Publishable final activity report

IMPART

Improving the understanding of the impact of nanoparticles on human health and the environment

Integrating Activity

Implemented as

Coordination Action

Contract number:	NMP4-CT-2005-013968
Project Co-ordinators:	
Phase I	CHALEX Ltd.
Phase II:	TEMAS AG
Report prepared by:	TEMAS AG
Reporting period:	from 01.02.2005 to 31.10.2008
Date of issue of this report:	23.02.2009

Project funded by the European Community
under the "Structuring the European Research Area" Specific Programme
Research Infrastructures action

1 Project execution

1.1 Project objectives: Improving the understanding of the impact of nanoparticles on human health and the environment

Nanotechnology is finding increased application in today's society and is being hailed as the next industrial revolution. Companies around the world are beginning to mass-produce nanoparticles (particles less than 100 nm in size) for use in everything from sunscreens to soil reclamation. The production of anthropogenically-derived nanoparticles will inevitably result in the introduction of these materials to the environment. However, despite rapid advances in nanotechnology, knowledge of the potential risks of nanoparticles to human health and the environment is limited. There is a concern that "size matters" with respect to toxicity, irrespective of the chemical composition. There are fears that materials that are biologically inert in bulk tend to become harmful in ultrafine particle form. Analogies have been drawn, for example, on the similarity of the structure of carbon Nanotubes to asbestos fibres, whose detrimental effects on human health are well documented. There is a need to encourage greater understanding of the short and long term implications of nanotechnology for health and the environment.

The primary aim of IMPART was to prevent knowledge of the health and environmental implications of nanoparticles from lagging behind the technological advances. In order to do this, IMPART has fostered communication links between numbers of regional, national and international initiatives in order to reduce duplication of effort, pool expertise and facilitate co-operation between networks. This has resulted in an improvement in the understanding of the potential impact of nanoparticles on human health and the environment.

The specific scientific and technological objectives of the IMPART co-ordination action have been:

1) To co-ordinate the efforts of regional, national and international initiatives represented in the consortium
2) To create and enhance good communication and permanent links between the partners
3) To carry out a review of the latest scientific and technological developments related to the risks of Nanoparticle exposure on human health and the environment
4) To disseminate the project's results through a specialised website and knowledge transfer workshops
5) To make recommendations to major funding bodies for the future research direction in the field
6) To produce guidelines and recommendations for the institution of future Nanoparticle standards and exposure limits

1.2 Contractors involved

1.2.1 Definition of the two phases of the IMPART project

The IMPART project was started February 1, 2005 with CHALEX Ltd. as coordinator. After the first year CHALEX was not able to provide all the necessary documents to the EC on time. Due to this situation the EC decided to suspend the project per June 14, 2006.

A new situation came up when the co-ordinator CHALEX Ltd., during the suspension phase, ceased trading on January 11, 2007. Additional to the co-ordinator two further partners (CODES and CMP Cientifica), which had close business relations with CHALEX Ltd., stopped there company business and, as a consequence the activities within the IMPART project.

Phase I: Duration from February 1, 2005 until June 14, 2006 (suspension)

Phase II: Duration from June 1, 2007 (lifting of the suspension) until July 31, 2008
Prolongation August 1, 2008 until October 31, 2008

1.2.2 Project partners

In order to reactivate the IMPART project after the suspension, and to bring it to a successful end, a new strong team for phase II with previous and new partners from NanoTox was established. Five out of twenty partners left the consortium and 5 new partners joined.

Overview of the IMPART partner phase 1 and phase 2:

Participant No.	Participant Short name	Participant Country	Particant Role	Participating Phases
1	Chalex	UK	CO	Phase 1
2	NFM	IL	CR	Phase 1+2
3	IPC	RO	CR	Phase 1+2
4	JSI	SI	CR	Phase 1+2
5	Uni Leicester	UK	CR	Phase 1
6	KTU	LT	CR	Phase 1+2
7	TUM	DE	CR	Phase 1
8	Codes	IRL	CR	Phase 1
9	UCv	RO	CR	Phase 1+2
10	FzK	DE	CR	Phase 1
11	VDI	DE	CR	Phase 1+2
12	CMP Cientifica	ES	CR	Phase 1
13	ULeu	BE	CR	Phase 1+2
14	UniS	UK	CR	Phase 1+2
15	Temas	CH	CR	Phase 1
	Temas	CH	CO	Phase 2
16	*Number never used*			
17	NIRDTP	RO	CR	Phase 1+2
18	DIT	IRL	CR	Phase 1+2
19	BioMaDe	NL	CR	Phase 1+2
20	LatTox	LV	CR	Phase 1+2
21	UniCrete	EL	CR	Phase 1+2
22	UMan	UK	CR	Phase 2
23	BAS	BG	CR	Phase 2
24	Nofer / NIOM	PL	CR	Phase 2
25	HUT / TKK	FIN	CR	Phase 2
26	EMPA	CH	CR	Phase 2

1.3 Work performed

1.3.1 Phase 1 incl. Suspension (February 2005 – May 2007)

The IMPART project was started February 1, 2005 with CHALEX Ltd. as coordinator.

Work package 1 (Project Management, led by CHALEX) and work package 2 (Co-ordination of Initiatives' Activities, led by FZK) began in Month 1 of the project, while work packages 3 (Risk Assessment of the Effect of Nanoparticles on Health and the Environment) and 4 (Dissemination and Knowledge Transfer) began in Months 14 and 13, respectively.

The network web site went online in the first month of the project: http://www.impart-nanotox.org. This site includes a project summary, diary of events, details of the project

consortium, discussion forum and a members' area for communication between partners. Once completed, a database of initiatives and activities in the field of nanotechnologies and health and environmental implications will be published online and updated regularly. Minutes of meetings and reports are published in the members' area of this web site and members are informed when additional content is made available.

The project kick-off meeting was held in Brussels, Belgium in Month 2 of the project. The first co-ordination seminar was held alongside the kick-off meeting. The aim of this seminar was to increase awareness of the consortium partners of other work being carried out in the field, such that they are able to adapt their own projects and make recommendations to minimise duplication of research efforts. The second seminar took place in Karlsruhe, Germany in Month 11.

Expert group leaders were appointed during the kick-off meeting in Brussels and the first meeting of the expert groups was held alongside the first co-ordination seminar in Brussels. People from the consortium were split into expert groups according to experience and field of work. Members were divided into four agreed subdivisions of the topics: materials for consideration; implications for human health and exposure; impact on the environment; and resulting legislative measures. The report of the deliberations from these meetings has been disseminated amongst consortium members and published online for the benefit of all those involved.

The second meeting of the expert groups was held alongside the second co-ordination seminar and involved general discussion about the project and status of the work of the expert groups. Progress of work was discussed and gaps identified. Further specialisation of topics was performed, with each major subject divided into subprojects. These contributions will sum up to an extended report from the expert meeting.

After the first year, CHALEX was not able to provide all the necessary documents to the EC on time. Due to this situation the EC decided to suspend the project per June 14, 2006.

Due to a TEMAS initiative an internal review meeting with the IMPART and NanoTox partners was held on September 12, 2006 in Zurich. At the meeting several actions were planned and decisions taken to reach the lifting of the suspension of the project as soon as possible. In order to reactivate the project and to bring it to a successful end, a new strong team under the new coordinator TEMAS with previous and new partners was established. Five out of twenty partners left the consortium and five new partner from NanoTox joint it for phase 2.

1.3.2 Phase 2 (June 2007 - October 2008)

In order to secure the main objectives of IMPART a new project planning, and new ANNEX 1 for phase 2 has been elaborated. The key deliverables have been defined as:

1. Input report for phase 2 as summary IMPART phase 1 and the NanoTox[1] projects (Working Report on the Status Quo of Nanomaterials Impact on Health and Environment)
2. Assessment of existing and identification of missing data

[1] During the internal review meeting (September 2006 in Zurich) with the IMPART and NanoTox project members, the EC officer Dr. P. Aguar announced, that the NanoTox project will to be continued and the interested members of NanoTox should become new partners of IMPART phase2.

3. Recommendation and Guidelines for:
    a. Legislation policy makers
    b. Research policy makers
    c. Industry, public and other stakeholders (Guidance Booklet)
4. Dissemination and knowledge transfer
    a. Homepage (Project website)
    b. Nano Safety & Risk database
    c. Main conference for policy makers
    d. Conference with opinion leaders
    e. National workshops

Results of Phase 2

1.3.2.1 Input report for phase 2 as a summary of IMPART phase 1 and NanoTox

The publicly available input report "Working Report on the Status Quo of Nanomaterials Impact on Health and Environment" can be down loaded from the IMPART data base:

www.impart-nanotox.org, Phase 2, data base or
with the direct access to the data base www.temas.ch/IMPART/IMPARTProj.nsf
Publication number "270508",
send a mailto: temas@temas.ch.

Summary of the content of the input report:

3 Exposure
- 3.1 Occupational exposure
- 3.2 Exposure and detection in biological samples/fluids

4 Environment
- 4.1 Natural Nanoparticles in Geological Systems
- 4.2 Nanotechnology and the Environment
- 4.3 Conclusions and Future Research

5 Law and Regulation
- 5.1 Protection of workers' health and safety against risks due to chemicals
- 5.2 ISO Technical Committee

6 Summary of knowledge gaps and recommendations

1.3.2.2 Assessment of existing and identification of missing data (internal reports)

1.3.2.2.1 Legislation

This internal report was included in order to:

- review and assess standards, legislation, ethical issues and policies at international and European level, which have been put in place or are under development
- discuss their implications and effectiveness
- examine ways in which existing legislation is applied to the macro scale counterparts of nanoparticles
- develop strategies for involving external organisations in this task and for encouraging their participation
- update the database with the latest results about legislation issues

This assessment report is not publicly available. For special needs please send an email with your specific needs to the coordinator: temas@temas.ch.

Content of the report "Existing legislation applicable to Nanomaterials":

1 Legislative basis
- 1.1 European Inventory of Existing Commercial Chemical Substances (EINECS)
- 1.2 The European List of Notified Chemical Substances (ELINCS)
- 1.3 Directive 67/548/EEC, classification and labelling

2 EC Regulations
- 2.1 Incremental approach
- 2.2 Chemicals: REACH
- 2.3 Products
- 2.4 Protection of workers' health and safety against risks due to chemicals
- 2.5 Environment

3 International activities
- 3.1 OECD
- 3.2 United States
- 3.3 Germany

1.3.2.2.2 Toxicology

This internal report was included in order to

- review and assess toxicology and hazard issues of nanoparticles at international and European level, including completed and ongoing activities
- identify gaps in existing knowledge
- develop strategies for involving external organisations in this task and for encouraging their participation.
- update the database with the latest results about toxicological issues

This assessment report is not publicly available. For special needs please send an email with your specific needs to the coordinator: temas@temas.ch.

The report "Toxicology" covers the following topics:

1.3.2.2.3 Risks

This internal report was included in order to:

- review and assess risks issues of nanoparticles at international and European level, including completed and ongoing activities
- identify gaps in existing knowledge
- develop strategies for involving external organisations in this task and for encouraging their participation
- update the database with the latest results about nanotechnological risks issues, including health and environment

This assessment report is not publicly available. For special needs please send an email with your specific needs to the coordinator: temas@temas.ch.

The report "Assessment of Risks" covers the following topics:

1 Introduction
  1.1 Structure of this Report
2 Metal Oxides
  2.1 Association between nanomaterial structure and hazard potential
  2.2 The health risks
  2.3 Controlling exposure
  2.4 Best Practices and Future
3 Ceramic Nanoparticles
4 Carbon Nanotubes
  4.1 Toxicology
  4.2 Risks of carbon nanotubes
  4.3 Conclusion and future
5 Quantum Dots
  5.1 Engineered Quantum Dots
  5.2 Engineered Quantum Dots: Risk Issues
  5.3 Risk Factors
  5.4 Environmental Exposure Routes
  5.5 Best Practices
  5.6 Future
6 Environmental Risks of Engineered Nanoparticles
  6.1 Nanotechnology and the Environment
  6.2 Binding of toxic elements and compounds to nanomaterials
  6.3 Mobility of nanoparticles within the environment
  6.4 Conclusions and Future Research
7 Risks of Engineered Nanoparticles – The future
  7.1 Precautionary Principle: Potential problems that need to be resolved before products of nanotechnology are fully deployed
8 References

1.3.2.2.4 Best practices

This assessment report is not publicly available. For special needs please send an email with your specific needs to the coordinator: temas@temas.ch.

The report was elaborated, as foreseen, based on the input from industry contacts. After the industry consultation, the results have been analysed and put together in the report "best practices", which is structured as follows:

1 Part 1: Industry Assessment
- 1.1 Introduction
- 1.2 Methodology
- 1.3 Results
- 1.4 Discussion
- 1.5 Conclusion

2 Part 2: Knowledge Gaps and Best Practice Recommendations
- 2.1 Introduction
- 2.2 Knowledge gaps in the safe handling of nanomaterials
- 2.3 Best practice procedures for handing nanoparticles
- 2.4 Detailed Procedures

1.3.2.3 Recommendations and guidelines for legislation policy makers

In order to provide legislation policy makers and related target groups with a decision basis for taking further steps in the field of nano-safety issues, recommendations have been elaborated based on the findings of work packages 2 and 3 of the project.

The main recommendations are the following:

- Recommendations by IMPART for future legislation to be realised as immediate measures are as follows:
  - The legislation policy makers should be prepared to adopt and implement several immediate measures necessary if more studies clearly show that ENP are harmful for safety and health of humans and the environment
  - Foster the development of new testing methods (especially toxicological testing) in order to evaluate the safety and health risks of engineered NP
  - Create new protection measures at the workplace for the people that manipulate nanomaterials. Existing threshold values – e.g. general dust limit values for the alveolar and breathable dust fraction or substance-specific limit values – must be observed
- Immediate protection measures which we recommend to be adapted include the substitution options for nanomaterials and technical as well as organizational protection measures.
- A specific long-term regulation on nanotechnology seems technically problematic and politically improbable at the moment. It is necessary to make a consistent use of existing legislation, as long as this can be easily applied as such or suitably amended, following also the conclusions of European Communities Report: Regulatory Aspects of Nanomaterials, June 17, 2008.

An overview of the recommendations elaborated within this report has been presented and discussed on the occasion of the Main IMPART Conference.

The publicly available guidelines for *legislation policy makers* can be down loaded form the IMPART data base:

www.impart-nanotox.org, Phase 2, data base or
with the direct access to the data base www.temas.ch/IMPART/IMPARTProj.nsf
Publication number "270528", or
send a mailto: temas@temas.ch.

Summary of the content of the guidelines for legislation policy makers:

1.3.2.4 Recommendations and guidelines for research policy makers

In order to provide research policy makers and related target groups with a decision basis for taking further steps in the field of nano-safety issues (such as defining research targets or funding opportunities), recommendations has been developed based on the findings of work packages 2 and 3 of the project. The aim was to produce added value compared to the huge amount of available publications in the field by giving explanations and interpretations of crucial results.

The publicly available guidelines for *research policy makers* can be down loaded from the IMPART data base:

www.impart-nanotox.org, Phase 2, data base or
with the direct access to the data base www.temas.ch/IMPART/IMPARTProj.nsf
Publication number "270530", or
send a mailto: temas@temas.ch.

In short, the following recommendations were developed:

- Immediate measures:
  - Develop, distribute and use manufactured reference NP material for toxicology studies (complete and accurate particle characterization)
  - Develop reference NP with low oxidative potential
  - Develop standardized, validated protocols for toxicity testing (attention to the parameters, systems, cellular components)
  - Develop models for predicting the potential impact on health and environment
  - Develop systems for evaluating the impact of engineered NP over their entire life
- Long-term measures:
  - Mandatory registration and health–screening of all workers dealing with bulk quantities of engineered NP
  - Long-term cohort studies to follow their health status
  - Establish a bio-bank for bio-material from these cohort members
  - Establish a fund/department to coordinate these long-term activities

An overview of the recommendations elaborated within this report has been presented and discussed on the occasion of the Main IMPART Conference.

Summary of the content of the guidelines for research policy makers:

1.3.2.5 Guidance Booklet on Safe Handling of Nanoparticles for Industry, public and other stakeholders

With the target groups industry, funding agencies and the broad public in mind, a public available brochure in the form of a guidance booklet has been produced with recommendations for the save handling of nanoparticles as well as recommendations for communication with the broad public.

The main conclusions drawn within this task are:

- There is a consensus among legislators that current legislation covers, in principle, potential risks with regard to nanomaterials, and is thus valid and applicable to nanospecific issues. This puts responsibility on all involved stakeholders in the area of nanotechnologies for the safety of human health as well as the environment with regard to risks that are specific to nanomaterials.
- Effective risk reduction for workers can be achieved by applying conventional measures known from the long experience in the chemicals sector. This is still on a generic level without considering nanospecific material properties, certain recommendations will have to be adapted when more data on nanoparticle specific behaviour are available.
- In order to secure the safe use of nanomaterials by consumers, it is necessary to make sure what type of nanoparticles might be present in what type of environment in any given consumer product, and clarify potential risks under those conditions as already known from other fields like workers' hygiene. Recommended measures according to this knowledge should then be communicated to sellers and/or customers.
- With regard to the environment the input of Engineered Nano Particles should be reduced wherever feasible.
- In any case, a rough estimation of potential risks of nanoparticles can be made on the basis of production volume, potential exposure to customers / workers/ environment, potential aerosol release during production / handling / processing, solubility, aspect ratio, and particle diameter.
- In view of the precautionary principle, two rules should always be obeyed:
    - seek alternative materials where necessary and feasible
    - in cases of doubt, start investigations or refrain from the use / application of the material in question
- New results in the field of nanoparticles and their impact on human health and environment will become constantly available. The crucial point will be their interpretation, implementation and communication. As a prerequisite for future safe application of nanomaterials, the strong interconnection along the whole life cycle and across all stakeholder areas, including NGOs and the broad public, is indispensible.

The guidelines were presented and discussed on the occasion of the Main IMPART Conference.

This booklet can be down loaded from the IMPART data base:

> www.impart-nanotox.org, Phase 2, data base or
> with the direct access to the data base www.temas.ch/IMPART/IMPARTProj.nsf
> Publication number "270529", or
> send a mailto: temas@temas.ch.

Summary of the content of the guidance booklet on safe handling of nanoparticles for industry, public and other stakeholders:

1.3.2.6 Data base on Nano Safety & Risk publications (NS&R)

Based on the existing infrastructure of TEMAS a database for the searchable collection of all relevant literature worldwide has been installed. Since September, 2007 the database http://www.temas.ch/Impart/ImpartProj.nsf is online and 548 publications on S&R have been implemented.

Technical information

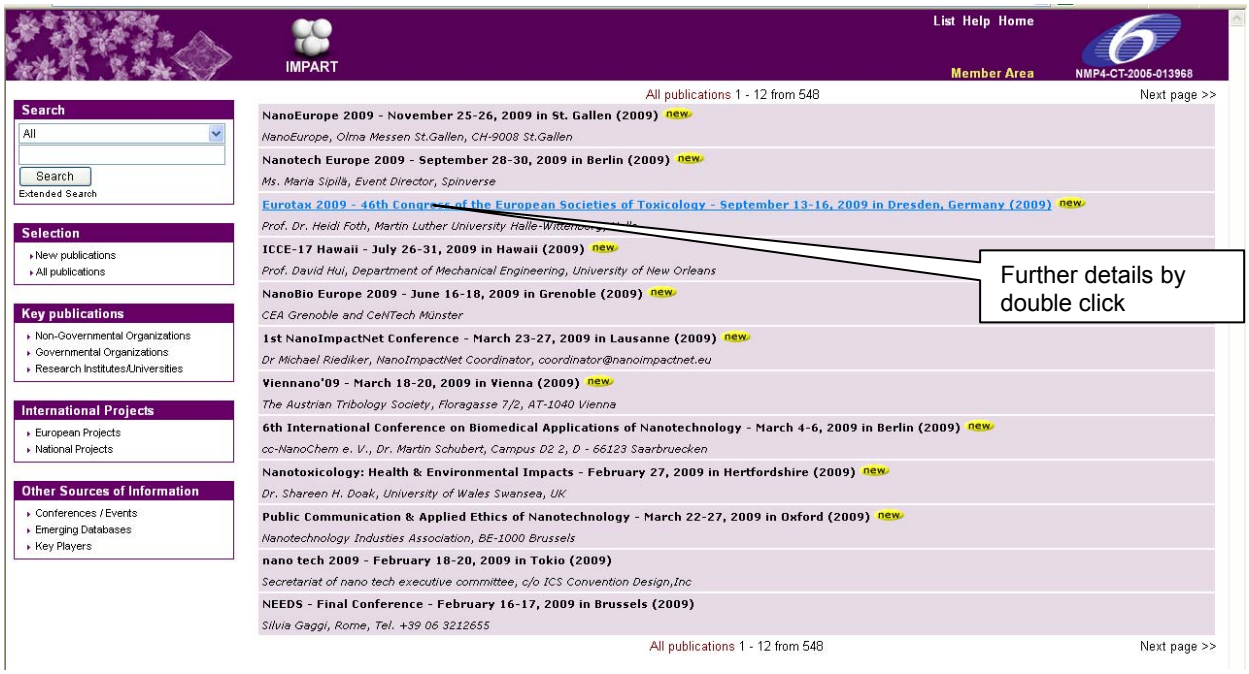
- Database based on LOTUS NOTES Domino, hosted on the TEMAS Web-Server
- Public access to more than 540 publications on NS&R
- Full text and pre-configured search engine
- Download of pdf-files
- Links from IMPART-NANOTOX website
- Links to emerging databases, further information, etc.

Pre-configured structure search functions

- All publications / New publications
- Key publications
    - Non-Governmental Organizations
    - Governmental Organizations
    - Research Institutes/Universities

- International Projects
  - European projects
  - National Projects
- Other sources of information
  - Conferences / Events
  - Newspaper Articles / Web Releases
  - Emerging Databases
  - Key Players

Access to the IMPART data base on Nano Safety & Risk publications



1.4 The degree to which the objectives were reached

WP No	Objectives	Degree to which the objectives were reached	Methodologies and approaches employed	Relation to the state-of-the-art
1	Coordination, management, quality assurance, Mid term review	All objectives have been reached	Standard management methods, kick-off-meeting, phone conferences, email exchange.	No special remarks
2	Co-ordination of initiatives activities and collection of data, Installation and ongoing up-date of the safety and risk data base	All objectives have been reached, the "input report" has been made public due to the high degree of actuality and quality of the content The safety and risk data base is publically accessible on www.impart-nanotx.org	Standard procedures with distribution of tasks, consolidating the individual reports and the final quality assurance have been applied. The IMPART safety and risk data base is a standard application of TEMAS based on Lotus Notes Domino.	This report was at its date of edition (June 2009) clearly above the available state-of-the-art overviews about "the status quo of Nanomaterials Impact on Health and Environment". The IMPART safety and risk data base is permanently up-dated and unique for the domain S&R.
3	Assessment of data: legislation, toxicology, risks, best practices	Four internal assessments of existing and missing data have been performed: ▪ Existing legislation applicable to Nanomaterials ▪ Toxicology ▪ Risks ▪ Best Practices	Standard procedures with distribution of tasks, consolidating the individual reports and the final quality assurance have been applied	Due to controversial discussions with experts about the-state-of-the-art, this internal report has not been published. Nevertheless for special needs, interested persons can ask the coordinator to get access to the four reports.

WP No	Objectives	Degree to which the objectives were reached	Methodologies and approaches employed	Relation to the state-of-the-art
4	Reports: recommendations and guidance booklet	All objectives have been reached. Three public documents have been elaborated: ▪ Legislation policy makers ▪ Research policy makers ▪ Industry, public and other stakeholders (Guidance Booklet) For all reports a down load on www.impart-nanotox.org and the S&R data base is installed.	Standard procedures with distribution of tasks, consolidating the individual reports and the final quality assurance have been applied	All reports are clearly above the-state-of-the-art. All stakeholders can now make use of the consolidated information.
5	Dissemination and knowledge transfer	All objectives have been reached: Three public documents have been elaborated: ▪ Coordination with ongoing activities ▪ www.impart-nanotox.org home page and promotion leaflet ▪ Consolidate conference for all stakeholders incl. NGOs (main IMPART conference, September 2009) ▪ National workshops to address opinion leaders and the public	Standard procedures with distribution the distribution of tasks.	N.A.

1.5 Impact of the project

The IMPART project has achieved all objectives.

No	Main achievements	Impact
1	Release of the suspension	IMPART with new members from NanoTox can now complete the project and concentrate on deliverables
2	Prefinancing with 7 months delay received and distributed, cleaning up IMPART phase I problems with EC administration	Get the planned resources for phase II released
3	Nano risk database operational	Access of the public of all relevant publications in the domain of Nano Risk & Safety issues.
4	Homepage www.impart-nanotox.org reactivated and permanently up-dated	High international visibility Access of the public to ongoing information from the consortium
5	Working Report on the Status Quo of Nanomaterials Impact on Health and Environment (Input report WP 2) completed, validated and released for the public.	Profound overview of the state-of-the-art with a comprehensive list of knowledge gaps and recommendations.
6	Assessment of existing data for internal use: - Existing legislation applicable to Nanomaterials" Deliverable D3.1 - Report on toxicology D3.2 - Report on risks D3.3 - Best practices D3.4	These reports delivered the input for WP 4, "Recommendations" These reports are available on request.
7	Recommendations for the stakeholders 1. Recommendations for legislation policy makers D4.2 2. Recommendations for research policy makers D4.3 3. Guidance booklet for on safe handling of nanoparticles D4.4	High value information with latest input of the state-of-the-art for policy makers, the industry, users, and the public. Recommendations and an outlook for future activities will support the future planning.
8	Main and final IMPART conference for opinion leaders, Brussels September 30, 2008	Valuable feedback of the presentations and the discussions. Participants The proceedings D5.3&D5.4 and the presentations are posted on www.impart-nantox.org. The conference satisfaction report confirms a medium to high appreciation of the IMPART project and the recommendations developed.

2 Dissemination and use

2.1 Exploitable knowledge and its use

The main exploitable results of IMPART are:

1. Data base on Nano Safety & Risk publications
2. Report "Working Report on the Status Quo of Nanomaterials Impact on Health and Environment"
3. Recommendations and guidelines for legislation policy makers
4. Recommendations an guidelines for research policy makers
5. Guidance Booklet on Safe Handling of Nanoparticles for Industry, public and other stakeholders

2.1.1 Data base on Nano Safety & Risk publications

In this data base all relevant publications on Nano Safety & Risk (NS&R) issues have been collected and structures as following:

Pre-configured structure search functions

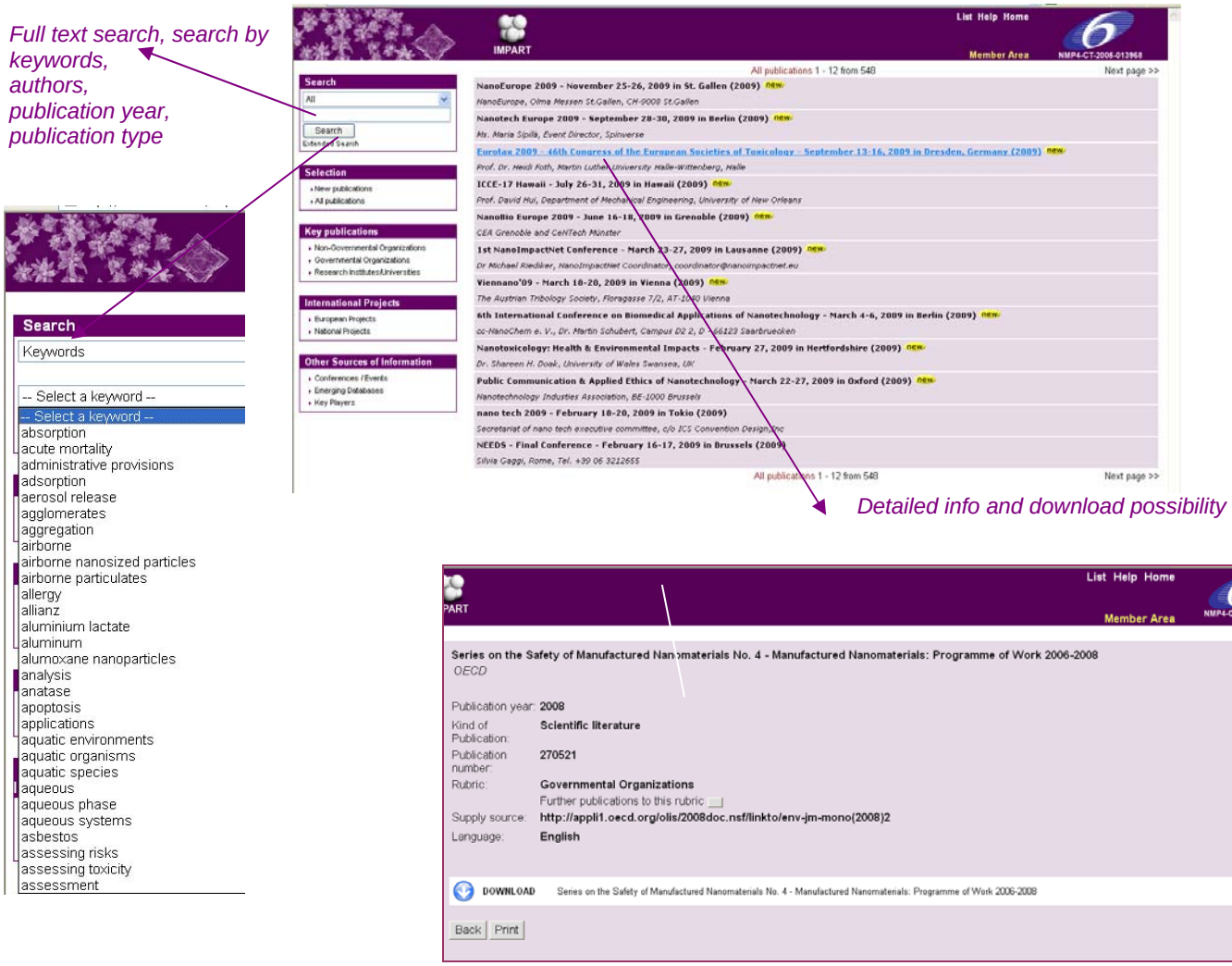
- All publications / New publications
- Key publications
  - Non-Governmental Organizations
  - Governmental Organizations
  - Research Institutes/Universities
- International Projects
  - European projects
  - National Projects
- Other sources of information
  - Conferences / Events
  - Newspaper Articles / Web Releases
  - Emerging Databases
  - Key Players

A full text search engine supports the pre-configured search functions.

The access to this data base is open to the public through:

- The IMPART home page www.impart-nanotox.org
- Direct access www.temas.ch/IMPART/IMPARTProj.nsf

Today the IMPART NS&R data base gives access to 548 publications



Exploitation

The access to the IMPART NS&R is free of charge. The *google* search on IMPART, nano safety and risks links to the IMPART NS&R data base.

Thanks to the EC initiative "CSA Workshop: Cooperation between Coordination and Support Actions in nanotechnology in the NMP programme", all important stakeholders across Europe have been informed and collaborations about the future use of the data base started.

The IMPART Nano Safety & Risk publication data base is continuously up-dated, furthermore also after the IMPART project has been completed. TEMAS will host and maintain this data base until collaboration with an ongoing or new project with similar objectives have been identified and an agreement of the transfer could be reached.

2.1.2 Reports

The main outcome of the IMPART project are the four published reports. A public access to all reports is given through the IMPART NS&R data base:

- The IMPART home page www.impart-nanotox.org
- Direct access www.temas.ch/IMPART/IMPARTProj.nsf

2.1.2.1 Working Report on the Status Quo of Nanomaterials Impact on Health and Environment (Input report)

Based on the input gained from the consolidation round, the final input report on the status quo of Nanomaterials impact on health and environment (Input report) was elaborated and made publicly available on the IMPART project homepage and the IMPART data base.

The final input report contains the following chapters:

1 Introduction
- 1.1 General considerations on nanotechnology and nanomaterials
- 1.2 Nanomaterials
- 1.3 Nanoparticle Properties
- 1.4 Risks of Nanomaterials
- 1.5 What is typical for “nanotoxicology” and different from bulk or other “toxicology”?

2 Health
- 2.1 Nanoparticles and Human Health
- 2.2 Is there a difference between “local” and “systemic” toxic effects?
- 2.3 How to express dosing
- 2.4 How good are the present protocols? Have we to apply new Tox-test? Do we need a new strategy?
- 2.5 Dissolution / precipitation of material within the biological system (organ specific)?
- 2.6 Cellular uptake and accumulation in “organelles” and “organs”?
- 2.7 How will we administer the materials for in vivo and in vitro tests?
- 2.8 What about long term studies at low (more realistic) concentrations?

3 Exposure
- 3.1 Occupational exposure
- 3.2 Exposure and detection in biological samples/fluids

4 Environment
- 4.1 Natural Nanoparticles in Geological Systems
- 4.2 Nanotechnology and the Environment
- 4.3 Conclusions and Future Research

5 Law and Regulation
- 5.1 Protection of workers’ health and safety against risks due to chemicals
- 5.2 ISO Technical Committee 229

6 Knowledge gaps and recommendations

7 Reference List

Exploitation

The Working Report on the Status Quo of Nanomaterials Impact on Health and Environment (Input report) is available free of charge and can be downloaded from:

- The IMPART home page www.impart-nanotox.org
- The SN&R data base www.temas.ch/IMPART/IMPARTProj.nsf

This report provides the researchers and other stakeholders about the state-of-the-art of the impact on health and environment.

2.1.2.2 Recommendations and guidelines for legislation policy makers

Recommendations by IMPART for future legislation to be realised as immediate measures are as follows:

- The legislation policy makers should be prepared to adopt and implement several immediate measures necessary if more studies clearly show that ENP are harmful for safety and health of humans and the environment
- Foster the development of new testing methods (especially toxicological testing) in order to evaluate the safety and health risks of engineered NP
- Create new protection measures at the workplace for the people that manipulate nanomaterials. Existing threshold values – e.g. general dust limit values for the alveolar and breathable dust fraction or substance-specific limit values – must be observed

Immediate protection measures which we recommend to be adapted include the substitution options for nanomaterials and technical as well organizational protection measures.

A specific long-term regulation on nanotechnology seems technically problematic and politically improbable at the moment. It is necessary to make a consistent use of existing legislation, as long as this can be easily applied as such or suitably amended, following also the conclusions of European Communities Report: Regulatory Aspects of Nanomaterials, June 17, 2008.

For the adaptation of future legislation to the requirements of nanoscale materials we recommend to establish already now the following general long-term strategies:

- in vivo long term toxicity assays for inhalation, oral, skin and injection exposure with the evaluation of markers for inflammation, cell proliferation in remote organs (e.g. liver, bone marrow, kidney)
- chronic nanotoxicity assay
- extended immunotoxicity studies
- development of new technologies for effective health and safety management in workplaces
- further epidemiological and toxicological data are required to determine the properties of nanomaterials in humans
- more measurements are needed in order to establish that will be no reason for concern at workplaces
- establishment of a standard guideline for workplaces and laboratories
- identification of protection measures and development of efficient metrology infrastructure

Exploitation

The recommendations for legislation policy makers are available free of charge as booklet and can be downloaded from:

- The IMPART home page www.impart-nanotox.org
- The SN&R data base www.temas.ch/IMPART/IMPARTProj.nsf

During the national and international events the recommendations are used address the respective stakeholders.

2.1.2.3 Recommendations and guidelines for research policy makers

The purpose of this Coordination Action was to develop guidelines for the production and application of nanoparticles, starting from the premise that at least some of these materials may be toxic to human health and the environment. For this purpose, the current report first assesses what is currently known about these materials and what legislation is in place to regulate them. Four classes of engineered nanoparticles have been examined; ceramics, metals and metal oxides, carbon and inorganic fullerenes, carbon and metallic nanotubes and quantum dots. The various routes of exposure have been considered and a summary is provided of the information which is available on the toxicity and health impact of these materials, derived from experimental studies. On the basis of this information an analysis has been made of the gaps which still exist in our knowledge of the impact of these materials and the procedures to minimize exposure. This has resulted in a series of recommendations for further research on these topics which are summarized in Chapter 4, Recommendations with regard to research policy.

Outlook on future activities:

The health, safety and environmental impact of nanoparticles will need to be addressed and monitored continuously for many years. On the short term, much of the focus will be on fundamental issues such as unravelling physiological responses to nanoparticles and establishing and understanding causal relationships between their presence and pathologies in cell culture and animal models. The credibility and broad acceptance of the results will depend on the establishment and use of standardized models, metrics, dosing and monitoring equipment. Legislation regulating the production, work-pace hygiene and application of these materials will be derived from these results. Nevertheless, mirroring the genetic engineering / food controversies of the past 20 years, one can expect a constant pressure from citizens' organizations, on the one hand, to prevent the application of nanoparticles, and from industries, on the other, to increase their application in consumer products and processes as a result of uncertainties in the extensibility of in vitro or animal model study results to humans.

Long-term cohort studies monitoring the health status of workers exposed to elevated levels of nanoparticles over extended periods will provide an upper limit of the threat which nanoparticles pose to human health. But over the same period, these materials will continue to diffuse in the environment and into the food chain in undefined ways and at virtually undetectable levels. One can expect, therefore, that if there are health hazards associated with certain classes of broadly used nanoparticles, they could well be untraceable and still have major impacts on our society. One needs only to look at the increasing incidence of breast cancer in women in the US and Western Europe or cancers which occur more selectively in other regions of the world to get a feeling for the intricacy of the link between human health, environment, customs, genetics and diet.

This IMPART study is a snapshot, in time, of the nanoparticle issue. It has identified areas where more research is needed and made recommendations which, when implemented will

bring more clarity to the discussions and controversies surrounding a technology that poses so many threats and, at the same time, hold so much promise.

Exploitation

The recommendations for legislation policy makers are available free of charge as booklet and can be downloaded from:

- The IMPART home page www.impart-nanotox.org
- The SN&R data base www.temas.ch/IMPART/IMPARTProj.nsf

During the national and international events the recommendations were used to address the respective stakeholders.

2.1.2.4 Guidance Booklet on Safe Handling of Nanoparticles for Industry, public and other stakeholders

Risk assessment and management for the production and use of nanomaterials containing nanoparticles is a highly complex issue, even more so when regarding both health and environmental issues along the whole lifecycle for any given type of nanoparticle.

There is a consensus among legislators that current legislation covers, in principle, potential risks with regard to nanomaterials, and is thus valid and applicable to nanospecific issues. This puts responsibility on all involved stakeholders in the area of nanotechnologies for the safety of human health as well as the environment with regard to risks that are specific to nanomaterials.

Effective risk reduction for workers can be achieved by applying conventional measures known from the long experience in the chemicals sector. This is still on a generic level without considering nanospecific material properties, certain recommendations will have to be adapted when more data on nanoparticle specific behaviour are available.

In order to secure the safe use of nanomaterials by consumers, it is necessary to make sure what type of nanoparticles might be present in what type of environment in any given consumer product, and clarify potential risks under those conditions as already known from other fields like workers' hygiene. Recommended measures according to this knowledge should then be communicated to sellers and/or customers.

With regard to the environment the input of Engineered Nano Particles should be reduced wherever feasible.

In any case, a rough estimation of potential risks of nanoparticles can be made on the basis of production volume, potential exposure to customers / workers/ environment, potential aerosol release during production / handling / processing, solubility, aspect ratio, and particle diameter.

In view of the precautionary principle, two rules should always be obeyed:

- seek alternative materials where necessary and feasible
- in cases of doubt, start investigations or refrain from the use / application of the material in question

New results in the field of nanoparticles and their impact on human health and environment will become constantly available. The crucial point will be their interpretation, implementation and communication. As a prerequisite for future safe application of nanomaterials, the strong interconnection along the whole life cycle and across all stakeholder areas, including NGOs and the broad public, is indispensible.

Exploitation

The recommendations for legislation policy makers are available free of charge as booklet and can be downloaded from:

- The IMPART home page www.impart-nanotox.org
- The NS&R data base www.temas.ch/IMPART/IMPARTProj.nsf

During the national and international events the recommendations were used to address the respective stakeholders.

2.1.3 Events

2.1.3.1 National dissemination

The following list summarises the events organised in national contexts by IMPART participants:

1. UniS (UK) organised a short course 'NANOMATERIALS' 7-11 April 2008 with specific discussion on IMPART draft recommendations and excellent feedback from delegates.
2. George Robillard (Netherlands) organised afternoon workshops for the meeting Nano4all on 15th October 2008 in Utrecht.
3. Marite-Arija Bake LATTOX (Latvia) was involved with the seminar: *'Nanotechnologies – opportunities and risks LATTOX Seminar within project IMPART'* on 15-16 June 2006 in Rīga/Ķegums, Puduri.
4. Maja Remškar (Jozef Stefan Institute, Slovenia) organized a symposium on Nanosafety and this included 3 IMPART contributions as presentations (P. Hoet, J. Hoeck, S. Tanasescu), and session chairing by M. Remškar and J. Hoeck
5. Margarita Apostolova (BAS) will organise the 10th Workshop NANOSCIENCE & NANOTECHNOLOGY-Sofia, November 27 - 28, 2008
6. DIT (Ireland): Ireland has a major nanotoxicology conference scheduled for spring 2009, and it is envisaged that IMPART results will be disseminated there.

2.1.3.2 International dissemination

The final IMPART International event, September 30, 2008, Brussels could address 65 registered participants.

The targeted audience for the combined meetings consisted of legislation policy makers, research policy makers, opinion leaders from industry and industry associations, researchers, public authorities and NGOs. All given presentations of the conference are available on the IMPART website (www.impart-nanotox.org).

Dissemination: The conference was designed to give enough space for discussions and answering of questions. The most important points covered are:

- Can we already draw up best practices for human and environmental safety? For the ecotoxicological investigations and tests at the moment this is not possible. For human health there is no black and white answer available, actually there is no agreement among the experts regarding this topic.
- Can we produce a list with potentially dangerous materials? This is not possible at the moment, and also not very likely in the future, because too many parameters need to be

assessed for every material (depending on all parameters a given material might be dangerous in one case, and safe in another).

- Is there a high priority for standard tests? This is true, purified standard samples are urgently needed for all test protocols.
- When talking about skin uptake of Engineered Nano Particles, it is absolutely necessary to refer to the type of skin: human, healthy, not burnt, not moved (massage). There is an actual gap in communicating results, this must be closed.
- The question was put up why, if we know so little, we should not take a moratorium on nanoparticles. The IMPART experts took the clear position that a moratorium would be contra-productive because it does not sufficiently differentiate between potentially harmful and harmless particles, thus banning a lot of needed functionalities. The measure to be taken is to spot the Engineered Nano Particles which already have a considerable production volume, and concentrate research and testing on them.
- Cohort studies are difficult in reality, because there is no clean baseline for such studies (non-smokers...).
- We do not have science in place to judge the risks. This is a main problem, we need to develop science first.
- When recommending more maintenance it is important to realise that more maintenance means also a higher risk of exposure.
- Why not include courses about nano and nanosafety in engineering schools, mainly about occupational health?
- Collaboration between industry and science needs to be strengthened, industry can define the real need for research

Outlook: With a summary of important steps to be taken, the coordinator gave a personal outlook on the necessary further developments in the field of nanosafety:

- Short term measures
    - Self declaration on a voluntary basis;
    - Existing regulations for chemicals, materials etc. such as REACH, Council Directives;
    - OECD test guidelines;
    - For engineered nanoparticles tools to estimate the risk potential for employees, consumers and the environment.
- Medium measures
    - Standardised test systems and reference materials;
    - Standardised, validated protocols for testing.
- Long term measures
    - Long-term studies;
    - Data base

He subsequently showed an example of measures already taken by Federal Offices of Public Health FOPH in Switzerland: the "Precautionary Matrix for Synthetic Nanomaterials" for a first assessment of risk potentials for specific nanomaterials in the frame of industrial self-control.

Access to the "Precautionary Matrix for Synthetic Nanomaterials":

- The IMPART home page www.impart-nanotox.org
- Direct access www.temas.ch/IMPART/IMPARTProj.nsf

2.1.3.3 Overview table

Exploitable Knowledge	Exploitable product(s) or measure(s)	Sectors(s) of applications	Timetable for commercial use	Patents or other IPR protection	Owner & other partner(s) involved
IMPART safety & risk data base	• Access to the data base • Data base	• Research • Policy makers • Industry • Public	Ready to apply	Public available, no IPR protection. For the data base, as a hole, a licence fee is foreseen.	• Content: IMPART project members • Data base, TEMAS
Working report on the status quo of NM impact on health and environment	Report as download from the IMPART data base	• Research • Policy makers • Industry	Ready to apply	Public available, no IPR protection, no copy right, reference to IMPART requested.	All IMPART members, main author Harald Krug, EMPA
Recommendations and guidelines for legislation policy makers	Report as download from the IMPART data base	• Policy makers • Public authorities • Funding agencies	Ready to apply	Public available, no IPR protection, no copy right, reference to IMPART requested.	All IMPART members, main author Esko Kauppinen, TKK
Recommendations and guidelines for research policy makers	Report as download from the IMPART data base	• Policy makers • Public authorities • Funding agencies	Ready to apply	Public available, no IPR protection, no copy right, reference to IMPART requested.	All IMPART members, main author George Robillard, BIOMADE
Guidance Booklet on Safety Handling of NP for industry, public and other stakeholders	Report as download from the IMPART data base	• Industry • Public • Other stakeholders	Ready to apply	Public available, no IPR protection, no copy right, reference to IMPART requested.	All IMPART members, main author Juergen Hoeck, TEMAS

2.2 Dissemination of knowledge

2.2.1 Overview table

Actual Dates	Type	Type of audience	Countries addressed	Size of audience	Partner involved
2005	Flyer of the IMPART – Nanotox CSA project	General public	All European countries	Not limited	Coordinator
2008	Promotion leaflet IMPART phase 2	General public	All European countries	Not limited	Coordinator
2008	Flyer, IMPART presents the final results	General public and specific stakeholders on nano safety & risk issues	All European countries	Not limited	Coordinator
2008	National course "NANOMATERIALS" with specific discussion on IMPART draft recommendations and excellent feedback from delegates	Specific stake holders	UK	50	Universities of Surrey and Manchester
2008	Meeting "Nano4all" Utrecht	General public	The Netherlands	60	BIOMADE
2006	'Nanotechnologies – opportunities and risks' in Riga/Kegums, Puduri	Specific stake holders	Latvia	20	LATTOX
2008	Nano safety and risks, Portoroz	Specific stake holders	Slovenia	> 100	Josef Stefan Institute
2008	NANOSCIENCE 6 NANOTECHNOLOGY-Sofia	Specific stake holders	Bulgaria	50	BAS
2009	Spring conference	Specific stake holders	Ireland	u.k.	DIT
2008	Final IMPART international conference, Brussels	Selected stake holders form science, government, funding agencies, EC officials, NGOs, etc.	Belgium	65	TEMAS / BAS
2005 - 2008	37 publications	Science and industry	NA	NA	For details see IMPART data base
2005 / 2008	IMPART – NanoTox website (www.impart-nanotox.org)	All stake holders and the public	NA	NA	CHALEX/ TEMAS
2008	IMPART data base www.temas.ch/IMPART/IMPARTProj.nsf	All stake holders and the public	NA	NA	TEMAS
2008	Direct mailings (2)	185 personally addressed persons	Europe	185	TEMAS

2.3 Publishable results

The IMPART CA has created public available reports on:

Improving the understanding of the impact of nanoparticles on human health and the environment

The publishable results are four reports and a data base with > 540 publications on nano safety and risk issues (NS&R).

Result	Market	Stage of development	Collaboration offered	Collaboration details	IPR	Contact details
IMPART safety & risk data base	NS&R stakeholders, general public	Completed, regularly up-dates ongoing	Collaboration to maintain the NS&R data base for the future	To be negotiated	Content: IMPART project members Data base, TEMAS	mailto:temas@temas.ch
Working report on the status quo of NM impact on health and environment	NS&R stake-holders from research, industry, government and public	Completed report prepared to download from the IMPART data base	Distribution of the report	To be negotiated	Public available, no IPR protection, no copy right, reference to IMPART project requested	
Recommendations and guidelines for legislation policy makers	NS&R policy makers, public authorities, funding agencies	Completed report prepared to download from the IMPART data base	Distribution of the report	To be negotiated	Public available, no IPR protection, no copy right, reference to IMPART project requested	
Recommendations and guidelines for research policy makers	NS&R policy makers, public authorities, funding agencies	Completed report prepared to download from the IMPART data base	Distribution of the report	To be negotiated	Public available, no IPR protection, no copy right, reference to IMPART project requested	
Guidance Booklet on Safety Handling of NP for industry, public and other stakeholders	Public, industry and other stake holders	Completed report prepared to download from the IMPART data base	Distribution of the report	To be negotiated	Public available, no IPR protection, no copy right, reference to IMPART project requested	