Exposure to nanoparticles

- Non-engineered particles
  - Volcanic eruptions
  - Fires
  - Industrial emissions

- Engineered particles
  - Free or in aerosol
  - Biopersistent
  - Catalytically active
## HARMFUL TO AQUATIC ORGANISMS

<table>
<thead>
<tr>
<th>Limits of Toxicity</th>
<th>L(E)C50 (mg/l)</th>
<th>Harmful to aquatic organisms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harmful</td>
<td>10 and 100</td>
<td>Risk phrase R52</td>
</tr>
<tr>
<td>Toxic</td>
<td>1 - 10</td>
<td>Danger symbol N, risk phrase R51</td>
</tr>
<tr>
<td>Very toxic</td>
<td>&lt;1</td>
<td>Danger symbol N, risk phrase R50</td>
</tr>
</tbody>
</table>

96-h LC50 for Fish, 48-h EC50 for daphnids, and 72-h EC50 for algae

Substances showing certain biological effects were classified

This classification was carried out according to the lowest effect concentration
Blaise Et Al. (2008) Classified Eleven Nanomaterials Using The Following

- L(E)C50 < 0.1 mg/l = extremely toxic to aquatic organisms;
- 0.1–1 mg/l = very toxic to aquatic organisms;
- 1–10 mg/l = toxic to aquatic organisms;
- 10–100 mg/l = harmful to aquatic organisms;
- >100 mg/l = non-toxic to aquatic organisms.
# The Potential Ecotoxicological Hazard Evaluation Of Seven NPs

<table>
<thead>
<tr>
<th>Limits of Toxicity</th>
<th>L(E)C50 (mg/l)</th>
<th>NPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harmful</td>
<td>10 - 100</td>
<td>Nano TiO2</td>
</tr>
<tr>
<td>Toxic</td>
<td>1 - 10</td>
<td>SWCNTs and MWCNTs</td>
</tr>
<tr>
<td>Very toxic</td>
<td>0.1 - 1</td>
<td>C60 fullerenes and nano CuO</td>
</tr>
<tr>
<td>Extremely toxic</td>
<td>&lt; 0.1</td>
<td>nano Ag and nano ZnO</td>
</tr>
<tr>
<td>No.</td>
<td>Group of organisms</td>
<td>Inorganic nanoparticles</td>
</tr>
<tr>
<td>-----</td>
<td>-------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mg TiO$_2$/l Nano TiO$_2$</td>
</tr>
<tr>
<td>1</td>
<td>Crustaceans</td>
<td>67.7 (10)</td>
</tr>
<tr>
<td>2</td>
<td>Bacteria</td>
<td>603 (4)</td>
</tr>
<tr>
<td>3</td>
<td>Algae</td>
<td><strong>65.5 (4)</strong></td>
</tr>
<tr>
<td>4</td>
<td>Fish</td>
<td>300 (4)</td>
</tr>
<tr>
<td>5</td>
<td>Ciliates</td>
<td>NF</td>
</tr>
<tr>
<td>6</td>
<td>Nematodes</td>
<td>80.1 (1)</td>
</tr>
<tr>
<td>7</td>
<td>Yeasts</td>
<td>20000 (1)</td>
</tr>
<tr>
<td>1-7</td>
<td>No. of data</td>
<td>24</td>
</tr>
<tr>
<td>1-7</td>
<td>Lowest L(E)C50</td>
<td>65.5</td>
</tr>
<tr>
<td>1-7</td>
<td>Most sensitive organisms</td>
<td>Algae</td>
</tr>
<tr>
<td>1-3</td>
<td>Classification (1-7)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>Classification (1-3)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th>No.</th>
<th>Group of organisms</th>
<th>Reference compounds</th>
<th>Most toxic chemical</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Bulk metal oxides</td>
<td>Metal ions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mg TiO$_2$/l Bulk TiO$_2$</td>
<td>mg ZnO/l Bulk ZnO</td>
</tr>
<tr>
<td>1</td>
<td>Crustaceans</td>
<td>20000 (3)</td>
<td>0.48 (3)</td>
</tr>
<tr>
<td>2</td>
<td>Bacteria</td>
<td>20000 (1)</td>
<td>20.0 (3)</td>
</tr>
<tr>
<td>3</td>
<td>Algae</td>
<td><strong>60 (1)</strong></td>
<td><strong>0.052 (2)</strong></td>
</tr>
<tr>
<td>4</td>
<td>Fish</td>
<td>500 (2)</td>
<td>1.8 (2)</td>
</tr>
<tr>
<td>5</td>
<td>Ciliates</td>
<td>NF</td>
<td>4.9 (1)</td>
</tr>
<tr>
<td>6</td>
<td>Nematodes</td>
<td>137 (1)</td>
<td>2.2 (1)</td>
</tr>
<tr>
<td>7</td>
<td>Yeasts</td>
<td>20000 (1)</td>
<td>134.4 (1)</td>
</tr>
<tr>
<td>1-7</td>
<td>No. of data</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>1-7</td>
<td>Lowest L(E)C50</td>
<td><strong>60</strong></td>
<td><strong>0.052</strong></td>
</tr>
<tr>
<td>1-7</td>
<td>Most sensitive organisms</td>
<td>Algae</td>
<td>Algae</td>
</tr>
<tr>
<td>1-7</td>
<td>Classification (1-7)&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>Classification (1-3)&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

PCP—Pentachlorophenol; NF—not found.

Assessment of the environmental effects of nanoparticles. The letter code indicates our assessment regarding the environmental effects for ENM categories: a): rather safe; b): uncertainty due to weak evidence; c): effects on the environment can be expected. This assessment does not express the relevance of the risks of ENM versus the risks of unintentionally produced nanoscale particles from traffic. Legend: +: results in increased exposure or stronger effect, ±: inconclusive data available, −: results in decreased exposure or lowered toxicity, n.a.: no data available.

<table>
<thead>
<tr>
<th>ENVIRONMENT</th>
<th>Ag(^{1})</th>
<th>ZnO(^{1})</th>
<th>TiO(_2)(^{1})</th>
<th>SiO(_2)(^{1})</th>
<th>Al(_2)O(_3)(^{1})</th>
<th>Montmorillonite(^{1})</th>
<th>CNT(^{1})</th>
<th>CB(^{1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication of hazardous effects at realistic exposure concentrations</td>
<td>+</td>
<td>+</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>n.a.</td>
<td>−</td>
</tr>
<tr>
<td>Dissolution in water increases the toxic effects (+ +), reduces toxic effects (− −)</td>
<td>++</td>
<td>++</td>
<td>−</td>
<td>−</td>
<td>++</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Tendency for agglomeration and sedimentation (− −) or no sedimentation (+ +)</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td>±</td>
<td>−</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Low removal rate during wastewater treatment (+ +), efficient removal rate during wastewater treatment (− −)</td>
<td>−</td>
<td>n.a.</td>
<td>−</td>
<td>±</td>
<td>−</td>
<td>n.a.</td>
<td>±</td>
<td>n.a.</td>
</tr>
<tr>
<td>Stable during waste incineration (+ +), burns during waste incineration (− −)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>n.a.</td>
<td>−</td>
</tr>
</tbody>
</table>

### Selected nanoparticles tested in a variety of living organisms in the biennium 2008–2010.

<table>
<thead>
<tr>
<th>Nanomaterial</th>
<th>NP size (nm)</th>
<th>Tested organism</th>
<th>Test</th>
<th>Reported results</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZnO</td>
<td>20</td>
<td>C. elegans</td>
<td>24-h LC$_{50}$</td>
<td>LC$_{50}$ (2.3 mg L$^{-1}$)</td>
</tr>
<tr>
<td>Al$_2$O$_3$</td>
<td>6050</td>
<td>(nematode)</td>
<td></td>
<td>LC$_{50}$ (82 mg L$^{-1}$)</td>
</tr>
<tr>
<td>TiO$_2$</td>
<td>10</td>
<td>Cucumis sativus</td>
<td>Germination</td>
<td>No toxicity observed</td>
</tr>
<tr>
<td>Au</td>
<td>7</td>
<td>Lactuca sativa</td>
<td>Bioluminescence</td>
<td></td>
</tr>
<tr>
<td>Ag</td>
<td>2</td>
<td>Photobacterium phoshoreum</td>
<td>Biogas production</td>
<td></td>
</tr>
<tr>
<td>Fe$_3$O$_4$</td>
<td>7</td>
<td>Anaerobic consortium bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ZnO</td>
<td>60</td>
<td>S. agalactiae</td>
<td>Bactericial action</td>
<td>Inhibition of cell division (95% at 0.12 M)</td>
</tr>
<tr>
<td>CeO$_2$</td>
<td>15 and 30</td>
<td>D. magna</td>
<td>Genotoxicity</td>
<td>CeO$_2$, damaged DNA</td>
</tr>
<tr>
<td>SiO$_2$</td>
<td>7 and 10</td>
<td>C. riparius</td>
<td>Mortality, growth, and reproduction</td>
<td>CeO$_2$, and SiO$_2$ increased mortality</td>
</tr>
<tr>
<td>TiO$_2$</td>
<td>7 and 20</td>
<td>Oryzias latipes</td>
<td>LC$_{50}$</td>
<td>LC$_{50}$ (1.03 mg L$^{-1}$)</td>
</tr>
<tr>
<td>Ag</td>
<td>20–37</td>
<td></td>
<td>Developmental toxicity</td>
<td>Edema abnormalities in the spine, fins, heart, brain, and eyes</td>
</tr>
<tr>
<td>TiO$_2$</td>
<td>6</td>
<td>D. magna</td>
<td>24-h LD$_{50}$</td>
<td>l-ALEX</td>
</tr>
<tr>
<td>Al (ALEX)</td>
<td>100</td>
<td>V. fischeri</td>
<td>48-h LD$_{50}$</td>
<td>48-h LD$_{50}$ of 107.588 mg L$^{-1}$</td>
</tr>
<tr>
<td>Al (l-ALEX)</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. As the nanotechnology industries increase production, nanoscale products and byproducts will enter the aquatic environment, posing a possible threat to aquatic organisms.

Increasing number of studies on ecotoxicity of NPs to aquatic organisms across several taxonomic groups (from bacteria to fish) underline the potential risk of NP exposure to aquatic life.

Significance of aquatic invertebrates as test species for ENP ecotoxicity: invertebrates represent about 95% of animal species, important ecological role, potential transfer through food chains.

Most ecotoxicological studies are performed on species used in regulatory testing (i.e. short-term lethality tests, chronic and life-cycle effects in freshwater crustaceans).
Little information is available on the effects and modes of action in marine organisms, especially those living in estuarine and coastal areas that can represent major depositional areas for NPs.
Besides the use of regulatory tests to evaluate the overall toxicity, more specific assays that can identify major toxic mechanisms like immunotoxicity, genotoxicity, oxidative stress, may help understanding the mode of actions that can be relevant for different NP types.
Assessing and managing risk in nanotechnology

Exposure
- Environment
- Occupational
- Industry

Structure/function Relationship
Relate characteristics to effects

Generation of standardised and relevant nanomaterial prep protocols

Models
- Environment
- Human
- Vertebrates
- Invertebrates
- Microorganisms

Susceptibility?

Predictive models and testing strategies

Which nanomaterials can be used in which applications?
Derivation of guidelines regarding the design of safe nanomaterials

Industry
Consumer
Policy makers
Nanotechnology Products

Consumer products using nanoscale materials have an increasingly presence in the market

Nanoparticle-based Cosmetics: L'oreal
WWW.SUPERDRUG.COM

CNT-based Nano Emissive Displays: Motorola
WWW.OPTICS.ORG

Structural Nanocomposite Parts: Hummer
WWW.IMAGES.BUSINESSWEEKS.COM

Will lipstick be safe?
Report: FDA to be poor watchdog of products using new technology
WWW.IMAGES.BUSINESSWEEKS.COM

Carbon Nanofiber Racquets: Wilson
WWW.IMAGES.BUSINESSWEEKS.COM

Ag-Nanoparticle Lined Refrigerator: Samsung
WWW.IMAGES.BUSINESSWEEKS.COM
Nanoparticles in environmental matrices

Differently sized nanoparticles

Ions dissolved from NPs

\( M^{n+} \quad M^{n+} \quad M^n \)

\( \text{pH} \quad + \quad \text{MATRIX} \)

Homocoagulated nanoparticles

Heterocoagulated nanoparticles

\( \text{pH} \)

Surface modified NPs

\( \text{DOC} \)

Natural colloids

Matrix ions

ENVIRONMENTAL MATRIX
Nanotechnology has the potential to substantially benefit environmental quality and sustainability through:

- Pollution prevention
- Treatment
- Remediation
- Information

The bad...


The good...
Nanotechnology for pollution prevention

- Synthetic or manufacturing processes which can occur at ambient temperature and pressure.
- Use of non-toxic catalysts with minimal production of resultant pollutants.
- Use of aqueous-based reactions.
- Build molecules as needed -- “just in time.”
- Nanoscale information technologies for product identification and tracking to manage recycling, remanufacture, and end of life disposal of solvents.
Nano in Bio → Medicine
The unique optical, electronic, structural properties of the dry side when added to biomolecules will result in powerful new medical treatments and diagnoses.

Bio in Nano → Materials/Devices
Manipulation and assembly of nanostructures from the dry side into materials and functional devices using machinery from the wet side will enable new technologies.

Nano-Bio in our Environment → Responsibility
Risk Assessment / Risk Reduction
Natural Nanoconjugates

1) Adsorption

2) Aggregation

3) Biotic Uptake
Nanotechnology and Environment

“A tool for sustainable development rather than an environmental liability”

- Enabling technologies to meet many needs
  - water, wastewater
  - hazardous waste
  - resource recovery
  - pollution prevention

- Environmental consequences of new technologies
  - focus on transport, transformation, and fate of nanostructures
  - proactive approach early in the process
Nanostructures: Environmental Impact?

Particle-mediated transport
- size
- surface chemistry (hydrophobic)

Potential for bio-assimilation
- direct consequences
- associated contaminants
Nanoparticles in Aqueous Environments

- Bio-uptake
- Deposition
- Transport
- Aggregation
- Sorption/desorption
- Naturally occurring particles
- Organic compounds/macromolecules/contaminants

Nanoparticles

$3A1, 3A2, 3A3$
Nanomaterial source (manufacture, use, disposal, accidental release...)

(Gaiser et al., 2010)
Nanoparticles may enter cells via:

- **Endocytosis**
  - Receptor activation for initiation
- **Membrane penetration**
  - Generally occurs with very hydrophobic particles
- **Transmembrane channels**
- **May be seen only with very small nanoparticles (< 5 nm)**
Many types of molecules will adsorb to nanoparticles in complex aqueous environments. Adsorbed molecules may dictate biological interactions, especially biouptake.

Biomolecules (i.e. proteins)
Synthetic chemicals (i.e. pesticides)
Factors Influencing Adsorption

• Occurs to a greater degree on:

- Hydrophobic particles
- Charged Particles

Amphiphilic or charged molecules most likely to adsorb

Macromolecules generally adsorb most strongly
Any evidence for this?

Many studies show facilitated transport of heavy metals, fertilizers, and pesticides into fish.
Chemicals adsorb to naturally occurring colloidal particles, resulting in tremendous increases in biouptake.
Environmental Applications for Nanomaterials

- Emulsified zero-valent iron for remediation efforts
- NM for filtration media

Water
Other fluids

- Cerium oxide as diesel fuel additive
Life Cycle of Nanomaterials

Manufacturing
- Nanomaterial manufacturing
- Nano-Intermediate Manufacturing
- Nano-enabled product manufacturing

Use

End of life
- Landfill
- Disposal
- Sewage

From: L. Gibbs 2006
Health, Safety, and Environmental Concerns Regarding NM

• Human implications

- NM toxicity not yet well understood; nano-size materials do not behave like their bulk counterparts
- Reactivity of NM due to large surface area
- Potential for bioaccumulation

• Environmental implications

- Contamination of water and soil from improper disposal of NM
- Bio-uptake of NM and accumulation in food chain
Possible mechanisms of nanomaterial toxicity to bacteria. Different nanomaterials may cause toxicity via one or more of these mechanisms.

- Disruption of membrane/membrane potential
- Produce reactive oxygen species (ROS)
- DNA
  - Damage DNA
- Protein
  - Oxidize/damage proteins
- CYP
- Release hazardous constituents, e.g., metals, ions
- Interrupt electron transport/respiration

Routes of release and hence exposure

- Incorporated into a formulation
- Mixed with waste products
- Interacting with biological systems
- Potential human exposure via foodchain
- Interacting with environmental chemicals/species
- Pristine NM

The Royal Society and Royal Academy of Engineers (2004)
Fate of NM in the environment
Interactions with other constituents and effects on bioavailability

OM

Salinity

Enhanced/reduced uptake (of NM/contaminant)

Effects on aggregation/dispersion
Workplace Studies
Workplace Studies

- Aerosol concentrations of NMs during handling of unrefined NMs material were low.
- More energetic processes likely needed to increase airborne concentrations of NM.
- Gloves were contaminated with NM.
- Results indicated importance of dermal contact as potential exposure route.

Maynard and coworkers (2004)
Exposures of largemouth bass to fullerenes for 48 hr produced lipid damage in brain tissues

Exposures of *Daphnia* to uncoated, water soluble fullerenes for 48 hr indicated an LC$_{50}$ of 800ppb

(E Oberdorster 2004)
Nanotechnology
where are we today?

- Limited number of NM have been evaluated to date
- Mechanisms for potential NM toxicity are an active area of research
- Specific NM properties, particularly their surface characteristics, clearly affect their toxicity
Nanomaterials available

- Products
- Powder
- Suspensions

- Batches
- Oxidised
- Pure/contaminated
- Coatings
- functionalised
Why do we need to test “chemicals”

“Ecological hazard” exposure data required for new and existing chemicals

- Industrial chemicals
- Plant protection products & biocide
- Pharmaceutical and veterinary medicines
What are Ecotox data used for?

- Classification and labeling requirements
- Chemical safety report
  - PNEC("predicted no effect concentration") derivation
- Safe use?
Figure 2-4. Diagram of quantal dose-response relationship.

The abscissa is a log dosage of the chemical. In the top panel the ordinate is mortality frequency, in the middle panel the ordinate is percent mortality, and in the bottom panel the mortality is in probit units (see text).
Mortality (%) vs. Chemical concentration (mg/l)

- **NOEC** - No observed effect concentration
- **LOEC** - Lowest observed effect concentration
- **LC50** - Lethal concentration for 50% of the population
Statistical extrapolation (SSD)

\[ PNEC = \frac{5\% SSD(50\% c.i.)}{AF} \]

AF = assessment factor between 1 and 5
STANDARD TEST GUIDELINES

- Many different test organisms/methods used internationally
- OECD and ISO
- Define test conditions
  + Species, temperature, water quality, feeding
- Performance criteria
  + Minimum control performance, water quality
- Most use standard “demographic” endpoints
  + survival, reproduction, growth
FACTORS AFFECTING TOXICITY

- Species
- Age
- Sex
- Condition of the animal
- Water temperature and water quality
- Chemical type
- Several LC$_{50}$ values may exist for the same chemical
DIVERSITY OF TEST ORGANISMS

Primary producers
- Micro alga
- Macro alga
- Rooted plant

Invertebrates
- Water column
- Substrate - epi or infaunal

Vertebrates
- Fish
- Others

Mode of feeding
- Suspension/particle feeder
- Deposit feeder
- Herbivore/carnivore
OECD STANDARD TESTS

- Organisation for Economic Co-operation and Development

- The OECD groups **30 member countries** sharing a commitment to democratic government and the market economy. With active relationships with some **70 other countries** and economies, **NGOs and civil society**, it has a global reach. Best known for its **publications** and its **statistics**, its work covers economic and social issues from **macroeconomics**, to **trade, education, development** and **science and innovation**.

- Chemicals Testing: OECD Guidelines for the Testing of Chemicals - Sections 1-5:
  - **Section 1**: Physical Chemical Properties
  - **Section 2**: Effects on Biotic Systems
  - **Section 3**: Degradation and Accumulation
  - **Section 4**: Health Effects
  - **Section 5**: Other Test Guidelines

http://www.oecd.org/document/22/0,2340,en_2649_34377_1916054_1_1_1_1,00.html
http://new.sourceoecd.org/vl=9729091/cl=13/nw=1/rpsw/cw/vhosts/oecdjournals/1607310x/v1n2/contp1-1.htm
Lethal and Sublethal Toxicity Tests using *Daphnia* species

- Freshwater Crustacean
- Reproduces by parthenogenesis (asexual reproduction in which females produce offspring without fertilization by a male) under stable conditions, produces males under stress conditions.

http://www.caudata.org/daphnia/
http://ebiomedia.com/gall/classics/Daphnia/daphnia_behave.html
Daphnia endpoints

1. Mortality
2. Reproduction
3. Population effects
4. Ephippia production
5. Development (abnormal?)
6. Growth (moulting, size)
7. Biochemical endpoints
Sediment Toxicity Tests

Many pollutants (e.g. lipophilic organic pollutants, metals) strongly bind to sediments/soils.

Organisms used include sediment dwelling amphipods and insect larvae (Chironomid larvae; non-biting midges).

Can be used to test toxicity of field samples or artificially spike clean sediments with a toxicant.

Usually involve lethal tests using a static exposure system, however, more sub-lethal tests are being adopted. Static-renewal tests more difficult due to difficulties in finding specimens within the sediment.
## Characterization of the particle

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphology and compositions</td>
<td>SEM-EDX, TEM-EDX</td>
</tr>
<tr>
<td>Size, size distribution</td>
<td>DLS (Nanosizer)</td>
</tr>
<tr>
<td>Surface charge</td>
<td>Zeta potential analyzer</td>
</tr>
<tr>
<td>Specific surface area</td>
<td>BET surface area analyzer</td>
</tr>
<tr>
<td>Metal contaminants</td>
<td>ICP, AA</td>
</tr>
</tbody>
</table>

- Transmission Electron Microscope (TEM)
- Scanning Electron Microscope (SEM)
- BET surface area analyzer
- Nanosizer
<table>
<thead>
<tr>
<th>Cell type</th>
<th>Size (nm)</th>
<th>Time (h)</th>
<th>Assay</th>
<th>IC₅₀ (µg/ml)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRL 3A</td>
<td>15</td>
<td>24</td>
<td>MTT</td>
<td>24</td>
<td>Hussain et al. 2005</td>
</tr>
<tr>
<td>BRL 3A</td>
<td>100</td>
<td>24</td>
<td>MTT</td>
<td>19</td>
<td>Hussain et al. 2005</td>
</tr>
<tr>
<td>NIH 3T3 (Mouse fibroblast)</td>
<td>1-100</td>
<td>24</td>
<td>MTT</td>
<td>&lt;50</td>
<td>Hsin et al. 2008</td>
</tr>
<tr>
<td>A10 (Rat vascular smooth muscle)</td>
<td>1-100</td>
<td>24</td>
<td>MTT</td>
<td>50</td>
<td>Hsin et al. 2008</td>
</tr>
<tr>
<td>HCT 116 (Human colon cancer)</td>
<td>1-100</td>
<td>24</td>
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