities of INIA in Madrid the 27th and 28th of November. More than half of the meeting was dedicated to break-out sessions were inter-WP and intra-WP discussions took place.



GUIDEnano Tool presentation

6-Month Meeting in Utrecht (05/2014)

6 Month Meeting was hosted by TNO on the 26-28th of May 2014 at the University of Utrecht. The project was held over the first two days where updates from each work package were presented by the WP leaders. The partner then split into groups for WP interactions. The plans were laid for the next 6 months of the project. The third day of the meeting was dedicated to the Exploitation Seminar Strategy (ESS) where an expert coached the consortium on potential results to be exploited from GUIDEnano. Based on previous partner contributions, there were several potential results identified.

Break-out sessions for intra/inter WP discussions

The first Scientific Committee

The first Scientific Committee (SC) meeting was held in Leiden, The Netherlands on the 16th of September. The SC, which consists of WP leaders, met to discuss the progress of the project after one year and monitor the activities of each WP. The Advisory Board (AB) meeting was held on the following day where the SC met with the members of the AB including BASF and NIA. The project technical advisor, Richard Moore (PTA) was also present. The AB was briefed on the progress of the project to date and discussions about what is expected from the project. Moreover, the coordinators from FP7 projects NANoREG and SUN were invited to the meeting to establish official interactions between the 3 projects.

Kick-Off meeting in Barcelona (12/2013)

GUIDEnano Kick-Off Meeting was held in December 2013 in Barcelona hosted by the coordinator LEITAT. The majority of the partners were present at the meeting where the project objectives were confirmed and plan of the first 6 months were laid.

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Our dissemination

GUIDEnano was disseminated at a number of European and international conferences, some examples are given in the following table:

CONFERENCE	DATE & LOCATION	TITLE	PARTNERS
The NSF Nanoscale Science and Engineering (grantee conference)	***9 - 10 / 12 / 2014*** *Arlington VA, USA*	*Assessment and mitigation of nano-enabled product risks on human and environmental health: Development of new strategies and creation of a digital guidance tool for nanotech industries*	
Workshop on Regulatory Challenges in Risk Assessment of NMs	***23 - 24 / 10 / 2014*** *Helsinki*	*Environmental fate modelling and measurement of nanomaterials*	
OECD WORKING PARTY ON MANUFACTURED NMs: Expert Meeting on Categorization of Manufactured NMs	***17 - 19 / 09 / 2014*** *Washington, USA*	*1) Nanomaterials classification considerations for environmental fate to the Workshops Session 4 on ENVIRONMENTAL FATE* *2) "The 'Source Domain' Concept: Different Release Process and Associated Exposure"*	
NANOON 2014	***5 – 7 / 11 / 2014*** *Brno, Czech Republic*	*Overall presentation of GUIDEnano objectives*	
Sustainable Nanotechnology Conference	***9 – 11 / 3 / 2015*** *Venice*	*The GUIDEnano strategy for nanomaterial environmental hazard assessment along the life cycle / Interactive splCP-Msdata treatment using Nanocount / Development of a initial Risk Assessment strategy within the GUIDEnano Project.*	
SETAC 2015	***3 – 7 / 05 / 2014*** *Barcelona, Spain*	*Non-toxic concentrations of ZnO nanoparticles enhance Cu nanoparticle toxicity in human and fish hepatoma cell lines*	

Events organization

1ST SUSTAINABLE NANOTECHNOLOGY SCHOOL:

Understanding the environmental, health and safety implications of manufactured nanomaterials to foster their sustainable applications (Venice, January 2015).

70 participants coming from Europe as well as United States and Brazil attended to the school. The SNS was organised in the frame of the major EU FP7 projects SUN, MARINA and GUIDEnano and the MODENA Cost Action.

SUSTAINABLE NANOTECHNOLOGY CONFERENCE 2015 : (Venice, March)

Was jointly organized by the Sustainable Nanotechnology Organization (SNO), a USA based non-profit organization dedicated to advancing sustainable nanotechnology, and two large EU FP7 nanosafety projects SUN and GUIDEnano.

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Collaborations with other projects

GUIDEnano / NanoREG / SUN

The aim of this collaboration is to increase efficiency and effectiveness of the three projects by avoiding duplication of work, by taking advantage of the possible synergies and by collaborating on operational and logistical level where possible. There were several meetings between the three projects to formalize the collaboration (collaboration agreement was circulated and discussed-not signed yet) and to plan some action points in the collaboration (proposed actions: Organization of joint dissemination activities, exchange public reports, WP leaders' interactions to avoid overlaps and to take advantages of synergies, potential integration of tools).

- Dissemination activities organized between GUIDEnano and SUN: Sustainable nanotechnology School (www.unive.it/sustainablenanotechschool; Venice, January 2015)

- SNO-SUN-GUIDEnano Sustainable Nanotechnology Conference 2015 (http://www.susnano.org/conferenceOverview2015SNO-SUN-GN.html; Venice, March 2015

GUIDEnano / NanoDefine

As a result of a joint workshop in Berlin in March 2015, a formal collaboration between the two NSC projects GUIDEnano and NanoDefine has been agreed. GUIDEnano aims at developing a guidance web-based tool to evaluate and manage the human and environmental health risks posed by nano-enabled products, considering the whole product life cycle. A central product of NanoDefine, besides the development of methods, instruments and software for nanoparticles analysis, will be a decision support e-tool for the selection of appropriate methods and classification of materials according to the EC nano-definition. In the course of the workshop, possibilities have been evaluated to link the two guidance tools together. Possible options were identified and will be worked out further by the involved IT specialists from both projects. The agreed collaboration leverages the outreach of the individual projects and maximises the benefit for nanosafety in Europe.

Potential Collaborations with other projects

MARINA

Risk assessment strategy is in line with GUIDEnano

e-Nanomapper

After a first face to face meeting to present the objectives of the two projects and discuss potential collaboration, a workshop will be organized in September 2015 involving other projects developing Tools/frameworks to further determine how to proceed

Nanomile

Collaboration has been discussed between the coordinators but further detailed actions in terms of data collation have to be agreed

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GUIDEnano Meet us - Upcoming events

CONFERENCES	DATE & LOCATION	+ INFO
EURONANOFORUM 2015	***10 - 12 / 06 / 2015*** *Riga, Latvia*	*www.euronanoforum2015.eu*
QEEN Workshop	***7 - 8 / 07 / 2015*** *Arlington, USA*	*nano.gov/QEENworkshop*
QualityNano Final Conference	***15 - 17 / 07 / 2015*** *Crete, Greece*	*www.qualitynano.eu*
Nanosafety Cluster meeting	***29 - 30 / 09 / 2015*** *Paris, France*	*www.marina-fp7.eu*
EFSA's 2nd Scientific Conference	***14 - 16 / 10 / 2015*** *Milan, Italy*	*http://www.efsaexpo2015.eu/*
Systems Biology in Nanosafety Research	***9 - 10 / 11 / 2015*** *Stockholm, Sweden*	*http://goo.gl/forms/1aTdAvorp4*
8th Nanotox Conference	***06 / 2016*** *Boston, USA*	

New projects

GUIDEnano partners are currently involved in further ongoing NanoSafety Cluster projects as well as EU/US and nationaland EU regional projects. These ongoing Cluster projects include NANOFASE, which is led by NERC and will start in September 2015.

On behalf of the GUIDEnano Consortium

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