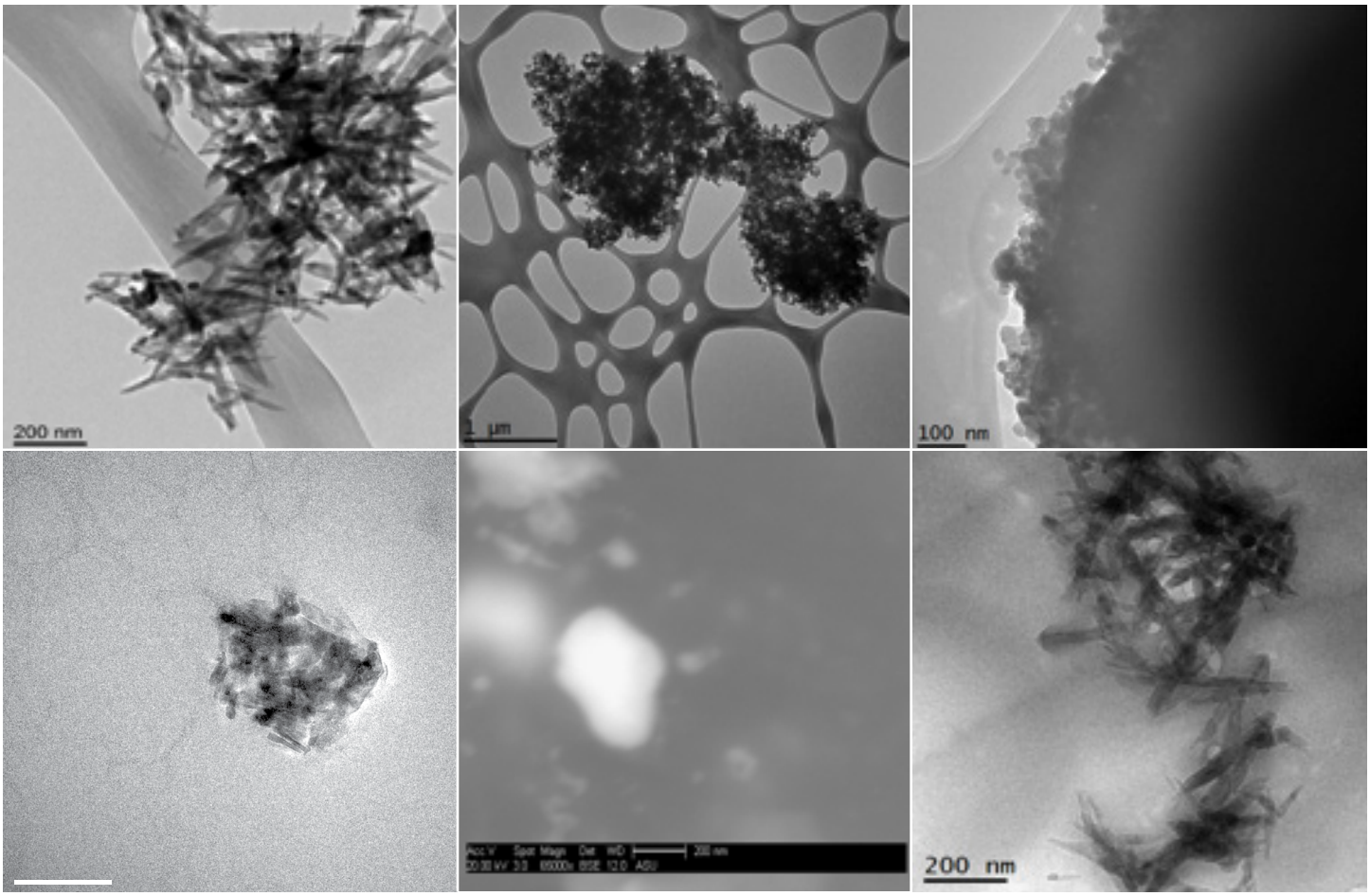
NANO-PARTICLES IN BABY FORMULA:

Tiny new ingredients are a big concern

Friends of the Earth



Electron microscopy images of nanomaterials found in baby formula provided by Arizona State University, see appendix B for additional information.

Acknowledgements

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About Friends of the Earth:

Friends of the Earth U.S., founded by David Brower in 1969, is the U.S. voice of the world's largest federation of grassroots environmental groups, with a presence in 74 countries. Friends of the Earth works to defend the environment and champion a more healthy and just world. Throughout our 47-year history, we have provided crucial leadership in campaigns resulting in landmark environmental laws, precedent-setting legal victories and groundbreaking reforms of domestic and international regulatory, corporate and financial institution policies. **www.foe.org**

Any errors or omissions in this report are the responsibility of Friends of the Earth U.S.

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Executive Summary

Unbeknownst to the general public, popular infant formulas sold throughout the United States contain infinitesimally small ingredients known as engineered nanoparticles or nanomaterials. While some nanoscale ingredients may offer potential benefits, their safety remains poorly understood, and a growing body of scientific research is raising concerns about their use in food and many other consumer products. **The groundbreaking analysis of nanomaterials in baby formula presented here by Friends of the Earth is meant to inspire greater public scrutiny, industry accountability and government regulation of nanotechnology, particularly in the food sector.** This analysis builds on our 2014 nanotechnology report, *Tiny Ingredients, Big Risks: Nanomaterials rapidly entering food and farming.*

Nano ingredients pose threats to human health but are not regulated or assessed for safety before they are put on the market. In the United States, the Food and Drug Administration (FDA) is charged with ensuring baby formulas are safe, however, the FDA does not approve the safety of infant formulas before they can be marketed. The FDA requires that baby formulas meet certain nutritional requirements and are screened for pathogens, and companies must register with the FDA and provide a notice before marketing a formula. However, these rules do not include screening or safety testing of nanomaterials or other potentially toxic synthetic ingredients. Baby formulas are intended for our most vulnerable population and should be regulated with the utmost of care. A product fed to millions of infants should not be permitted to go to market if we are not certain that the ingredients it contains are safe for human consumption. All infant formulas should be thoroughly tested for safety.

To put the nanoscale in context: a strand of DNA is 2.5 nm wide, a red blood cell is 7,000 nm wide, and a human hair is around 80,000 nm wide. One nanometer is one billionth of a meter. One way to understand how incredibly tiny these particles are is to consider a tennis ball in comparison with planet Earth. On scale, a tennis ball is the same size in relation to Earth as a nanoparticle is to a tennis ball.

Major baby formula brands contain nanomaterials

This analysis by Friends of the Earth reveals the use of engineered nanomaterials in baby formulas sold throughout the United States. We commissioned independent laboratory studies with a world-class nanotechnology research facility at the Arizona State University (ASU) to learn more about the presence of engineered nanomaterials in popular baby formulas. To our knowledge, these are the first laboratory studies focused on the detection of engineered nanomaterials in baby formulas that are marketed to the public.

Friends of the Earth tested a selection of six baby formula samples gathered from retailers in the San Francisco Bay Area.

We found nano-sized structures and particles of potential concern in all six of the baby formulas tested, including: Nano-hydroxyapatite (nano HA) in needle-like and non needle-like form, nano titanium dioxide (TiO2), and nano silicon dioxide (SiO2) (the nano TiO2 and SiO2 results were inconclusive). TiO2 was tentatively identified using a scanning electron microscope (SEM) in the Similac® Advance® OptiGRO™ (liquid) product, though after purchasing a second sample several months later and using a different separation process and transmission electron microscopy (TEM) analysis, the presence of TiO2 could not be confirmed.

Nanoparticles found in popular baby formulas tested by Friends of the Earth

Baby Formula Brand	Nanoparticles Found
Gerber® Good Start® Gentle	Nano-hydroxyapatite (nano HA)
Gerber® Good Start® Soothe	Titanium dioxide and silicon dioxide (limited amount of particles detected)
Enfamil™	Nano-hydroxyapatite (nano HA) in needle-like and non needle-like form
Similac® Advance® OptiGRO™ (liquid)	Titanium dioxide (nano TiO2 laboratory results inconclusive)
Similac® Advance® OptiGRO™ (powder)	Nano silicon dioxide (laboratory results inconclusive)
Well Beginnings™ Advantage®	Nano-hydroxyapatite (nano HA)

Nanomaterials present novel risks to human health

Recent studies have found that these nanomaterials may pose risks to human health if ingested or inhaled. Especially concerning: the nanomaterials

found in the three powdered formulas we tested provide a probable inhalation hazard for babies, parents and other care givers, as well as workers involved in the manufacturing of these products.

Nanomaterials have unique properties that offer many new opportunities for food industry applications. They can be used as nutritional additives, flavoring and coloring, anti-caking agents or as antibacterial ingredients for food packaging. However, **the same properties exhibited at the nanoscale that make these materials attractive for use in the food industry may also result in greater toxicity for humans and the environment.** (See full report for summary of the latest science).

At the nanoscale, the physical, chemical, and optical properties of familiar substances differ from those of the same substances in larger particle form. Nanoparticles can be more chemically reactive and more bioactive than larger particles. Because of their very small size, nanoparticles are more likely than larger particles to enter cells, tissues and organs.

The European Union Scientific Committee on Consumer Safety (SCCS) finds that needle-like nano-hydroxyapatite — one of the nanomaterials we found in Gerber®, Well Beginnings™, and Enfamil™ formulas — is potentially toxic, could be absorbed by and enter cells, and should not be used in cosmetics such as toothpaste, teeth whiteners and mouth washes. A material that should not be used in cosmetics raises greater concern when used in food.

Nanomaterials are already used widely in the commercial sector

Nanotechnology is a rapidly expanding, multi-billion dollar industry involving manipulation of matter at the nanoscale. As of August 2008, the Project on Emerging Nanotechnologies estimated that over 800 manufacturer-identified nanotech products were publicly available, with new ones hitting the market at a pace of three to four each week.

Many nanomaterials have already entered wide-scale commercial use and can be found in hundreds of products available on supermarket shelves, including transparent sunscreens; light-diffracting cosmetics; penetration enhanced moisturisers; stain, moisture and odor repellent fabrics and clothing; long-lasting paints and furniture varnishes; anti-bacterial household appliances such as vacuum cleaners; refrigerators and air conditioners; and sporting equipment.

Beyond baby formulas, other children's products that contain engineered nanoparticles include skincare products and sunscreens, supplements, food containers, pacifiers, teethers, blankets, toys and stuffed animals, baby bottles, toothbrushes, baby carriages, bibs, baby clothing and many other products.

Nanotechnology is currently in the first generation of innovation. In coming years and decades, the next generation nanotechnology is forecast to bring more complex nanodevices, nanosystems, and nanomachines. Nanobiotechnology may be used to manipulate the genetics of humans, animals and agricultural plants at the atomic scale and to incorporate synthetic materials into biological organisms and biological materials into synthetic structures.

EU responsible technology policies

European regulators have enacted a range of precautionary policies for nanotechnologies. The European Parliament is working towards a moratorium on novel foods containing nanomaterials. France, Belgium and Denmark have implemented mandatory registries for nanomaterials, and the EU has implemented a nanofood-labeling regime.

U.S. regulatory inaction

In stark contrast to the EU, the United States has not developed any mandatory regulations or safety assessments for nanomaterials used in food or consumer products. It is important for U.S. consumers to know that manufacturers are not

required to list nanomaterial ingredients on product packaging in the United States. In our investigation, Friends of the Earth did not find any baby formulas that listed nanoparticles as ingredients, including the samples we found — via laboratory testing — to contain nanoparticles.

Nanotechnology raises ethical and social justice concerns

Serious ethical and social justice concerns must be addressed in the regulation of nanotechnology. In the case of baby formula, infants may be at greater risk of suffering health harms because of their more vulnerable physiology. Children's immune, central nervous, reproductive, and digestive systems are still developing, and at certain early stages of development, exposure to toxicants can lead to irreversible damage which can increase risk of disease later in life.

Food sector workers represent another vulnerable population as they may come into contact with nanomaterials during production, packaging, transport and waste disposal of food, food packaging and agrochemicals. As one example, the U.S. Occupational Health and Safety Administration states that nanoscale titanium dioxide, which we found in baby formula samples, is a potential occupational carcinogen.

Friends of the Earth and allied organizations demand regulatory action

In response to mounting scientific evidence on the potential harms of nanotechnology, non-governmental organizations worldwide, including Friends of the Earth, are calling for precautionary action. More than 70 groups from six continents have endorsed a guiding document published in 2007 called *Principles for the Oversight of Nanotechnologies and Nanomaterials*.

In 2011, the Center for Food Safety, along with Friends of the Earth and other organizations, filed a lawsuit calling out the FDA for failure to take action on a 2006 citizen petition to regulate nanotechnology. In response to the lawsuit, the FDA released voluntary, non-binding recommendations for industry that were finalized in 2014.

Given the potentially serious health and environmental risks and social implications associated with nanofoods, Friends of the Earth calls for a moratorium on the further commercial release of food products, food packaging, food coatings, food contact materials and agrochemicals that contain engineered nanomaterials until nanotechnology-specific safety and labeling laws are established and the public is involved in decision-making.

Friends of the Earth recommends the FDA conduct a thorough review of the nanoparticle ingredients found in baby formulas. The agency must, in the meantime, use its authority to enforce manufacturer recall of baby formulas containing engineered nanoparticles, as these ingredients may put people at risk.

We also demand greater accountability and transparency from food producers and retailers to allow consumers to make informed choices about

this novel set of technologies. If nanotechnology is to be developed safely, responsibly and transparently, there is an urgent need for further research and dissemination of information to policy makers, regulators, consumers and the scientific community.

Summary of recommendations:

For a detailed description of the following recommendations, see the full report.

What government must do:

- Enact a moratorium on new commercial nanotech products
- Assess safety of and recall baby formulas with nanoparticle ingredients
- Regulate nanomaterials as novel substances
- Extend the size-based definition of nanomaterials up to 500 nm in size
- Protect workers
- Ensure transparent, mandatory safety assessment and product labeling

What industry must do:

- Recall formula containing nanomaterials
- Remove nanomaterials from product formulas
- Create nanomaterial policies
- Ensure transparency in the supply chain

What concerned parents, individuals and organizations can do:

Until government and companies manage nanotechnology in a responsible and transparent manner, there are steps we can take to protect our health.

- Breastfeed when and if possible
- Hold government and industry accountable: Join Friends of the Earth to demand a moratorium on the use of nanotechnology in the food sector and urge policy makers to regulate and label food, food packaging and agricultural products containing manufactured nanomaterials
- Contact baby formula manufacturers and ask them to remove nanomaterials from their products

Visit our website to learn more about nanotechnology, take action and support our efforts to create a safe, just, resilient and sustainable food system. http://www.foe.org/nanotechnology

Nano ingredients pose threats to human health but are not regulated or assessed for safety before they are put on the market. A product fed to millions of infants should not be permitted to go to market if we are not certain that the ingredients it contains are safe for human consumption.

1. Introduction

Unbeknownst to the general public, popular infant formulas sold throughout the United States contain infinitesimally small ingredients known as engineered nanoparticles or nanomaterials.[1] The safety of these nanoscale ingredients remains poorly understood and a growing body of scientific research is raising concerns about their use in food and many other consumer products. The groundbreaking analysis of nanomaterials in baby formula presented here by Friends of the Earth is meant to inspire greater public scrutiny, industry accountability and government regulation of nanotechnology, particularly in the food sector. This analysis builds on our 2014 report, *Tiny Ingredients, Big Risks.*

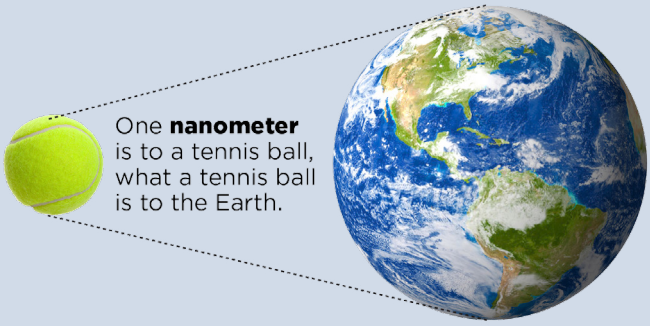
Nanotechnology is a rapidly expanding, multi-billion dollar industry involving manipulation of matter at the molecular scale. As of August 2008, the Project on Emerging Nanotechnologies estimated that over 800 manufacturer-identified nanotech products were publicly available with new ones hitting the market at a pace of three to four each week (Project on Emerging Nanotechnologies (PEN), 2015a).

Nanomaterials have unique properties that offer many new opportunities for food industry applications. They can be used as nutritional additives, flavoring and coloring, anti-caking agents or as antibacterial ingredients in food packaging. However, the same properties exhibited at the nanoscale that make these materials attractive for use in the food industry may also result in greater toxicity for humans and the environment.

At the nanoscale, the physical, chemical and optical properties of familiar substances differ from those of the same substances in larger particle form. Nanoparticles can be more chemically reactive and more bioactive than larger particles. Because of their very small size, nanoparticles are more likely than larger particles to enter cells, tissues and organs.

Nano ingredients pose novel threats to human health but are not regulated or assessed for safety before they are put on the market. There is no nanotechnology-specific regulation or safety assessment required before manufactured nanomaterials can be used in food, food packaging or agricultural products in the United States. The U.S. Food and Drug Administration is charged with ensuring baby formulas are safe, however, according to the agency's own assertion, "The FDA does not approve infant formulas before they can be marketed" (U.S. Food and Drug Administration, 2014a)**.** The FDA requires that baby formulas meet certain nutritional requirements and be screened for pathogens, and companies must register with the FDA and provide a notice before marketing a formula (FDA, 2014a). However, these rules do not include screening or safety testing of nanomaterial ingredients. All infant formulas should be thoroughly tested for safety before entering the market.

The use of minimally tested, unlabeled nanoscale materials in children's products, a broad array of consumer products, food and agriculture is growing despite evidence that these materials can be toxic to human health and the environment. While regulators in the EU have taken action to regulate nanomaterials in food and consumer products, the lack of safety assessment, oversight and labeling of nanomaterial ingredients in the United States further exacerbate concerns.



To put the nanoscale in context: a strand of DNA is 2.5 nm wide, a red blood cell is 7,000 nm wide, and a human hair is 80,000 nm wide. One nanometer is one billionth of a meter. One way to understand how incredibly tiny these particles are is to consider a tennis ball in comparison with planet Earth. On scale, a tennis ball is the same size in relation to Earth as a nanoparticle is to a tennis ball.

a. Breastfeeding: Benefits and barriers

It is estimated that worldwide, baby food and formula sales will amount to 30 billion USD in 2015 (Nielsen, 2015). Yet, data proves that breast milk is indisputably the healthiest food for a growing infant and helps to reduce health risks for both mother and child (U.S. Department of Health and Human Services, 2011). However, mothers face myriad obstacles to breastfeeding. The U.S. Office

1 Nanotechnology is the engineering of functional systems at the molecular scale. For the purposes of this report, we use the term "nano" to include particles up to 500nm in size, due to the evidence of nano-specific problems associated with particles up to this size range. We use the terms nanomaterial and nanoparticle interchangeably.

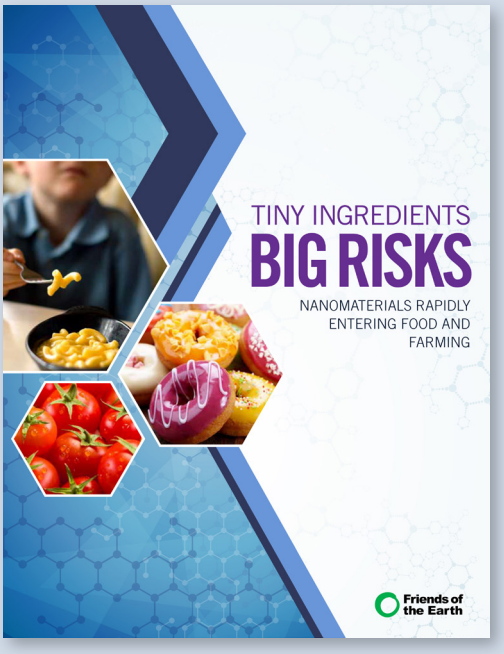
of the Surgeon General has identified many of these barriers, which range from the influence of social norms and the marketing of breast milk substitutes to health problems, employment and childcare, lack of support or fear of stigma (U.S. HHS, 2011). These barriers make it essential for families to have a safe and healthy alternative for feeding (U.S. HHS, 2011). It is also important to note that in many cases mothers may not be able to or choose not to breastfeed.

b. Nanotechnology raises ethical and social justice concerns

Serious ethical and social justice concerns must be addressed in the regulation of nanotechnology. In the case of baby formula, infants may be at greater risk of suffering health harms from exposure to toxics like nanomaterials because of their more vulnerable physiology (Moya, Bearer, & Etzel, 2004). Children's immune, central nervous, reproductive and digestive systems are still developing, and at certain early stages of development, exposure to toxicants can lead to irreversible damage which can increase risk of disease later in life.

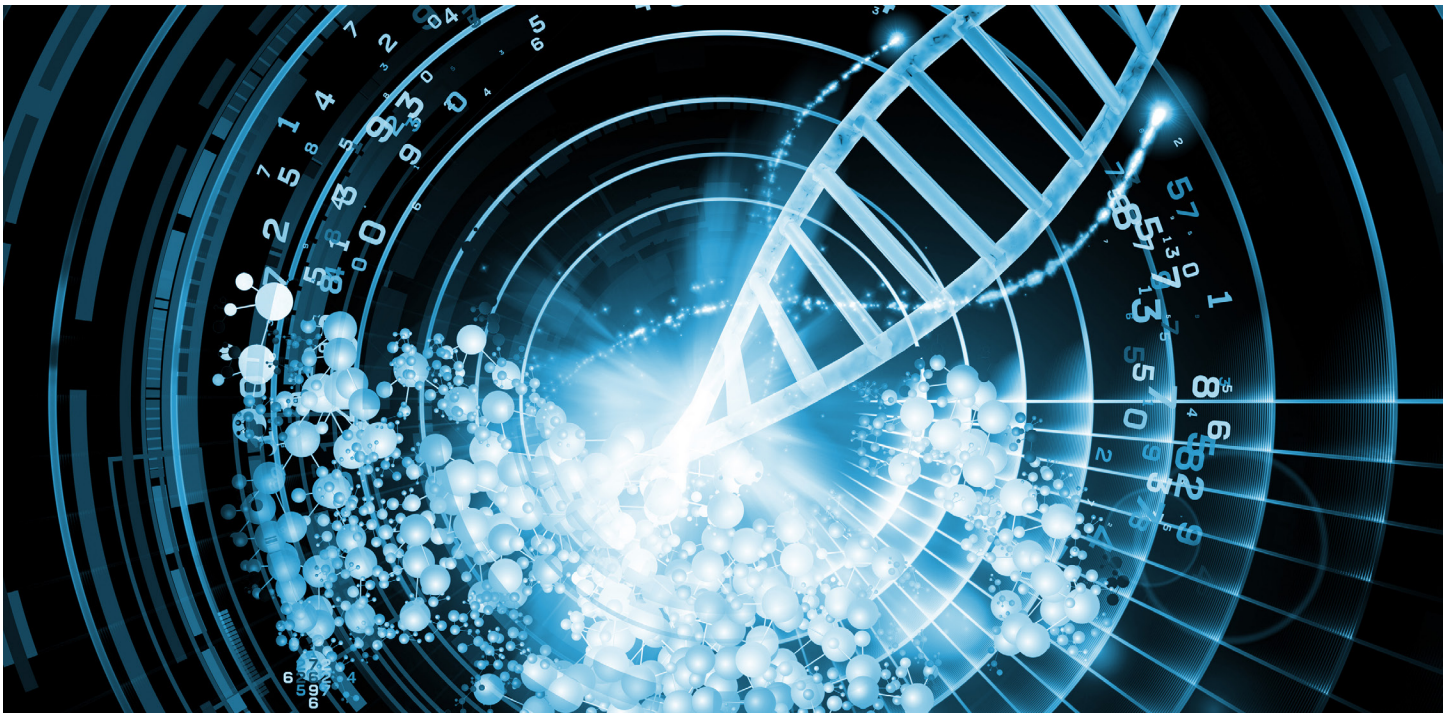
An additional concern is that low-income families are given baby formulas at no cost via the U.S. Special Supplemental Nutrition Program for Women, Infants and Children (WIC) (Kent, 2006), thereby increasing their children's potential exposure to nanomaterials in baby formula.

Food sector workers represent another vulnerable population as they may come into contact with nanomaterials during production, packaging, transport and waste disposal of food, food packaging and agrochemicals. As one example, OSHA states that nanoscale titanium dioxide, which we found in some of the baby formula samples we tested, is a potential occupational carcinogen.



Nanotechnology and the Environment

The data presented here focus on human health concerns. For an overview of environmental risks associated with nanotechnology, see our 2014 report, *Tiny Ingredients, Big Risks: Nanomaterials rapidly entering food and farming*



Arizona State University laboratory.

2. Findings & Analysis

Friends of the Earth commissioned independent laboratory testing of baby formulas with a world-class nanotechnology research facility at the Arizona State University (ASU). Table 1 below provides a summary of our test results. This section also provides a brief summary of toxicological concerns for the nanoparticles found. Descriptions of the likely function of these nano ingredients were drawn from publically accessible information from manufacturers, scholarly articles, government documents and other media and research materials. See Appendix A for details on study methodology and Appendix B for additional details about laboratory results.

a. Major baby formula brands contain nanomaterials

Friends of the Earth tested a selection of six baby formula samples gathered from retailers in the San Francisco Bay Area. We found nano-sized structures and particles of potential concern in all six of the baby formulas tested, including: Nano-hydroxyapatite (nano HA) in needle-like and non needle-like form, nano titanium dioxide (TiO2), and nano silicon dioxide (SiO2) (the nano TiO2 and SiO2 results were inconclusive).

TiO2 was *tentatively* identified using a scanning electron microscope (SEM) in the Similac® Advance® OptiGRO™ (liquid) product, though after purchasing a second sample several months later and using a different separation process and transmission electron microscopy (TEM) analysis, the presence of TiO2 could not be confirmed.

To our knowledge, these are the first laboratory studies focused on the detection of engineered nanomaterials in baby formulas that are marketed to the public.

- The Gerber® Good Start® Gentle, Well Beginnings ™ Advantage® and Enfamil ™ formula samples were found to contain nano-hydroxyapatite (note: two separate samples of Gerber® Good Start® Gentle were tested three times and found to contain nano HA; duplicate tests were conducted on all samples).
- The Gerber® Good Start® Soothe baby formula likely contains nano titanium dioxide (TiO2) and nano silicon dioxide (SiO2) (note: limited amount of particles detected).
- The Similac® Advance ® OptiGRO™ (liquid) baby formula likely contains titanium dioxide nanoparticles (nano TiO2) (note: laboratory results were inconclusive).
- The Similac® Advance® OptiGRO™ (powder) baby formula likely contains nano silicon dioxide (note: laboratory results were inconclusive).

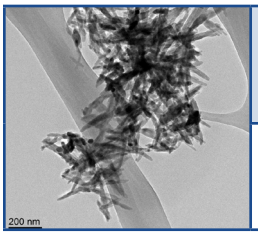
Table 1: Nanoparticles found in popular baby formulas tested by Friends of the Earth

Baby Formula Brand	Nanoparticles Found
Gerber® Good Start® Gentle	Nano-hydroxyapatite (nano HA)
Gerber® Good Start® Soothe	Titanium dioxide and silicon dioxide (limited amount of particles detected)
Enfamil™	Nano-hydroxyapatite (nano HA) in needle-like and non needle-like form
Similac® Advance® OptiGRO™ (liquid)	Titanium dioxide (nano TiO2 laboratory results inconclusive)
Similac® Advance® OptiGRO™ (powder)	Silicon dioxide (laboratory results inconclusive)
Well Beginnings™ Advantage®	Nano-hydroxyapatite (nano HA)

Baby formulas are intended for our most vulnerable population and should be regulated with the utmost of care. A product fed to millions of infants should not be permitted to go to market if we are not certain that the ingredients it contains are safe for human consumption.

Recent studies have suggested that these nanomaterials may pose risks to human health if ingested or inhaled (see below health concerns for each nanomaterial found). **Especially concerning: the nanomaterials found in the three powdered formulas we tested provide a probable inhalation hazard for babies, parents and other care givers, as well as workers involved in the manufacturing of these products** (Note: inhalation concerns would not pertain to the liquid version of the Similac® Advance® formula).

Baby formulas are intended for our most vulnerable population and should be regulated with the utmost of care. A product fed to millions of infants should not be permitted to go to market if we are not certain that the ingredients it contains are safe for human consumption.



b. INGREDIENT: Nano-hydroxyapatite (nano HA)

FORMULAS: Gerber®, Well Beginnings ™ and Enfamil™

Potential Uses

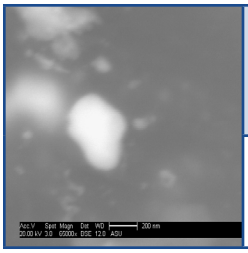
Nano-hydroxyapatite is most likely a calcium source for these baby formulas. It can also be used to stabilize the ingredients in the formula mixture. Conventional hydroxyapatite is used as a calcium source for supplements and is derived from the bones of cows. Hydroxyapatite forms 70 percent of our bones (International Osteoporosis Foundation, 2015). Through nanotechnology, hydroxyapatite can now be manufactured into needle-like nanoparticles to take advantage of properties at the nanoscale. Nano HA is described in scientific literature as a novel ingredient used experimentally for rebuilding bones in surgery and to repair tooth enamel (Huber et al., 2006; McArthur et al., 2013; Tschoppe et al., 2011). Toothpaste containing nano HA can be purchased in the United States, many brands and dozens of products are available for purchase online (Amazon, 2015). Friends of the Earth did not find any description of nano HA use in baby formula, however, some manufacturers list a food use for this ingredient among other advertised applications (Del Nanbio Technology GMBH, 2015).

Health Concerns

In October of 2015, the European Union Scientific Committee on Consumer Safety (SCCS) provided evidence that needle-like nano-hydroxyapatite is potentially toxic, could be absorbed and enter cells and should not be used in cosmetics such as toothpaste, teeth whiteners and mouth washes (EU SCCS, 2014; EU SCCS, 2015). The SCCS opinion states: "The available information indicates that nano-hydroxyapatite in needle form is of concern in relation to potential toxicity. Therefore, needle-shaped nano-hydroxyapatite should not be used in cosmetic products."

Some chemical company material safety data sheets (MSDS) list hydroxyapatite as an inhalation hazard and cite the lack of data available to provide a complete safety profile (Sigma-Aldrich, 2008; Merz NA, Inc., 2015). Other similarly shaped needle-like nanoparticles have been shown to have the potential to cause diseases in the lungs similar to those caused by inhalation exposure to asbestos, including mesothelioma and lung cancer (Poland et al., 2008; Jacobs, 2014; HHS et al., 2013). Additionally, a 2014 study found that both nano HA and nano titanium dioxide (TiO2) increased reactive oxygen species (ROS) and inflammation in cells (Tay et al., 2014).

Further research could ascertain if the needle-like shape of nano HA could become an inhalation hazard for parents and children as the formula is sold in powder form. Another important research question would be to understand if the nano version of this calcium supplement could produce an undesirable increase in calcium intake. Increased calcium absorption can cause hypercalcemia and interfere with brain and heart function (Mayo Clinic, 2015).



c. INGREDIENT: Nano titanium dioxide (TiO2) (note: laboratory results inconclusive)

FORMULA: Similac® Advance ® liquid version; Gerber® Good Start® Soothe

Potential Uses

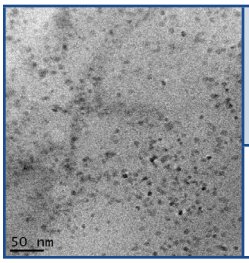
Nano TiO2 is a brightener or whitener for food and beverage products and is also used as an anti-caking agent.

Health Concerns

In contrast to bulk particles of titanium dioxide, nanoscale titanium dioxide is biologically very active. Studies show that titanium dioxide can damage DNA (Trouiller et al., 2009), disrupt the function of cells, interfere with the defence activities of immune cells and, by adsorbing fragments of bacteria and 'smuggling' them across the gastro-intestinal tract, can provoke inflammation (Ashwood et al., 2007; Donaldson et al., 1996; Dunford et al.,

1997; Long et al., 2006; Lucarelli et al., 2004; Wang et al., 2007b). A single high oral dose of titanium dioxide nanoparticles was found to cause significant lesions in the kidneys and livers of female mice (Wang et al., 2007b).

Nano titanium dioxide is highly mobile in the body and has been detected in both humans and animals in the blood, liver and spleen (Landesanstalt für Umwelt, Messungen und Naturschutz Baden-Württemberg (LUBW), 2010). A 2015 study found that food grade TiO2 can be absorbed in the bloodstream (Laetitia et al., 2015). A study using pregnant mice found that nanoparticles of titanium dioxide were transferred from mother to offspring and was associated with brain damage, nerve system damage and reduced sperm production in male offspring (Takeda et al., 2009).



d. INGREDIENT: Nano silicon dioxide (SiO2) (note: laboratory results inconclusive)

FORMULA: Similac® Advance® OptiGRO™ powder version; Gerber® Good Start® Soothe

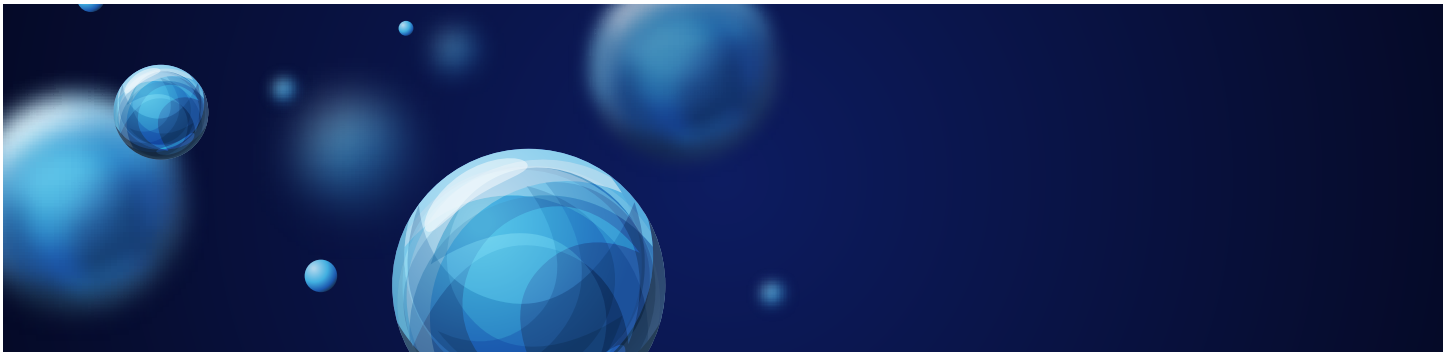
Potential Uses

Used as a 'trickle and flow' aid in powdered food products, as a clearing agent in beer and wine, as a food additive (amorphous silicon found to be nano) and as a food coating.

Health Concerns

Nanosilicon has been found in the livers of rats and mice after oral administration. In vitro studies show a significant percentage of the nanosilicon remains undissolved and that "the presence of undissolved nanosilicon particles in the gut in vivo is considered likely" (Dekker et al., 2013; SRU, 2011). Animal studies have shown placental transfer and foetal uptake of silicon. Scientists have warned that the enhanced sensitivity of the foetus may mean that even low doses of nanomaterials may cause adverse effects (Correia et al., 2015).

Arizona State University (image 1) Arizona State University laboratory where baby formulas were tested.



3. Background: An introduction to nanotechnology

The term "nanotechnology" does not describe a singular technology but rather encompasses a range of technologies that operate at the scale of the building blocks of biological and manufactured materials — it constitutes manipulation of matter on an atomic, molecular and supramolecular scale.

The term nanotechnology is generally understood to encompass both nanoscience and the broad range of technologies that operate at the nanoscale:

- Nanoscience: The study of phenomena and materials at the atomic, molecular and macromolecular scales, where properties differ from those at the larger scale.
- Nanotechnology: Design, characterization, production and application of structures, devices and systems by controlling shape and size at the nanoscale.
- Nanomaterials: articles, nanotubes, nanowires, quantum dots, fullerenes (Buckyballs) etc.

a. Defining nanomaterials for health and safety

There is still no internationally accepted set of definitions and measurement systems for nanotechnology, although work towards these has begun. **For the purpose of this report we use the term "nano" to include particles up to 500 nm in size due to the evidence of nano-specific problems associated with particles up to this size range. We urge regulators to adopt this definition — the health and environmental hazards of nanoparticles should be based on physiological and anatomical behaviors of small particles rather than arbitrary size distinctions.**

The definition of nanomaterials is in flux. The U.S. Food and Drug Administration uses a definition of 1-1,000 nm for drugs and requests information for ingredients less than 1,000 nm in size for other products it regulates. The European Medicines Agency also defines nanotechnology in a size range of less than 1,000 nm across.

Despite these definitions, there is an emerging trend to define nanotechnology as only applying to materials, structures and systems that measure no more than 100 nm in size. This distinction is artificial, especially from the viewpoint of biological interactions. Many particles, which measure more than 100 nm, present a suite of physiological and anatomical behaviors, for example greater reactivity, bioactivity and bioavailability (Garnett & Kallinteri, 2006). When considering the health and environmental implications of nanoparticles, their size range must be more broadly defined. It is essential to also consider the hazards associated with sub-micron (100-1,000 nm) particles and microparticles (greater than 1,000 nm).

The problematic nature of the arbitrary 100 nm ceiling is underscored by studies showing that small particles outside this size range can pose greater health hazards than particles within it. Wang et al conducted an *in vivo* study in which 20 nm and 120 nm particles of zinc oxide powder were fed to mice (Wang et al., 2007). Both nanoparticles resulted in organ damage and thickening of the test animals' blood, but it appeared that the larger nanoparticles actually resulted in greater liver damage. In another *in vivo* experiment, mice were fed high doses of 58 nm and 1,058 nm zinc powder. The microparticle zinc caused more severe liver damage, while the nanoparticle zinc caused anaemia and more severe kidney damage (Wang B, 2006).

In a 2010 report, the UK's House of Lords Science and Technology Committee recommended that any definition of a nanomaterial must be based on evidence for behavior that is different from that seen in the bulk, rather than some arbitrary size such as 100 nm (Nature Nanotechnology, 2010). The authors of a review of the nanotoxicological implications of nanomedicines suggest that: "In practice, the useful range of nanomedicines more normally falls within the range of 5-250 nm as these tend to have a similar range of properties based on physiological and anatomical consequences" (Garnett & Kallinteri, 2006). Researchers investigating the biological effects of nanoparticles have also defined their relevant size range to be up to a few hundred nanometres (Hansen et al., 2006). Still other researchers publishing in the drug delivery (Des Rieux et al., 2006) and food (Sanguansri & Augustin, 2006) (Mozafari et al., 2006) literature have argued that a useful size definition for nanomaterials used in these fields is 1-1,000 nm.

b. Manufactured vs. incidental nanoparticles

Manufactured nanoparticles are those that are deliberately produced, in contrast to nanoparticles that "exist in nature," or are by-products of other human activities. Manufactured nanomaterials include nanoparticles (e.g. metal oxides) and also nanostructures such as nanotubes, nanowires, quantum dots, dendrimers and carbon fullerenes (Buckyballs), among others.

"Incidental" nanoparticles (also called ultrafine

particles in the study of air pollution and its epidemiology) are a by-product of forest fires, volcanoes, vehicle combustion and high-temperature industrial processes including combustion, welding and grinding (Institute of Occupational Medicine, 2004).

c. Nanomaterials are already used widely for their novel properties

Many nanomaterials have already entered wide-scale commercial use and can be found in hundreds of products available on supermarket shelves, including transparent sunscreens; light-diffracting cosmetics; penetration enhanced moisturisers; stain-, moisture- and odor-repellent fabrics; long-lasting paints and furniture varnishes; anti-bacterial household appliances such as vacuum cleaners, refrigerators and air conditioners; and sporting equipment (Project on Emerging Nanotechnologies (PEN), 2015a).

Beyond baby formulas, children's products that contain engineered nanoparticles include skincare products and sunscreens, supplements, food containers, pacifiers, teethers, blankets, toys and stuffed animals, baby bottles, toothbrushes, baby carriages, bibs, baby clothing and many other products (PEN, 2015b)**.**

Nanotechnology is currently in the first generation of innovation. In coming years and decades, next generation nanotechnology is forecast to bring more complex nanodevices, nanosystems and nanomachines (Roco, 2001). Nanobiotechnology may be used to manipulate the genetics of humans, animals and agricultural plants at the atomic scale, and to incorporate synthetic materials into biological organisms and biological materials into synthetic structures (Roco & Bainbridge, 2003).

d. Why are food and agriculture companies interested in nanotechnology?

At the nanoscale, the physical, chemical and optical properties of familiar substances differ from those of the substances in larger particle form. For example, in larger particle form zinc oxide (ZnO) is white and opaque, as a nanoparticle zinc oxide is transparent, enabling it to be used to provide UV protection in products such as transparent cling wrap packaging. In nanoparticle form, the antimicrobial properties of silver are far greater, a property which has encouraged manufacturers to use it in chopping boards, refrigerators, food storage containers and food packaging.

Altered properties of nanoparticles are a result of both the influence of quantum mechanics[1] and the much greater relative surface area that nanomaterials have compared with larger particles. The large surface area of nanomaterials results in their increased chemical reactivity and biological activity (Nel et al., 2006), making them attractive for use in food fortification (adding micronutrients to foods) or as antimicrobials in food packaging. However, the altered properties of nanomaterials, especially their high chemical reactivity and greater capacity to penetrate biological membranes, also present serious new toxicity risks (Royal Society & Royal Academy of Engineering, 2004).

Nanotechnology has existing and potential applications in all aspects of agriculture, food processing, food packaging and even farm and food monitoring. These include:

- Methods to enable foods such as soft drinks, ice cream, chocolate, or chips to be marketed as "health" foods by reducing fat, carbohydrate or calorie content or by increasing protein, fiber or vitamin content;
- Production of stronger flavoring, coloring, nutritional additives and processing aids to increase the pace of manufacturing and to lower costs of ingredients and processing;
- Development of foods with novel colors, flavors or nutritional properties to suit consumers' dietary needs, allergies or taste preferences;
- Packaging or edible coatings to increase food shelf life by detecting spoilage, bacteria or the loss of food nutrients, and to release antimicrobials, flavors, colors or nutritional supplements;
- Re-formulation of on-farm inputs to produce more potent fertilizers, plant growth treatments and pesticides that respond to specific conditions or targets.

1 A fundamental branch of physics concerned with describing the interactions and motions of tiny molecules, atoms, and even smaller matter.

4. Health Concerns: Novel risks from nanomaterials and nanofoods

The lack of standards and internationally recognized measurement methods coupled with the lack of transparency of the nanotechnology industry create significant challenges to understanding where engineered nanoparticles are being used and what the potential routes of exposure are.

Nanomaterials have unique properties that offer many new opportunities for food industry applications. However, the same properties exhibited at the nanoscale which make these materials attractive for use in the food industry may also result in greater toxicity for humans and the environment.

Nanoparticles pose new risks because:

- They can be more chemically reactive and more bioactive than larger particles of the same chemicals.
- Due to their very small size, nanoparticles have been demonstrated to be more likely than larger particles to enter cells, tissues and organs.
- Greater bioavailability and greater bioactivity may introduce new toxicity risks.

a. Permeability and absorption

Numerous *in vivo* experiments using rats and mice have demonstrated gastrointestinal uptake of nanoparticles (Chen et al., 2006; Desai et al., 1996; Hillyer & Albreicht, 2001; Wang et al., 2007; Wang et al., 2007b) and small microparticles (Hazzard et al., 1996; McMinn et al., 1996; Wang et al., 2006).

The absorption rate of substances via the gastrointestinal tract appears to depend on properties such as size and surface structure. In one study looking at rats, the smaller the nanoparticles, the higher the uptake via the digestive tract. (LUBW, 2010) In another study, mice were fed 4 nm gold particles; these were later detected in the liver, kidney, spleen, lung and brain. Larger particles (58 nm) remained in the gastrointestinal tract (Sachverständigenrat für Umweltfragen (SRU), 2011). Nanoparticles also show greater adhesion to biological surfaces within our bodies versus larger particles (for example, the walls of our gastrointestinal tract), which can increase rates of uptake (Chen et al., 2006a).

Powell *et al* have observed that the daily exposure of people in the Western world to sub-micrometer-sized mineral particles has resulted in "pigmented cells" in parts of the intestinal tract, meaning cells loaded with these particles (e.g. aluminosilicates titanium dioxide). The particles have been observed to be composed of aluminosilicates, titanium dioxide and a small percentage of non-aluminum-containing silicates such as silicon (SiO2) and magnesium trisilicate (talc) (Powell et al., 2010; Powell et al., 1996).

In the July 19, 2012, report, "Effects of Silver Nanoparticles on the Liver and Hepatocytes in vitro," published in Toxicological Sciences, author Birgit Gaiser, Ph.D., states,

> At the moment, there is not much information available on the topic of ingested nanoparticles and human health. There is evidence that a small percentage of these particles or particle components [of nano titanium dioxide or nano silver]...can move on from the intestinal tract into the blood, and reach other organs. This is why we believe it is important to assess the risk of even small amounts of particles in the human body (Belli, 2012).

Studies have shown that nanomaterials may affect the human intestine. When human colon cells were treated with nano-sized polystyrene, which is commonly used in food packaging, the cells became more permeable to iron (Spiegel, 2012).

b. Crohn's disease and immune system dysfunction

It is well known that people with asthma are especially susceptible to air pollution. In effect, asthma sufferers act as the proverbial "canary in the coal mine," alerting those around them that air pollution levels are getting dangerously high. Scientists have more recently suggested

that the growing prevalence of Crohn's disease — a damaging and chronic inflammation of the gastrointestinal tract that can lead to cancer — may be a similar warning signal in relation to microparticles in our food (Ashwood et al., 2007).

Some data suggests that existing levels of nanoparticles up to a few hundred nanometers in size in processed food may be associated with rising levels of immune system dysfunction and inflammation of the gastrointestinal tract, including Crohn's disease (Ashwood et al., 2007; Gatti et al., 2004; Lomer et al., 2001; Lucarelli, et al., 2004). Individuals with Crohn's disease or colon cancer have been found with nanomaterials in their intestinal tissue (SRU, 2011).

This data points to the need for more research. The relationship between the development of Crohn's disease and factors such as genetic susceptibility, immune system health, psychological health and environmental factors, including exposure and physiological response to nano or microparticles, remains poorly understood. Other theories point to abnormal or exaggerated response to the individual's intestinal bacteria as a mechanism of action for Crohn's.

c. Additional health concerns

Nanoparticles of silver, titanium dioxide, zinc and zinc oxide — materials now used in nutritional supplements, food packaging and food contact materials — have been found to be toxic to cells in test tube and animal studies.

In 2009, a team led by Roel Schins at the Environmental Health Research Institute in Düsseldorf, Germany, published research suggesting that some nanoparticles, including silicon and titanium dioxide, can induce DNA damage in human intestinal cells (Gerloff et al., 2009).

d. Wastewater and environmental concerns

The final disposition of nanomaterials and their entry into the environment is also of concern. Nanomaterials from products or food, such as leftover formula, can end up going down drains and arrive in wastewater treatment plants. Wastewater treatment plants (WWTPs) are concerned about nanomaterials because they do not behave the way relevant bulk materials behave. WWTPs are especially concerned about nano-metals because some metals — such as silver and copper — are more toxic to aquatic animals. These issues have been highlighted by various U.S. agencies/ associations (Tri-TAC, 2011; National Association of Clean Water Agencies (NACWA), 2015).

Preliminary environmental studies also suggest that these substances may be toxic to ecologically-important species such as water fleas (Bang et al., 2011). For more on environmental concerns, see the Friends of the Earth report *Tiny Ingredients, Big Risks.*

e. Occupational health and safety concerns

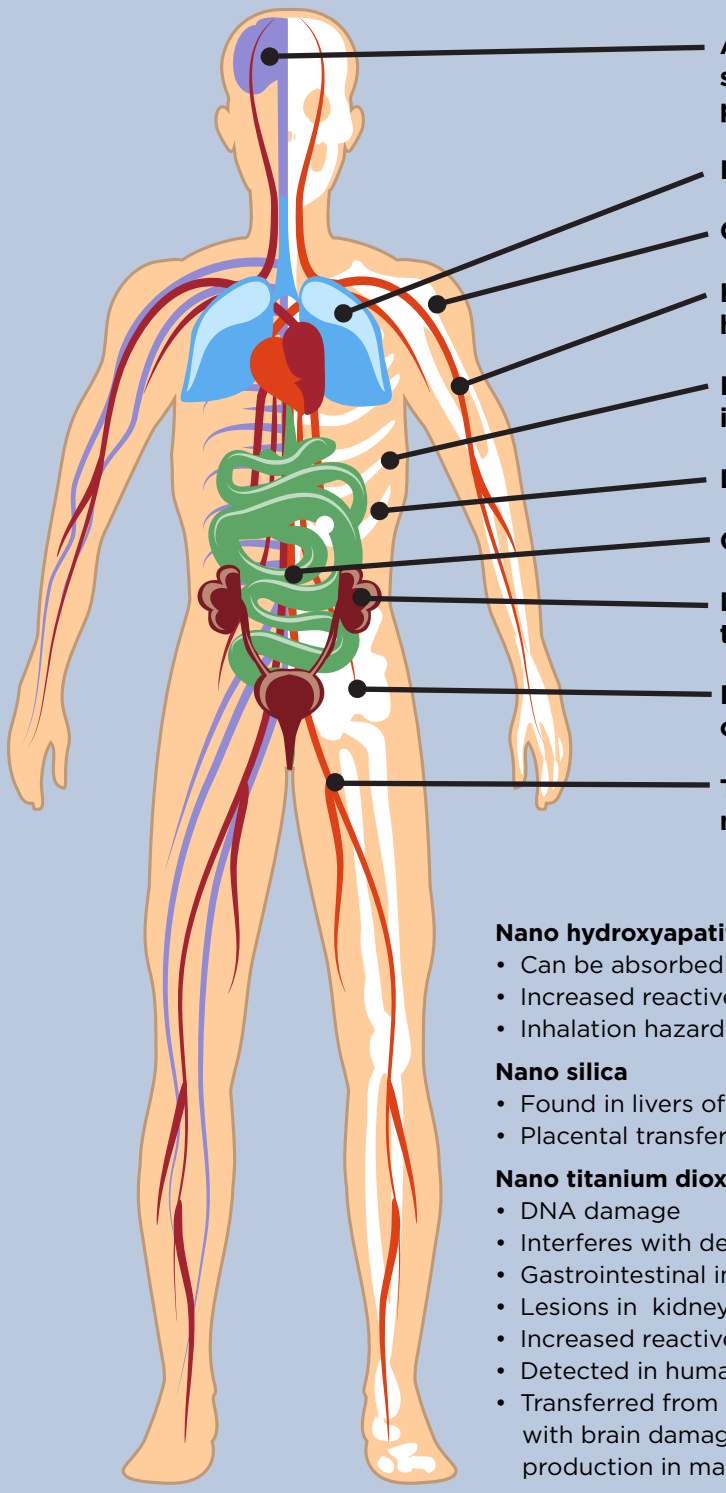
In the food sector, workers may come into contact with nanomaterials during production, packaging, transport and waste disposal of food, food packaging and agrochemicals (European Food Safety Authority (EFSA), 2009). However, in the absence of a mandatory registration, worker notification or product labeling, many workers may be unaware that they are handling nanomaterials or that they may need to use protective equipment. Additionally, it is not currently clear in the literature if existing Personal Protective Equipment (PPE) can protect individuals from nanoscale particles.

To date, there is very little data relating to the exposure of workers to nanomaterials. A number of nanomaterials used in the food industry, such as zinc oxide and titanium dioxide, have been shown to be harmful when inhaled, raising occupational health and safety concerns for workers handling these materials. The U.S. Occupational Safety and Health Administration (OSHA) has cautioned, "... certain inhaled nanoparticles may be deposited in the respiratory tract and may cause inflammation and damage to lung cells and tissues" (OSHA, 2013). OSHA has furthermore stated that, nanoscale TiO2 particles have higher mass-based potency than larger particles and that occupational exposure (by inhalation) to nanoscale TiO2 particles is considered a potential occupational carcinogen (OSHA, 2013).

Studies have also shown that nanomaterials can enter the bloodstream via the lungs, raising major occupational health and safety concerns (Oberdörster et al., 2005).

POTENTIAL HEALTH EFFECTS OF NANOPARTICLES FOUND IN BABY FORMULA

*Summary of scientific data**



Associated with brain damage, nerve system damage and reduced sperm production in male mouse offspring

Inhalation hazard

Can be absorbed by and enter cells

Highly mobile throughout body; detected in human blood, liver and spleen

Increased reactive oxygen species and inflammation in cells

DNA damage

Gastrointestinal inflammation

Lesions in kidney and liver of mice exposed to high oral dose

Interferes with defense activities of immune cells

Transferred from mother to offspring in mouse studies

Nano hydroxyapatite
- Can be absorbed by and enter cells
- Increased reactive oxygen species and inflammation in cells
- Inhalation hazard

Nano silica
- Found in livers of rats and mice after oral administration
- Placental transfer and fetal uptake

Nano titanium dioxide
- DNA damage
- Interferes with defense activities of immune cells
- Gastrointestinal inflammation
- Lesions in kidney and liver of mice exposed to high oral dose
- Increased reactive oxygen species and inflammation in cells
- Detected in human blood, liver and spleen
- Transferred from mother to offspring in mouse study; associated with brain damage, nerve system damage and reduced sperm production in male offspring

** Drawn from studies of nano hydroxyapatite, nano silicon and nano titanium oxide; not all impacts pertain to each nanoparticle. For complete details see report.*

5. Regulation of Nanotechnology

Research and regulation are not keeping up with the pace of commercialization of nanotechnologies. Yet, governments, scientists and scientific bodies such as the U.S. National Research Council have presented more than sufficient evidence to justify a proactive regulatory regime and a properly funded research program that will effectively target areas of greatest environmental and health concern.

a. Principles for the Oversight of Nanotechnologies and Nanomaterials

In response to mounting evidence of harm and the lack of government oversight, in 2007 a coalition of domestic and international advocacy groups, including Friends of the Earth, called for strong, comprehensive, oversight of the technology and its products and urged action based on eight principles: 1) a precautionary foundation, 2) mandatory nano-specific regulations, 3) health and safety of the public and workers, 4) environmental protection, 5) transparency, 6) public participation, 7) inclusion of broader impacts and 8) manufacturer liability. These demands were published as the *Principles for the Oversight of Nanotechnologies and Nanomaterials*, which was endorsed by more than 70 groups from six continents.

b. Nanomaterials Policy Recommendations

Responding to rising concern about manufacturers using unregulated nanomaterials in food, a coalition of advocacy groups in the U.S. and abroad, led by As You Sow, released *Nanomaterials Policy Recommendations* (As You Sow et al., 2015) for companies in food-related industries to assist them in avoiding or reducing the risks from nanomaterials in food products and packaging.

The recommendations urge companies to:

- Adopt a detailed public policy explaining their use of nanomaterials, if any;
- Publish a safety analysis for any nanomaterials being used;
- Issue supplier standards;
- Label all products that contain nanoparticles smaller than 500nm; and
- Adopt a hierarchy of hazard controls approach to prevent exposure of employees to nanomaterials.

The nanomaterials policy recommendation is accompanied by a fact sheet (As You Sow, 2015) to inform companies and consumers about the potential risks of nanomaterials. The goal of the policy is to provide a single set of recommendations for food manufacturers endorsed by groups working on nanomaterials policy issues to avoid confusion and multiple sets of recommendations. However, we recognize that voluntary measures do not fill the gaping hole left by a lack of regulation to guide industry and protect workers, public health and the environment.

c. Organic certifiers say no to nanotech

The largest organic certifiers in several countries have banned the use of engineered nanoparticles in food as part of their standards of organic production and processing, including the UK's Soil Association (Smithers, 2008), the Biological Farmers of Australia (Biological Farmers of Australia (BFA), 2012) and the Canada General Standards Board (Organic & Non-GMO Report, 2010).

d. Responsible regulation in the European Union

Regulators in the European Union (EU) have taken various steps to protect public health vis a vis nanotechnology. The European Parliament is negotiating a possible moratorium on novel foods containing nanomaterials (European Parliament, 2014). France, Belgium and Denmark have implemented mandatory registries for nanomaterials, and the EU has implemented a nanofood-labeling regime.

In relation to one of the nano-ingredients found in our study (nano-hydroxyapatite or nano HA) the European Commission, which is the main executive body of the European Union, states, "The Commission has concerns on the use of Hydroxyapatite in nano form because of the potential for nanoparticles of Hydroxyapatite to be absorbed and enter into the cells" (EU Scientific Committee on Consumer Safety (SCCS), 2014). In October of 2015, the EU Commission's Scientific Committee on Consumer Safety (SCCS) published an opinion on nano HA stating, "The available information indicates that nano-hydroxyapatite in needle form is of concern in relation to potential toxicity. Therefore, needle-shaped nano-hydroxyapatite should not be used in cosmetic products" (SCCS, 2015).

e. U.S. regulatory inaction

In stark contrast to the precautionary action being taken in the EU, the U.S. response has largely been one of regulatory inaction. The U.S. Food and Drug Administration (FDA) is charged with ensuring the

safety and security of our nation's food supply, yet the agency has not developed binding guidance for industry on the use of nanomaterials in food and consumer products.

U.S. consumers remain in the dark about the presence of nanomaterials in products they purchase. No product registry or labeling requirements are in place. The lack of established regulations allows foods with nano ingredients to remain on the market while the public unknowingly takes on potential health risks. It is important for U.S. consumers to know that manufacturers are not required to list nanomaterial ingredients on product packaging in the United States.

Friends of the Earth was unable to find any baby formula products in which include nanoparticles were listed ingredients, including the samples we found to contain nanoparticles via laboratory testing.

Governments, scientists and scientific bodies such as the U.S. National Research Council have presented more than sufficient evidence to justify a proactive regulatory regime and a properly funded research program that will effectively target areas of greatest environmental and health concern.

f. Demanding regulatory action: FOE joins forces to sue the FDA

In 2006, a group of eight non-profit organizations, including Friends of the Earth, submitted a citizens petition to the U.S. Food and Drug Administration demanding that the government formally recognize the inherent differences of nanomaterials and address their associated new risks to human health and the environment by regulating their use in consumer products. In response, the FDA took a number of preliminary actions including forming a task force, which issued a report and recommendations, holding multiple public meetings and workshops and publishing a number of FDA scoping documents and guidance.

However, by 2011, the FDA had still not issued binding regulations. In December 2011, the Center for Food Safety, along with Friends of the Earth and four other non-profit organizations, filed a lawsuit regarding the agency's failure to respond to their 2006 petition.

None of the baby formulas found to contain nanoparticles listed nano ingredients on the label. U.S. consumers remain in the dark about the presence of nanomaterials in products they purchase.

In stark contrast to the precautionary action being taken in the EU, the U.S. response has largely been one of regulatory inaction. The U.S. Food and Drug Administration (FDA) is charged with ensuring the safety and security of our nation's food supply, yet the agency has not developed binding guidance for industry on the use of nanomaterials in food and consumer products.

In its formal response to the lawsuit, FDA took steps in the right direction by acknowledging that there are differences between nanomaterials and their bulk counterparts and that nanomaterials have potential new risks and may require new testing.

In 2014, the agency finalized a voluntary, non-binding guidance for industry. In the guidance, FDA proposed classifying nanomaterials as food additives, which would require premarket testing and approval. The FDA states in its guidance that they "are not aware of any food ingredient…on the nanometer scale for which there are generally available data sufficient" to determine that the ingredient is Generally Recognized As Safe (U.S. FDA, 2014b).

In other words, FDA likely will not accept industry claims that nano-scale food substances can be assumed to be safe simply because their macro-scale counterparts are deemed to be safe. However, the agency continues to decline to enact mandatory regulations.

In alignment with FDA's 2014 guidance, Friends of the Earth believes that the nanoparticles we found in commercially available baby formulas must undergo premarket safety assessment and approval.

6. Research Priorities

Although sufficient data exists to inform precautionary action on nanotechnology, there is a pressing need for more research to understand, identify, assess, control and remediate potential impacts of nanomaterials.

In 2012, the U.S. National Research Council (NRC) set out an environment, health and safety research strategy for beginning to deal with the gigantic gaps in knowledge surrounding the environmental and human health impacts of nanomaterials. That research strategy became part of the National Nanotechnology Initiative in the U.S., in what was supposed to be an integrated, collaborative effort by many departments to ensure that the development of nanotechnology industries was done well. A year later, the NRC report, *Research Progress on EHS Aspects of Engineered Nanomaterials* (NRC, 2013) analyzed progress to date. Of the 20 indicators NRC used to assess progress, there has been little or no progress in 19. The report noted, "...despite increasing budgets for nanotechnology-EHS research and a growing number of publications, regulators, decision makers and consumers still lack the information needed to make informed public health and environmental policy and regulatory decisions" (NRC, 2013).

The U.S. President's Council of Advisors on Science and Technology, in its 2013 assessment of the National Nanotechnology Initiative, expressed concerns about "...a lack of integration between nanotechnology-related [environmental health and safety] research funded through the NNI and the kind of information policymakers need to effectively manage potential risks from nanoparticles" (Sargent, 2014). Additionally, the European Food Safety Authority has admitted that risk assessments for nano-products in food and feed will inevitably have significant uncertainties because testing methods and data on risk and exposure are missing (EFSA, 2008).

A 2013 report by the Food and Agriculture Organization of the United Nations and the World Health Organization further expresses the need to better understand the novel properties of nanoparticles, particularly pertaining to safety:

> Additional safety concerns may arise owing to the characteristic properties of nanomaterials that make them different from their microscale/macroscale counterparts. For example, the very high surface area of engineered nanomaterials has consequences that need to be considered in their risk assessment. Nanoparticles may interact with other substances present in the food matrix, and such effects and interactions of engineered nanomaterials need to be characterized. Understanding their fate in the environment is also important, as it may result in indirect human exposure (Food and Agriculture Organization of the United Nations and World Health Organization, 2013).

In relation to food and other products containing nanomaterials, there are significant gaps in our knowledge, including information on:

- The extent to which nanomaterials from packaging, surfaces and coatings migrate into foods.
- Where and how nanomaterials distribute in the human body following ingestion.
- The long-term chronic effects of ingesting nanomaterials, including impacts on sensitive and vulnerable populations.
- How nanomaterials interact with the human body and in the environment (European Environment Agency, 2013).
- How, where and in what quantities nanomaterials enter the environment (Royal Commission on Environmental Pollution, 2008).
- Once nanomaterials are released, how durable they are and the extent to which they are transformed in the environment (NRC, 2013; SRU, 2011)
- The fate, behaviour and ecotoxicity of nanomaterials throughout their life cycle; How to characterize, track and detect nanomaterials in complex environments (NRC, 2013).

7. Policy Recommendations

Friends of the Earth urges our govenment regulators to further investigate the safety of nanomaterials and establish manditory pre-market safety assessment and oversight of nanotechnology. We also demand greater accountability and transparency from food and consumer producers and retailers to allow consumers to make informed choices about this novel set of technologies.

If nanotechnology is to be developed safely, responsibly and transparently, there is an urgent need for further research and dissemination of information about its current uses and associated human and environmental health concerns to inform the scientific community, companies, policy makers, regulators and consumers. Friends of the Earth's vanguard study has helped to shed light on the use of engineered nanomaterials in baby formulas. Nevertheless, focused efforts by our government, industry and academia will be required in order to inform about the totality of engineered nanomaterial products already on the market.

Nanotechnology-enabled agricultural inputs and food ingredients continue to be developed and discussed in the scientific literature, yet the public is left in the dark about their use, while regulators stand idle in addressing the potential knowledge gaps and human and environmental health concerns. As we enter a new era of greater food awareness, public demand for healthy and sustainable food, and for transparency, is growing. People are demanding more information about the food they eat — what it contains, how it is produced, and how it may impact human health and the environment — so they can make informed choices about what they feed their families.

While independent and university scientists are hard at work creating methodologies and systems to detect engineered nanoparticles, government regulators should deny these products access to the market while we learn more about their safety, and how to properly manage them to protect human health and the environment.

Friends of the Earth believes future non-governmental organization, academic and especially government initiatives to further investigate the use and safety of engineered nanoparticles in baby formulas and other commercially available foods and products is of utmost importance to ensure the safe and sustainable development of nanotechnologies.

Given the potentially serious health and environmental risks and social implications associated with nanofoods, especially products created for infants, Friends of the Earth is calling for a moratorium on the further commercial release of food products, food packaging and coatings, food contact materials and agrochemicals that contain engineered nanomaterials until nanotechnology-specific safety and labeling laws are established and the public is involved in decision-making.

Given the potentially serious health and environmental risks and social implications associated with nanofoods, especially products created for infants, Friends of the Earth is calling for a moratorium on the further commercial release of food products, food packaging and coatings, food contact materials and agrochemicals that contain engineered nanomaterials until nanotechnology-specific safety and labeling laws are established and the public is involved in decision-making.

For additional recommendations, please refer to *Principles for the Oversight of Nanotechnologies and Nanomaterials* (CFS, 2007).

a. What government must do:

Enact a moratorium on new commercial nanotech products

Government regulators should deny products produced with nanomaterials access to the market until they determine how to properly assess and manage them to protect human health and the environment.

Assess safety of and recall baby formulas with nanoparticle ingredients

Friends of the Earth recommends that the FDA conduct a thorough review of the nanoparticle ingredients found in baby formulas. The agency must, in the meantime, use its authority to enforce a manufacturer recall of baby formulas containing engineered nanoparticles as these ingredients may put human health at risk.

Regulate nanomaterials as new substances

All deliberately manufactured nanomaterials must be subject to rigorous nano-specific health and environmental impact assessment and must be demonstrated to be safe prior to approval for commercial use in foods, food packaging, food contact materials, agricultural applications or other consumer products.

Extend the size-based definition of nanomaterials to 500 nm

All particles up to 500 nm in size must be considered to be "nanomaterials" for the purposes of health and environment assessment given the early evidence that they may pose health risks similar to particles less than 100 nm in size which have to date been defined as "nano."

Protect workers

- The Occupational Health and Safety Administration should adopt nano-specific regulations to protect workers from and inform them of potential exposure.
- Research on occupational exposure and personal protective devices in the workplace should be a priority.

Ensure transparency in safety assessment and product labeling

- All relevant data related to safety assessments and the methodologies used to obtain them must be placed in the public domain.
- All manufactured nano-ingredients must be clearly indicated on product labels to allow members of the public to make an informed choice about product use.
- The presence of nanomaterials must be disclosed to workers and other downstream users along the supply chain.
- Public involvement in decision-making is required.

b. What industry must do:

Recall formula containing nanomaterials

Manufacturers should remove all baby formulas containing nanoparticles from store shelves until the safety of these ingredients can be substantiated and appropriately regulated by the FDA.

Remove nanomaterials from product formulas

All baby formula and food manufacturers should review the ingredients contained in their products to ensure they are free from manufactured nanomaterials; this may involve inquiries with third party ingredient suppliers.

Create nanomaterial policies

- Companies should create clear policies to avoid the use of engineered nanomaterials in their products until nanotechnology-specific regulation is put in place to protect the public, workers and the environment from potential new hazards associated with nano-toxicity.
- Manufacturers should refer to the *Nanomaterials Policy Recommendations* published by a coalition of domestic and international advocacy groups, including Friends of the Earth, to help inform companies and consumers about the potential risks of nanomaterials (As You Sow et al., 2015).

Ensure transparency in the supply chain

- If companies continue to use nano-ingredients, they must be clearly indicated on product labels, allowing members of the public to make informed choices about product use.
- Companies producing baby formulas containing nanomaterials must create a registry of potential side effects as reported by consumers (parents of babies consuming these products). This should be modeled after the registries that pharmaceutical companies are required to create which both receive reports of side effects of new products and incorporate this information into required consumer education inserts at point of sale.

c. What concerned parents, individuals and organizations can do:

Until government and companies manage nanotechnology in a responsible and transparent manner, there are steps we can take to protect our health.

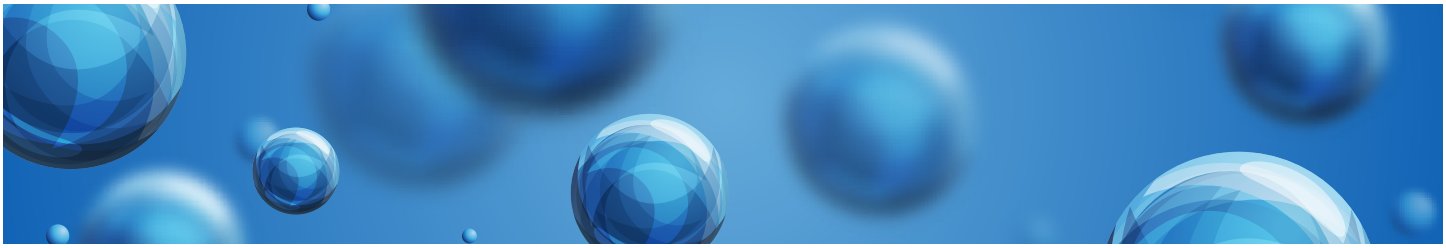
Avoid foods that potentially contain nanomaterials

- Breastfeed when and if possible.
- Eat fresh food when and if possible. Processed and packaged foods are more likely than fresh foods to be a source manufactured nanoparticles.

Hold government and industry accountable

- Write to your local representatives and members of regional, state and federal government requesting their support for a moratorium on the use of all nanotechnology in the food sector. Demand that governments regulate and label food, food packaging and agricultural products that contain manufactured nanomaterials before allowing any further commercial sales.
- Ensure that food and agricultural manufacturers take seriously public concerns about nanofoods. Contact the manufacturers of the baby formulas or foods you consume often and ask them about what steps they are taking to keep unsafe, untested nanomaterials out of the food they sell.

Visit our website to learn more about nanotechnology, take action and to support our efforts to create a safe, just, resilient and sustainable food system. Friends of the Earth-United States http://www.foe.org/nanotechnology



8. APPENDICES

Appendix A: Methodology

Friends of the Earth commissioned independent laboratory testing of baby formulas with a world-class nanotechnology research facility at the Arizona State University (ASU). This study was lead by Paul Westerhoff PhD, PE, BCEE, Professor, Ira A. Fulton Schools of Engineering at Arizona State University, Dr. Robert Reed (Postdoctoral Researcher at ASU) and Jared Schoepf (PhD candidate at ASU). Additional details about the study are included in the Analysis Report prepared by the laboratory.

Friends of the Earth tested a selection of six baby formula samples gathered from the following three retailers in the San Francisco Bay Area: Walgreens in Berkeley and Safeway in Berkeley and Oakland. We encourage the replication of our study and additional analysis geared towards learning more about the presence of engineered nanoparticles in baby formula and other consumer products.

Sample preparation details

The foods (~0.125 g each) were suspended in 40 mL ultrapure water and sonicated for 30 minutes to suspend particles. These samples were centrifuged at 15,000 G for 15 minutes to settle any particles present. The organics-rich supernatant was poured off, leaving a pellet of particulate matter in the centrifuge tube. This was re-suspended in 20 mL ultrapure water and sonicated for five minutes, then 100 uL volumes were pipetted onto a copper/lacey carbon transmission electron microscopy grid and allowed to dry. Microscopy was performed on a Philips CM200 transmission electron microscope with energy dispersive spectroscopy. Mean particle diameter was measured manually with ImageJ software. Particle number size distributions were developed and the percentage of particles less than 100 nm in width determined.

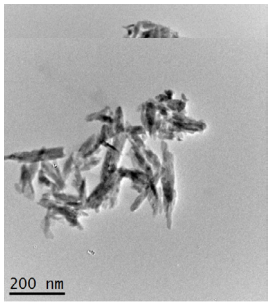
The detection of nanoparticles is a complex matter requiring state-of-the-art, experimental and costly devices and techniques, especially when attempting to quantify or characterize engineered nanoparticles in a complex matrix such as baby formula. The lack of standards and internationally recognized measurement methods coupled with a lack of transparency from the nanotechnology industry, reinforced by the lack of U.S. regulation of nanotechnology, creates significant challenges to understanding where engineered nanoparticles are being used.

Advanced analytical methods were employed to detect nanoparticles in the baby formulas tested. The samples were tested by transmission electron microscopy (TEM) and energy dispersive X-ray detection (EDX), including centrifugal ultrafiltration of the Gerber® sample prior to TEM to ensure that the crystal structures were not "artifacts" of sample drying.

EDX elemental peak readings for the Gerber® 'Gentle' formula suggested the nanostructures observed contained both Calcium and Phosphorous. The EDX reading combined with a comparison of similar electron microscopy images suggest the formula likely contains nano hydroxyapatite (nano HA). Similar readings and conclusions were also made for the Enfamil™ and Well Beginnings ™ baby formula samples. To confirm the presence of nano HA in the formulas, two food grade hydroxyapatite products were analyzed by TEM and EDX to find out if the hydroxyapatite (HA) formed in the sample preparation process for TEM or if it is an additive to the baby formula. The sample preparation was maintained the same as with all six of the baby formulas. One food-grade reference sample was composed solely of needle-like HA (Product 1) while the other sample had majority spherical-shaped HA (Product 2). It was concluded that the sample preparation process does not solely form HA needle-like structures. The analysis provides positive confirmation that detected HA in baby formulas was likely added, rather than an artifact of any sample handing.

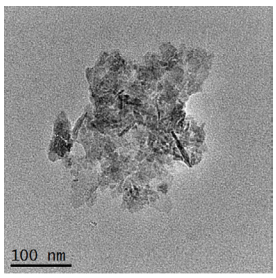
TiO2 was *tentatively* identified using a scanning electron microscope (SEM) in the Similac® Advance® OptiGRO™ (liquid) product, though after purchasing a second sample several months later and using a different separation process and transmission electron microscopy (TEM) analysis, the presence of TiO2 could not be confirmed.

Summary of reference food grade hydroxyapatite



Hydroxyapatite Food-Grade Product 1

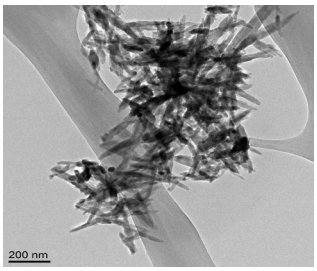
- 99% pure food-grade product purchased from USA manufacturer (American Elemental)
- Needle-like hydroxyapatite structures dominated the product

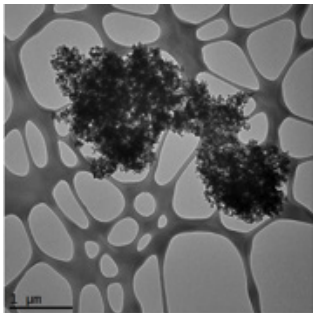
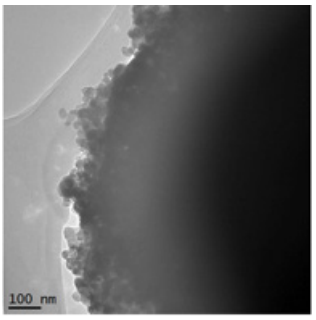
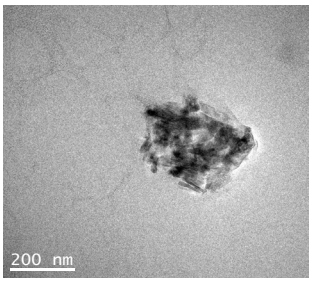
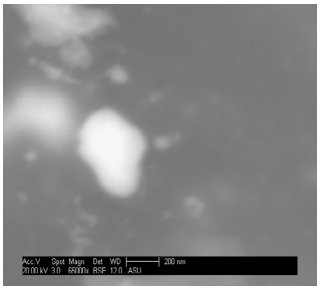


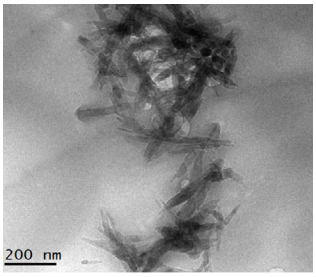
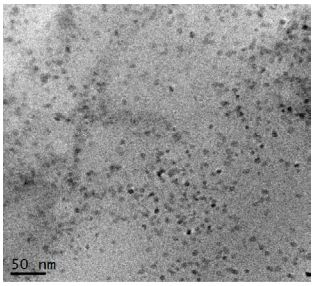
Hydroxyapatite Food-Grade Product 2

- Dietary supplement purchased from USA manufacturer (NOW® Foods) Calcium Hydroxyapatite
- Spherical-shaped hydroxyapatite dominated the product

Appendix B: Results summary

Baby formula brand and purchase location	Laboratory analysis image of nanoparticles (TEM/EDS)	Nanoparticles found and particle size	Ingredient uses	Health concerns
Gerber® Good Start® Gentle Purchased at Safeway® (Berkeley, CA) 		Nano-hydroxyapatite (nano HA) Average individual particle size of 28 ± 7 nm (width) 237 ± 119 nm (length)	Nano HA is most likely a calcium source for the formula. It can also be used as a stabilizer	The European Union has provided evidence in their SCCS opinion that needle-like nano-hydroxyapatite is potentially toxic, could be absorbed and enter cells and should not be used in cosmetics (SCCS, 2014; SCCS, 2015). Some chemical company material safety data sheet (MSDS) list hydroxyapatite as an inhalation hazard and further cite the lack of toxicology studies available (Sigma-Aldrich, 2008; Merz NA, Inc., 2015).

Baby formula brand and purchase location	Laboratory analysis image of nanoparticles (TEM/EDS)	Nanoparticles found and particle size	Ingredient uses	Health concerns
Gerber® Good Start® Soothe Purchased at Walgreens (Berkeley, CA) 	 (SiO2)  (TiO2)	Nano titanium dioxide (TiO2) and silicon dioxide (SiO2) (limited amount of particles detected) Particles under 100 nm	TiO2 is a brightener or whitener for food and beverage products, anti-caking agent SiO2 is used as a 'trickle and flow' aid in powdered food products, as a clearing agent in beer and wine, as a food additive (amorphous silicon found to be nano) and as a food coating	Studies show that titanium dioxide can damage DNA (Trouiller et al., 2009), disrupt the function of cells, interfere with the defense activities of immune cells and, by adsorbing fragments of bacteria and 'smuggling' them across the gastro-intestinal tract, can provoke inflammation (Ashwood et al., 2007; Donaldson et al., 1996; Dunford et al., 1997; Long et al., 2006; Lucarelli et al., 2004; Wang et al., 2007b). A study using pregnant mice found that transfer nanoparticles of titanium dioxide to their offspring. This resulted in brain damage, nerve system damage and reduced sperm production in male offspring (Takeda et al., 2009). See Similac® Advance® OptiGRO™ summary results for more information about SiO2 health concerns.
Enfamil™ Purchased at Safeway® (Oakland, CA) 		Mixture of needle-like and non needle-like nano-hydroxyapatite (nano HA) Average particle size of 11 nm (width) and 75 nm (length)	Nano HA is most likely a calcium source for the formula. It can also be used as a stabilizer	The European Union has provided evidence in their SCCS opinion that needle-like nano-hydroxyapatite is potentially toxic, could be absorbed and enter cells and should not be used in cosmetics (SCCS, 2014; SCCS, 2015). Some chemical company material safety data sheet (MSDS) list nano hydroxyapatite as an inhalation hazard and further cite the lack of toxicology studies available (Sigma-Aldrich, 2008; Merz NA, Inc., 2015).
Similac® Advance® OptiGRO™ (liquid) Purchased at Walgreens (Berkeley, CA) 		Titanium dioxide nanoparticles (laboratory results inconclusive) Particle sizes between 16 and 530 nm, average particle size is unknown	TiO2 is a brightener or whitener for food and beverage products, anti-caking agent	Studies show that titanium dioxide can damage DNA (Trouiller et al., 2009), disrupt the function of cells, interfere with the defense activities of immune cells and, by adsorbing fragments of bacteria and 'smuggling' them across the gastro-intestinal tract, can provoke inflammation (Ashwood et al., 2007; Donaldson et al., 1996; Dunford et al., 1997; Long et al., 2006; Lucarelli et al., 2004; Wang et al., 2007b). A study using pregnant mice found that transfer nanoparticles of titanium dioxide to their offspring. This resulted in brain damage, nerve system damage and reduced sperm production in male offspring (Takeda et al., 2009).

Baby formula brand and purchase location	Laboratory analysis image of nanoparticles (TEM/EDS)	Nanoparticles found and particle size	Ingredient uses	Health concerns
Well Beginnings™ Advantage® Purchased at Walgreens (Berkeley, CA) 		Needle-like nano-hydroxyapatite (nano HA) Average size 28 ± 5 nm (width) 160 ± 30 nm (length)	Nano HA is most likely a calcium source for the formula. It can also be used as a stabilizer	The European Union has provided evidence in their SCCS opinion that needle-like nano-hydroxyapatite is potentially toxic, could be absorbed and enter cells and should not be used in cosmetics (SCCS, 2014; SCCS, 2015). Some chemical company material safety data sheet (MSDS) list nano hydroxyapatite as an inhalation hazard and further cite the lack of toxicology studies available (Sigma-Aldrich, 2008; Merz NA, Inc., 2015).
Similac® Advance® OptiGRO™ (powder) Purchased at Walgreens (Berkeley, CA) 		Nano silicon dioxide (laboratory results inconclusive) Average diameter of 7 ± 1 nm	Used as a 'trickle and flow' aid in powdered food products, as a clearing agent in beer and wine, as a food additive (amorphous silicon found to be nano) and as a food coating	Nano silica has been found in the livers of rats and mice after oral administration. In vitro studies show a significant percentage of the nano silica remains undissolved and that "the presence of undissolved nano silica particles in the gut in vivo is considered likely" (Dekker et al., 2013; SRU, 2011). Animal studies have shown placental transfer and foetal uptake of silica. Scientists have warned that the enhanced sensitivity of the foetus may mean that even low doses of nanomaterials may cause adverse effects (Correia et al., 2015).

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