# « Safety evaluation of manufactured nanomaterials by characterisation of their potential genotoxic hazard »

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# **An European Joint Action**

- approved in July 2009
- 6.2 millions of Euros , 46% funded by EC.
- Start in March 2010, for 3 years

### **Context :**

Human exposure to manufactured nanomaterials (MNs) used in consumer products may occur during several phases of their life cycle.

The lack of scientific knowledge make regulation difficult. The JA general objectif is to support and add value to the Member



# **Objectives :**

- States' policies and to contribute to increasing the safe use of MNs in the European Union.
- \* To obtain detailed physicochemical properties for each MN at the bulk powder and individual particle level
- \* To determine the influence of exposure media on MNs dispersability and to identify the optimum preparation protocols for the specific MNs
- \* To generate in vitro genotoxicity data on MNs
- \* To determine relevant doses and sampling time for biodistribution and in vivo genotoxicity studies, and to identify MN accumulation in organs for in vivo genotoxicity tests
- \* To perform a round robin test on in vitro genotoxicity testing of MNs
- \* To generate data from in vivo genotoxicity selected tests, and to assess the correlation between in vivo and in vitro results taking into account the kinetic results



# **Partners**

Main Partner: Afsset (Fr)

16 Associated Partners (11 countries): ISS(IT), CLMC/IMB-BAS (BULG), FIOH (Fin), NRCWE(DK), BfR (DE), NIOM (PL), RIVM (NL), UAB (ESP), VAR/IPH(BE), INSA (PT), and AFSSA/IPL/INRS/CEA (FR)

Synergy with other activities

- OCDE sponsorship program
- ISO TC229
- Strong interaction with all participants

# **Scientific Work Package**

Tests will follow the available international guidance documents

#### **Characterisation:** NRCWE (DK)

SOP for full characterisation of NMs including MN suspension in test media

#### In vitro genotoxicity: FiOH (FI)

- Comet and micronucleus assays + specific tests (MLA and lymphocytes micronucleus assay)
- Different cell lines : pulmonary, intestinal for all MNs and human skin model for TiO<sub>2</sub>
- \* A ring test with the most promising assays on selected MN s

In vivo genotoxicity: ANSES (ex-Afssa) (Fr)

#### 12 collaborating partners:

- 7 ministries (FR, IT, NL, DE, FI, ESP, BE)
- 5 Institutes JRC (CE), HPA (UK), UCD (IR), LNE (FR), AFSSAPS (FR)

	0	8	12	15	18	20	24		30		36	
	borocto	ricoti										
VVP4 - CI	laracte	IISau										
Primary Chra	cteristics											
Analytical an	d dispersio	n protoco	ols									
SOPs for chra	acterization	of select	ed MNs									
VN data sets	s with reque	ested phy	/sico-chemica	l propertie	s							
WP5 - <i>ir</i>	n vitro											
<i>n vitro</i> geno	toxicity stu	idies (con	net and micro	nucleus on	intesti	inal, lung ar	d skin cells)					
						<i>In vitro</i> rir	g test					
Evaluation of	f the results	s from the	e <i>in vitro</i> and	in vivo tes	sts for d	correlation a	and used to	formulate a	strategy fo	or genotox	icity testi	ng of MNs
WP7 - T	oxicoki	netic										
WP7 - To Analytical teo	<b>oxicoki</b> chniques fo	netic r determi	ination of MN	ls in blood	and tis	sue (with W	/P4)					
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- \* On rat, 3 doses, 5 animals/dose,
- Gavage and instillation
- \* 5 target organs
- Correlation with in vitro tests and toxicokinetics

#### Toxicokinetics: RIVM (NL)

- Performed before in vivo genotoxicity testing
- Oral route and IV (TiO2 and SiO2), only IV (CNT)
- Dose range finding for genotoxicity tests: development of sample preparation and detection method.
- Determination of organ at risk for MN accumulation and genotoxicity tests

## www.nanogenotox.eu

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15 MNs commercially available will be tested
NTC (7)
TiO<sub>2</sub> (4)

anses.fr



**SiO**<sub>2</sub> (4)