caLIBRAte
nano risk governance

# Testing scheme and input sensitivity of nanomaterial risk, exposure and hazard assessment tools

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## In short

Establishment of a web-based nano-risk governance portal with well-documented and tested tools is one of the key products of the caLIBRAte project. As part of the project, we tested the tools and models available for nanomaterial (NM) risk, exposure and hazard assessment for the input sensitivity. To carry out this task and to implement a feasible and efficient methodological testing approach, information was needed on model input requirements along with data formats. This included technical information on 20 models identified in early stage of the caLIBRAte project. Generation of such information was the first step to implement the sensitivity testing and data gap analysis in caLIBRAte. Finally, eleven NM risk, exposure and hazard assessment models were identified for sensitivity testing.

## Input sensitivity

Input values → Run the model with *N* different values → Output values

Explore parameter space | Study model response

- **Sensitivity analysis** is defined as a study on model output value variation, when model input values are changed. The model is run with a pre-determined set of input values yielding a set of outputs.
- **Testing methods:**
  - ✓ One-at-a-time (OAT)
  - ✓ Monte-Carlo
  - ✓ Tailored regression analysis and diagnostic methods
- **Objective:** find the input parameters that show no, lowest or highest sensitivity.

## Input requirements

Input data
- NM size, etc.

Data format
- Keyboard/Mouse
- File .txt, .xls, etc.

→ Model platform:
- Excel
- Web tool
- Code based

→ Output data
- Exposure, Risk, etc.

Data format
- Screen
- File .txt, .xls, etc.

- **The majority of inputs** required by the models are very heterogeneous. We mapped a total of 1190 different input parameters, and overlaps were not in the majority.
- **The predominant platforms** for model implementations are Excel sheets (8/20) and web interfaces (8/20).
- **The data formats** ranged from in situ user keyboard and screen input to files in Excel, text, or other formats.

## Model testing results

### 64 input parameters classified as most sensitive

- Presence of nanomaterials in the production, release rate/ concentration, duration of cycle/ process, weight fraction of nanomaterial in product, redox/ catalytic/ ROS/ inflammation potential and stability/ half-life of the nanoparticles

### 43 input parameters classified as least sensitive

- Duration of handling/ duration of activity in work cycle, ventilation rate, room volume, origin of nanomaterial/product type, ENP/ Primary particle diameter and activity level/ handling activity.

### Unexpected behavior

- Eight models have non-sensitive parameters (most common unexpected behavior)
- Two of the models produced nonlinear output when linear behavior was expected
- One of the models had outliers in the output values
- Three of the models produced sudden jumps in the output data
- No model crashes or fails were encountered during the models runs

## Models

SUN DS
Nanosafer CB
GUIDEnano
ConsExpo nano
BAUA Sprayexpo 2.3
LICARA nanoscan
ECETOC TRA v3.1
EGRET2
SimpleBox4Nano
ISO/TS 12901-2:2014
GWAVA
RedNano
n-SSWD
MendNano
NanoDUFLOW
Swiss Precautionary Matrix
Stoffenmanager Nano
nanoQSAR
Control banding nanotool
ANSES

The input requirement mapping was performed on all models, whereas only the models marked in orange were sensitivity tested.

## Implications

- The most and least sensitive input parameters, serve as a **guidance for data collection needs.**
- **The highly sensitive parameters** identified here indicate that **high-quality data of these is key in obtaining better risk estimates, and in reducing uncertainty**. Hence, data collection for these parameters has a high likelihood of having a high value.
- In contrast, the need for collecting large amount of data on the parameters that have low sensitivity is not as high, as it is not as likely that better data substantially improves the risk estimates.
- Therefore, **performance testing and** the **users are suggested to put more emphasis on the most sensitive parameters**, since they affect the model outcome the most.

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