NanoScale's Metal Oxides

Composition

FAST-ACT is comprised of magnesium oxide and titanium dioxide, both non-toxic materials commonly found in consumer products including food products.

Particle Size

The commonly accepted definition for nanotechnology or a nanomaterial is one that is engineered or takes advantage of a dimension, in at least one direction, of 100 nanometers or less. The component materials of FAST-ACT (magnesium oxide and titanium dioxide) have crystallite sizes engineered to be less than 10 nm as measured by powder X-ray diffraction (calculated by Scherrer Equation). However, the large surface energy of these nanocrystals causes them to agglomerate to form extremely porous agglomerates that are much larger, the median particle size is approximately 3-5 microns as measured using laser light scattering (Malvern Mastersizer 2000; the capability (measurable size range) of this instrument is 0.02 to 2,000 microns). The average particle sizes are given below

$d_{0.1}$ is 1.023 μm, $d_{0.5}$ is 3.84 μm and $d_{0.9}$ is 9.916 μm; volume weighted mean is 4.8 μm

In **none** of the cases were particles smaller than 209 nm (0.209 μm) detected.

These micron sized particles will not deagglomerate and become nanoparticulate during handling, or use. ***Therefore, FAST-ACT is not composed of nanoparticles, but rather micron sized agglomerates of nanocrystals which are 30-50 times larger than nanoparticles. Because of this, there is no inherent danger associated with the particle size.***

Toxicity Testing

NanoScale has completed several third party toxicology studies on the materials, all of which have shown them to be non-toxic. The U.S. Army Center for Health Promotion and Preventive Medicine (CHPPM) is currently completing a Subacute Inhalation Toxicity study in which male and female rats were exposed to 5, 25, and 100 mg/m^3 of a FAST-ACT for 6 hours a day for 20 days. Gross necropsy findings were negative.

In regard to the carcinogen status of TiO_2, NanoScale actually just completed a review of relevant human and animal studies and have updated our MSDS, (see attached). In February 2006 an IARC (International Agency for Research on Cancer) review resulted in the classification for Titanium Dioxide being changed from 'Not classifiable for human carcinogenicity' to: 'Possible human carcinogen'. The reason for this was ***entirely*** due to animal studies. The IARC concluded there was 'insufficient evidence of carcinogenicity in humans' and 'sufficient evidence of carcinogenicity in experimental animals'. The IARC rules state: there is "*Sufficient evidence of carcinogenicity: …if… two or more independent studies in one species*

carried out at different times or in different laboratories or under different protocols" show evidence of tumors. The IARC expert group judged three studies on rats as qualifying.

Although the three studies showed evidence of tumors it is important to realize that these studies tested pigmentary and ultrafine titanium dioxide. As stated in the IARC *draft* monograph, volume 93, primary particle sizes for pigmentary titanium dioxide are typically between 0.2 and 0.3 μm. Ultrafine grades range from 10-50 nm. NanoScale's NanoActive® Titanium Dioxide particles are larger and do not fall into the pigmentary or ultrafine classifications. Also, as realized in studies reviewed by NIOSH, the toxicity seems to be more related to the particle size rather than the chemical itself.

Furthermore, the National Institute for Occupational Safety and Health (NIOSH) in a *draft* Current Intelligence Bulletin, has reviewed the relevant animal and human data for assessing the carcinogenicity of Titanium Dioxide and concluded: A) the tumorigenic effects of Titanium Dioxide exposure in rats appear not to be chemical specific or a direct action of the chemical substance itself. Rather, these effects appear to be a function of particle size and surface area acting through a secondary genotoxic mechanism associated with persistent inflammation; and B) Current evidence indicates that occupational exposures to low concentrations of Titanium Dioxide produce a negligible risk of lung cancer in workers. ***On the basis of these findings, NIOSH has determined that insufficient evidence exists to designate Titanium Dioxide as a "potential occupational carcinogen" at this time.***