



# An ISA-TAB-Nano compliant data management system for nanosafety modeling

**MOD**eling the **EnviR**onmental and human health effects of **N**anomaterials  
(MODERN)

*Robert Rallo, Universitat Rovira i Virgili*



# Overall project objectives

- **Challenges**

- Development of **computational approaches for nanodescriptors and in silico toxicity models** to assess nanoparticle effects
- **Identification of NP categories** from their physicochemical, structural and toxicological properties, including environmental and human health endpoints

- **Objectives/Activities**

- Build a **database of eNPs** with a comprehensive description of their structural, molecular and physicochemical properties
- **Develop and validate in silico models** of biological activity of eNPs in organisms and in the environment from in vitro/in vivo profiling data
- **Define and implement a categorization and hazard ranking methodology** for eNPs based on structural similarity principles and toxicological profiles

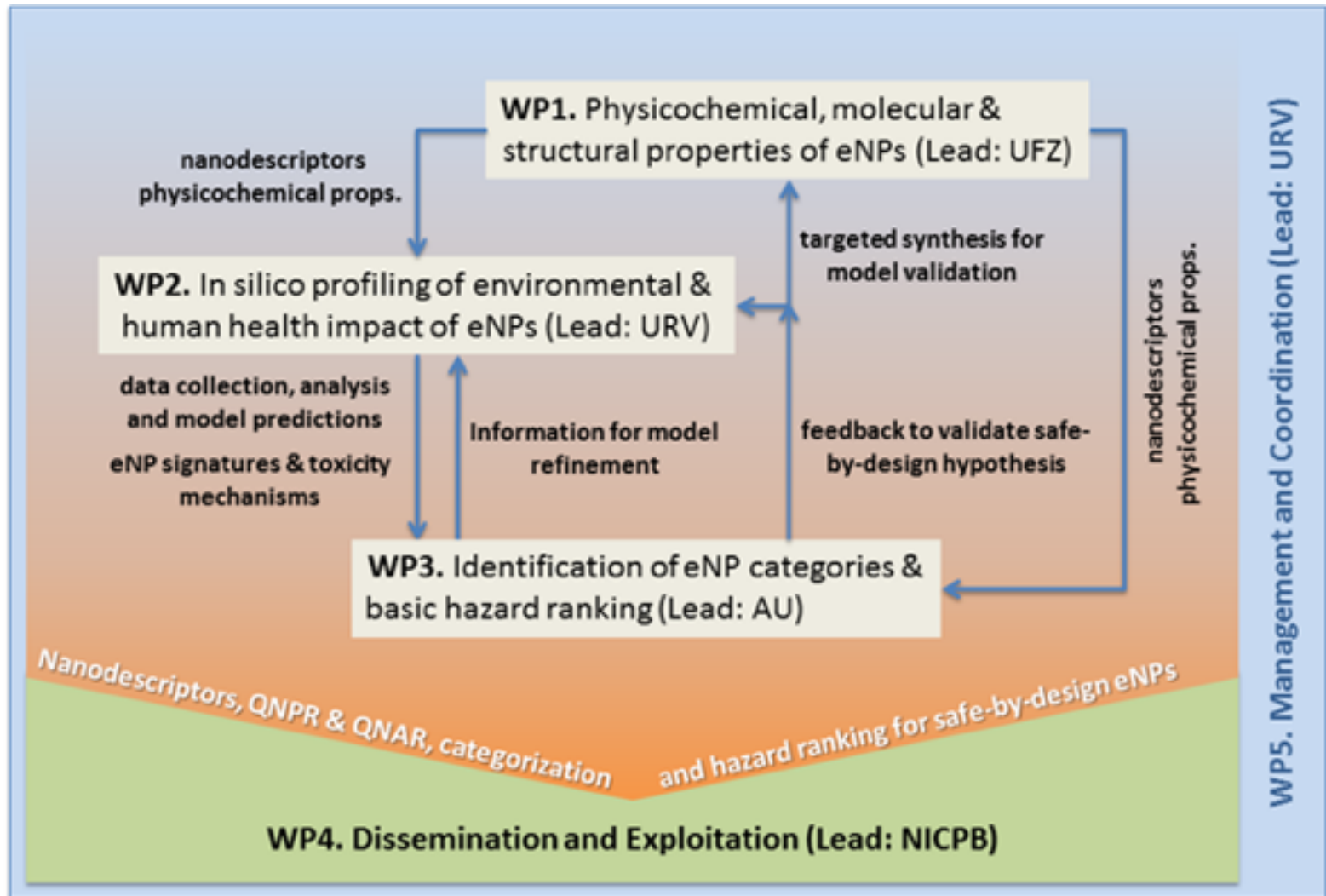


# MODERN consortium

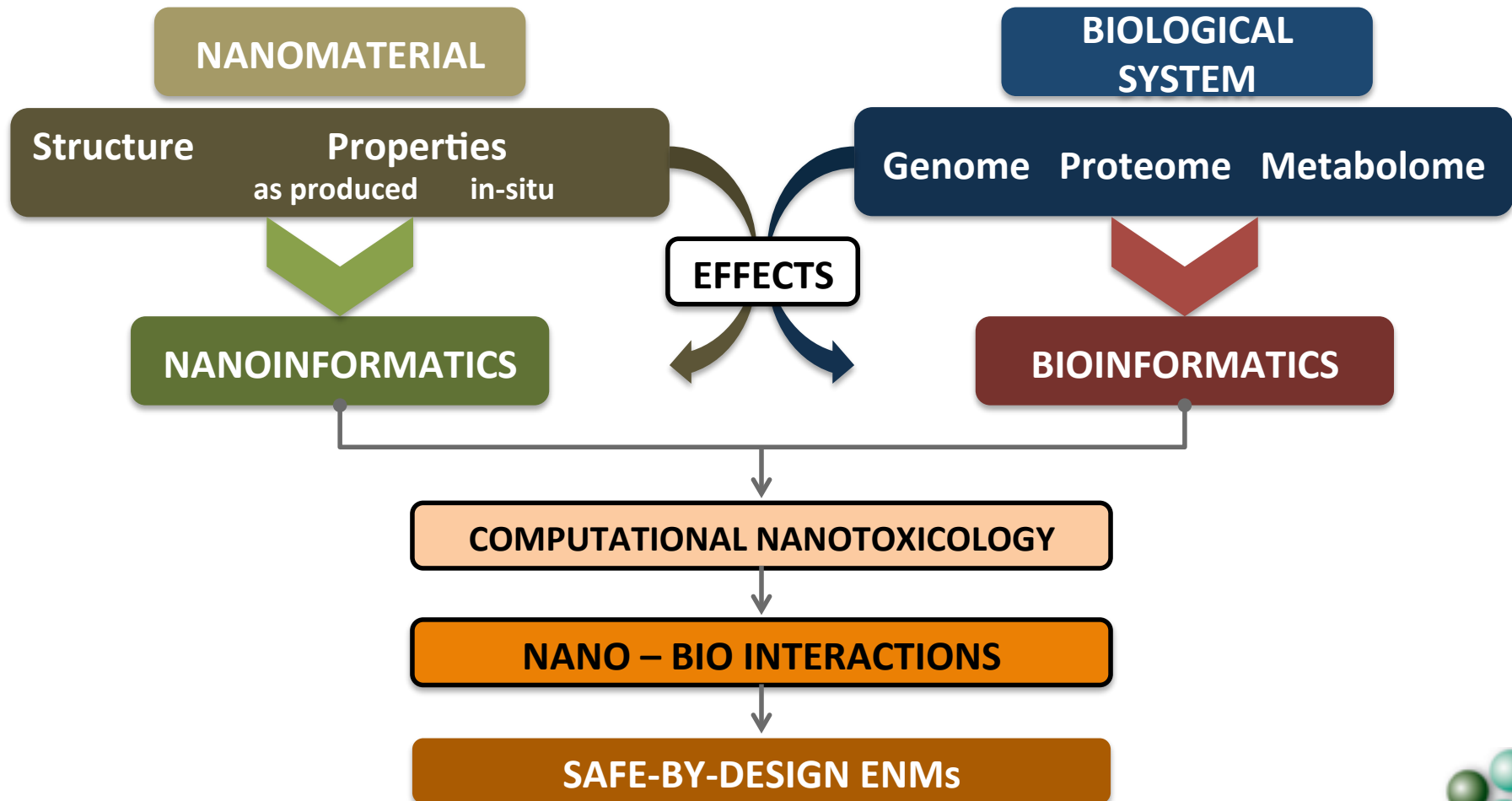
- Universitat Rovira i Virgili (URV) - *coordinator*
- Helmholtz Centre for Environmental Research (UFZ)
- Aarhus University (AU)
- National Institute of Chemical Physics and Biophysics (NICPB)
- Universität Bremen (UniHB)
- Tartu Ülikool (UT)
- University of California, Los Angeles (UCLA)



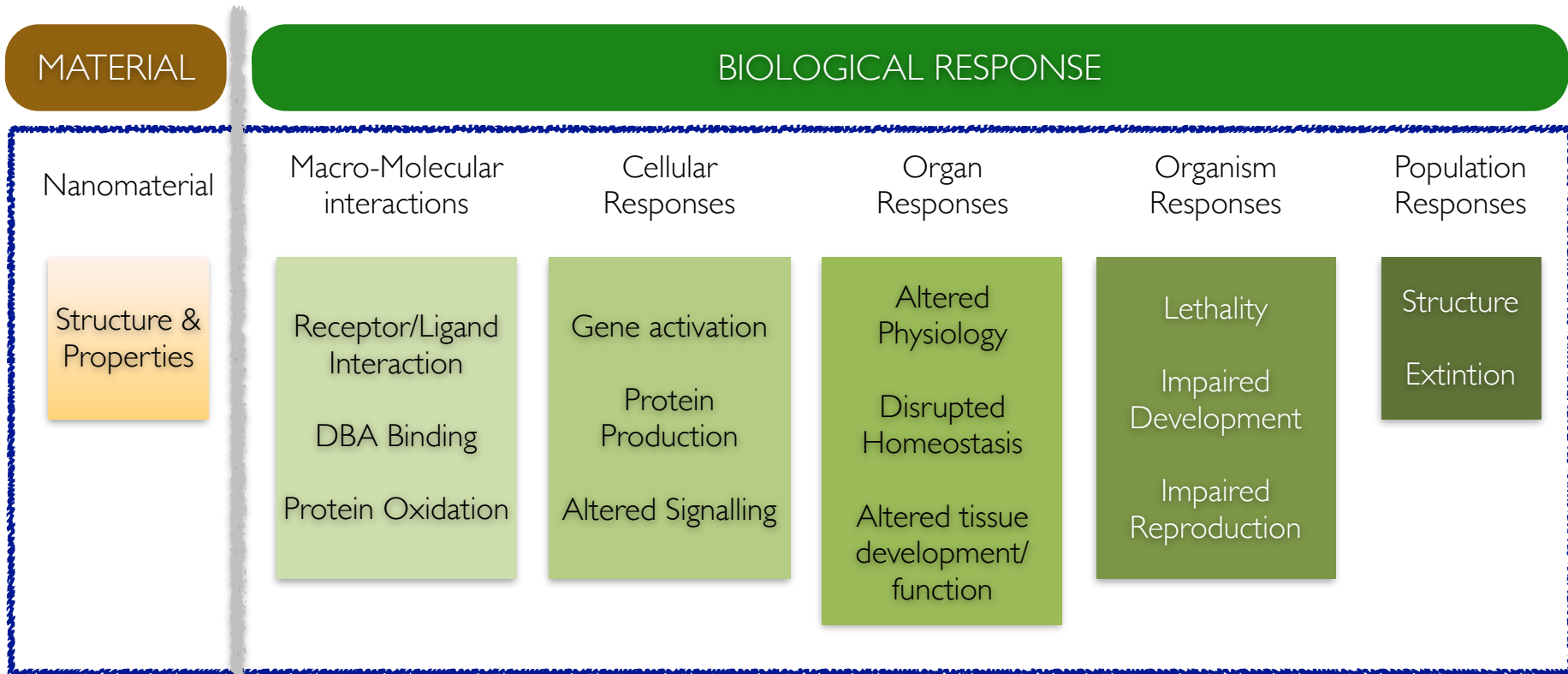
# Project structure



# MODERN approach to safe-by-design



# Computational nanotoxicology and nano-bio interactions



OECD Adverse Outcome Pathway Framework



# Establishment of a data repository

## 1. Design and implementation of an ISA-TAB Nano compliant data management system

- Web-based ISA-TAB Nano validator (v1.1, v1.2)
- Federated data management system with ontology support

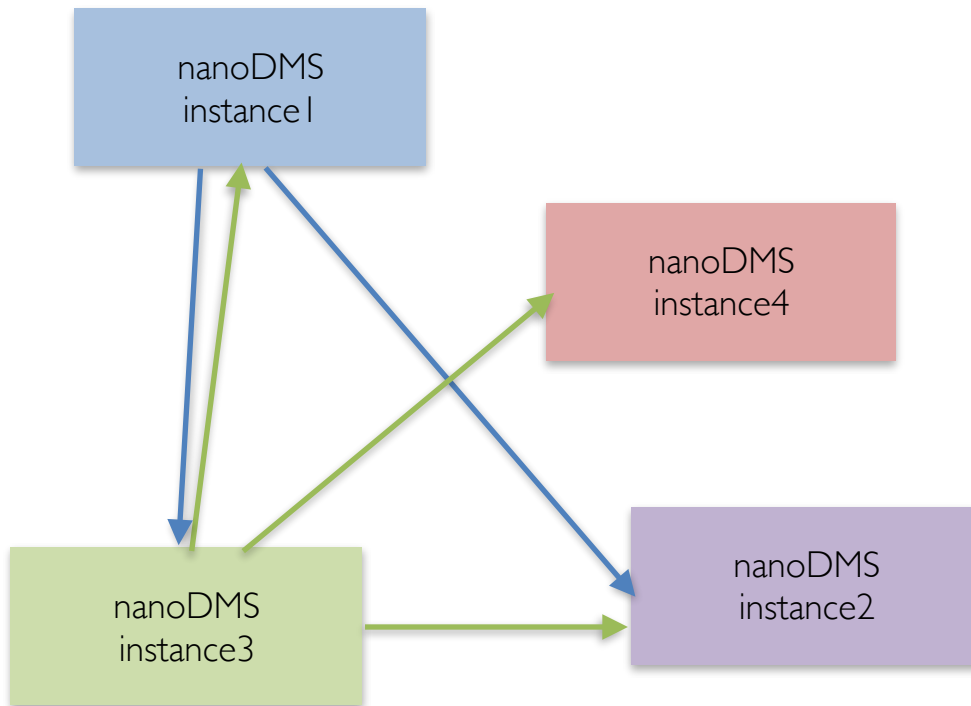
## 2. Data collection to populate the data repository

- Data use agreements
- Harmonized database



# Design & implementation

## nanoSafety Data Management System (nanoDMS): Architecture and features



### Features:

- Web-based application
- Import/Export
- Ontology support
- Federation mechanisms
- Data protection
- ISA-TAB-Nano validation

- Administrative interface with
  - Support for multiple users and projects
  - Join/leave federation
- Project sharing among federated instances

Tools publicly available from MODERN website:  
<http://modern-fp7.biocenicat.cat/tools.html>

The screenshot shows the nanoDMS web interface with a table of file information. The table has columns for File Name, Project, Reference, Sample Name, Date, Time, Size, and Status. The data is as follows:

| File Name | Project   | Reference   | Sample Name   | Date       | Time     | Size   | Status |
|-----------|-----------|-------------|---------------|------------|----------|--------|--------|
| File 1    | Project 1 | Reference 1 | Sample Name 1 | 2010-10-10 | 10:10:10 | 100 MB | Ready  |
| File 2    | Project 2 | Reference 2 | Sample Name 2 | 2010-10-10 | 10:10:10 | 100 MB | Ready  |
| File 3    | Project 3 | Reference 3 | Sample Name 3 | 2010-10-10 | 10:10:10 | 100 MB | Ready  |





# Data curation workflow

## Selection of ontologies

- Import from Bioportal
- Automatic term completion
- automatic generation of TERM ACCESSION NUMBER and TERM SOURCE REF



## Definition of the Investigation

- Investigation data: descriptive information
- Investigation publications: with PUBMED and DOI links to the publisher
- Investigation contacts: list of people involved in the investigation

### ONTOLOGY SOURCE REFERENCE

**Add**

|  |   |
|--|---|
| Term Source Name: MO<br>Term Source File: <a href="http://purl.bioontology.org/ontology/MO">http://purl.bioontology.org/ontology/MO</a><br>Term Source Version: v. 1.3.1.1<br>Term Source Description: MeSH Ontology | Term Source Name: NPO<br>Term Source File: <a href="http://purl.bioontology.org/ontology/npo">http://purl.bioontology.org/ontology/npo</a><br>Term Source Version: v. 2011-02-12<br>Term Source Description: NanoParticle Ontology                  |
| Term Source Name: UD<br>Term Source File: <a href="http://purl.bioontology.org/ontology/UD">http://purl.bioontology.org/ontology/UD</a><br>Term Source Version:<br>Term Source Description: Unit Ontology            | Term Source Name: CHEBI<br>Term Source File: <a href="http://purl.bioontology.org/ontology/CHEBI">http://purl.bioontology.org/ontology/CHEBI</a><br>Term Source Version: v. 80<br>Term Source Description: Chemical Entities of Biological Interest |
| Term Source Name: PATO<br>Term Source File: <a href="http://purl.bioontology.org/ontology/PATO">http://purl.bioontology.org/ontology/PATO</a><br>Term Source Version:<br>Term Source Description: Phenotype Ontology | Term Source Name: NCI<br>Term Source File: <a href="http://ncit.nci.nih.gov/">http://ncit.nci.nih.gov/</a><br>Term Source Version: v. 11.1.1d<br>Term Source Description: NCI Thesaurus   |

### INVESTIGATION

#### INVESTIGATION DATA

Investigation Identifier: [L\\_TALE\\_HMM-JParkNatureM2012](#)

Investigation Title: TALE\_HMM-JParkNatureM2012

Investigation Description: In order to overcome the immunosuppressive nature of the tumor environment, nanoscale liposomal polymeric gels were developed (lipopolygels, nLQs), which comprise drug-complexed cyclodextrin and cyclodextrin-encapsulating biodegradable polymers that can deliver small molecule inhibitors and water soluble protein cyclotaxins in a sustained fashion to the tumor environment.

Investigation Submission Date:  
Investigation Public Release Date:  
Investigation Disease: **BLCA**

Investigation Outcome: nLQs releasing TGF beta inhibitor and L-D significantly delayed tumour growth, increased survival of tumour-bearing mice, and increased the activity of natural killer cells and of rituximab-activated CD80 T-cell stimulation. It was demonstrated that the efficacy of nLQs in tumor immunotherapy results from a crucial mechanism involving activation of both innate and adaptive immune responses.

#### INVESTIGATION PUBLICATIONS

#### INVESTIGATION CONTACTS

### INVESTIGATION

#### INVESTIGATION DATA

#### INVESTIGATION PUBLICATIONS

**Add**

Investigation Publied ID: [1271927](#)

Investigation Publication DOI: [10.1038/nm2005](#)

Investigation Publication Author List:

- Park J
- Shownkeen DR
- Stern E
- Lock M
- DiCorleae J
- Raybale R
- Jay SM
- DiCorleae SL
- Aggarwal S
- Lucero-Prisco P
- Fernandez AF
- Cornejo D
- Halperin A
- Russell RK
- Fahmy TM

Investigation Publication Title: Combination delivery of TGF-beta inhibitor and L-D by nanoscale liposomal polymeric gels enhances tumour immunotherapy.

Investigation Publication Status: **BLCA**

#### INVESTIGATION CONTACTS



# Data curation workflow

## Creation of nanomaterial files

- Flexible definition of the structure of the material file
- spreadsheet-like editor
- support for ontology terms



## Definition of the Study

- Flexible definition of the structure of study files
- web-based entry forms for: Study definition, design, publications, factors, protocols and contacts
- support for the definition of assays

MATERIAL

File entries:

| MATERIAL SOURCE NAME | MATERIAL NAME    | MANUFACTURER LOT IDENTIFIER | MATERIAL DESCRIPTION                      |
|----------------------|------------------|-----------------------------|---|
| NCL-01               | g4_Pls_dendrimer |                             | G4 trihydroxyl terminated PAMAM dendrimer |
| NCL-01               | g4_Pls_sera      |                             |   |
| NCL-01               | g4_Pls_merck     |                             |   |
| NCL-01               | g4_Pls_grow      |                             |   |

Buttons: Add, Set File

Material list:

- m.NCL-01.csv - NCL-01
- m.NCL-02.csv - NCL-02
- m.NCL-03.csv - NCL-03
- m.NCL-04.csv - NCL-04
- m.NCL-05.csv - NCL-05
- m.NCL-06.csv - NCL-06

Set File

Field Type...

- MATERIAL SOURCE NAME
- MATERIAL NAME
- MANUFACTURER LOT IDENTIFIER
- MATERIAL DESCRIPTION
- MATERIAL SYNTHESIS
- MATERIAL DESIGN RATIONALE
- MATERIAL INTENDED APPLICATION
- MATERIAL TYPE
- MATERIAL CHEMICAL NAME
  - dendrimer branch(NPC:APC\_17N)
  - dendrimer generation
  - molecular weight(NPC:APC\_117F)
- UNIT
- MATERIAL CONSTITUENT
- MATERIAL LINKAGE NAME
- MATERIAL LINKAGE TYPE
- MATERIAL DATA FILE
- MATERIAL DATA FILE TYPE
- MATERIAL DATA FILE DESCRIPTION

Buttons: Save File Structure

STUDIES

File entries:

- NCL200812A-Size

Buttons: Add

Study list:

- NCL200812A-CytotoxicityLLC-PR3

STUDY

Study Identifier: NCL200812A-Size

Study Title: Hydrodynamic Size-Flow Distribution via Dynamic Light Scattering (DLS)

Study Description: Dynamic light scattering(DLS) technique was used to measure the hydrodynamic size of dendritic nanoparticles. The effects of sample concentration, buffer and temperature on the hydrodynamic size (DLS) size were investigated.

Study Submission Date: 2008-11-01

Study Public Release Date: 2008-11-01

Study Overview:

Study Overview: Hydrodynamic size (diameter) of the dendrimer samples NCL01, NCL02 and NCL03 were measured in aqueous solutions using DLS at 25 °C and 37 °C, in suspension with a backscattering detector also used for these measurements in acryl made (in backscattering). This technique does not have the missing power of differentiating monomers and dimers without fractionation. Samples were weighed, dissolved in deionized (DI) water, aliquoted, lyophilized and resuspended in deionized buffer solutions in a final concentration of 1 mg/ml, and filtered through a 0.2 µm filter, unless otherwise indicated. The measurements were taken in saline (154 mM NaCl) and phosphate buffered saline (PBS) at pH 7.4. These measurements were done for each sample. For NCL01, the size is slightly larger when dispersion in saline compared to PBS, in PBS, the size is independent of temperature. This is in contrast to NCL02, which is larger in PBS than in saline. NCL03 size shows temperature dependence, as its size decreases slightly with increased temperature in PBS. Finally, NCL03 is larger when dispersion in PBS compared to saline. For each sample, the intensity weighted mean diameter (D<sub>avg</sub>) derived from the cumulative analysis and the diameter after conversion to volume-weighted distribution are provided in the following table.

Study File Name: n-cl-01-01.csv

File entries:

| SOURCE NAME | MATERIAL TYPE       | TERRA accession number | TEMP SOURCE REF | PROVIDER                |
|-------------|---------------------|------------------------|-----------------|-------------------------|
| NCL-01      | nanoparticle sample | NPL_1434               | NPL             | Osse Technologies, Inc. |
| NCL-02      | nanoparticle sample | NPL_1434               | NPL             | Osse Technologies, Inc. |
| NCL-03      | nanoparticle sample | NPL_1434               | NPL             | Osse Technologies, Inc. |

Buttons: Add, Set File

# Data curation workflow

## Creation of assay files

- Flexible definition of the structure of the assay file
- spreadsheet-like editor
- generation of QSAR-ready datasets



## Supplementary files & permissions

- File upload
- Project-based access control

The screenshot shows the 'STUDY ASSAYS' section of a web application. It includes a sidebar with navigation options: STUDY, STUDY DESIGN, STUDY PUBLICATIONS, STUDY FACTORS, and STUDY ASSAYS. The main content area has a 'Study Assay Measurement Type' dropdown set to 'raw measurement', a 'Study Assay Technology Type' dropdown set to 'dynamic light scattering', and a 'Study Assay Measurement System' dropdown set to 'DLS'. Below this is a table of assay data with columns: PROTOCOL REF, MEASUREMENT VALUE (planned), UNIT, TUBIN ACQUISITION NUMBER, and TUBIN SOURCE REF. The table contains 8 rows of data. At the bottom right, there are two green buttons: 'QSAR-ready data' and 'Get File'.

The screenshot shows the 'FILES' section of the web application. It features a table with three columns: 'File Name', 'Type', and 'Remove'. The table contains one row with the file name 'Nanoscale\_2013.pdf', type 'pdf', and a red 'X' icon in the 'Remove' column. Below the table is a green button labeled 'Add File'.

The screenshot shows the 'PERMISSIONS' section of the web application. It has a 'Select visibility:' label and a dropdown menu currently showing 'Public'.



# Additional information

- The nanoDMS system can be downloaded from:
  - <http://nanodms.biocentit.cat>
- A test server is accesible from:
  - <http://biocentitc-deq.urv.cat/nanodms>
- The ISA-TAB-Nano Validation service is accesible from:
  - <http://biocentitc-deq.urv.cat/nano-validator>

