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Technical report:

HENVINET

Evaluation questionnaire - Causal chain for nanoparticles

Aileen Yang[1)] and Alena Bartonova[1)], Editors

Authors:
Qamar Rahman[2)], Suchi Smita[2)], Shailendra K. Gupta[2)]

[1)] Norwegian Institute for Air Research, Kjeller, Norway
[2)] Integral University, Lucknow, India

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Introduction

With your help we will evaluate the quality of the scientific knowledge of various aspects of the cause-effect relationship between nanoparticles, Environment and Human health.

The goal is to identify knowledge gaps and areas of disagreement between you and your expert colleagues, as well as areas of agreement. Ultimately, the aim is to discuss the implications of these for policy and research.

The evaluation consists of two separate parts. In part A you will be asked to comment on the completeness and structure of a diagram illustrating our current understanding of the cause effect relationship of intentional and unintentional nanoparticles on environment and their subsequent impact on human health. In part B you will be asked to give comments and express your confidence in scientist's ability to predict the magnitude of a disease burden that are expected to occur as a result of release of nanoparticles in the environment.

We ask for your considered opinion based on the quality of your scientific work and trust your broad experience in the field will help achieve an understanding of the issues discussed here.

Questionnaire replies will be considered alongside a thorough review of the literature on this issue. These will be used to provide recommendations to policy makers. Content of the literature review are provided as background information before each question section.

If you have any questions or concerns, please contact Dr. Qamar Rahman (qamar_15@sify.com) .

We appreciate your participation and thank you for your time.

Prelude

Thank you very much for participating in this study of the HENVINET project. Before beginning, we would ask that you provide some basic information about yourself.

- Name:_______________________________________
- Email address: _______________________________________
- Institutional affiliation: _______________________________________
- Disciplinary Background:_____________________________________
- 5 keywords describing your area of expertise:

1.______________ 2.______________ 3._______________ 4._____________
5.______________

PART A: Effect of Nanoparticles on Environment & Health: Causal diagram

As a growing and widely applied science, nanotechnology has a global socioeconomic value, with applications ranging from electronics to biomedical uses.
Because of their extremely small size (less than 100 nm) and the resultant very high surface to volume ratio, engineered nanoparticles (ENP) usually display an enormously elevated reactivity potential. Engineered NPs can be assigned to a transitional range between single atoms or molecules and bulk material. The physicochemical features of ENP differ substantially from those of their respective bulk materials.

On one hand, the new features of designed ENP's provide them with so far unprecedented technical capabilities and sometimes enable them to perform absolutely novel tasks in technology and science, unfortunately, on the other hand, just the same new qualities can concurrently also include undesired intrinsic features, which sometimes lead to harmful interactions with exposed organisms.

At the moment it is unclear whether the benefits of nanotech outweigh the risks associated with environmental release and exposure to nanoparticles. There are concerns that nanoparticles can also lead to a new class of environmental hazards. Till date, few studies have investigated the toxicological effects of direct and indirect exposure to nanomaterials released in the environment; however no clear guidelines exist to quantify these effects. Two independent studies have shown that certain carbon nanotubes if inhaled, can cause the onset of mesothelioma – cancer previously thought to be only associated with asbestos exposure (Poland et al. 2008; Takagi et al. 2008). As the nanoparticles produce in bulk are widely released in the environment and may also show a similar toxicological behavior with long-term exposures. Both industry and regulatory bodies are aware of the potential risk of nanoparticles but due to limited information, the issues of nanoparticles have a low priority among the regulatory bodies at the moment. Although it is not possible to generalize the risk of nanoparticles because of differences in size, surface properties, shape, chemical composition etc., yet, we urgently need to develop and design guidelines for the safe use of engineered nanoparticles and raise our concern about the harmful impact of nanoparticles released intentionally / unintentionally in the environment and their impact on human health (Papp et al., 2008).

Background:

Natural NPs have existed in the environment since the beginning of Earth's history. They influence lots of environmental processes because of their large surface area. Naturally occurring as well as unintentionally generated ambient NPs are quite heterogeneous in size and can be transported over thousands of kilometers and remain suspended in air for several days. It is estimated that around 50,000 kg / year of such NPs are being produced through unintended anthropogenic sources such as diesel-exhaust and other combustion-related processes (Borm et al. 2006).

With the advancement of industrial processes and nanotechnology, large number of ENP are been manufactured and it is inevitable that during their use, ENP are released in the air, water and soil knowingly or unknowingly. Most of these ENP are made up of carbon, silicon, titanium, metal or metal oxides and are believed to adversely effect the environment and human health directly or indirectly (Powell and Kanarek 2006). Some investigations have been already reported the accumulation of ENP in various environmental samples such as blue green algae, fish and other aquatic organism as well as soil and sediments.

To identify knowledge gaps and potential agreement or disagreement on the effect of nanoparticles on various environmental processes and their impact on human health, a causal diagram, based on current understanding of the various toxicity reports of ENP is developed. The diagram is developed on the basis of latest toxicity reports and review articles available. The confidence and correctness of causal effect diagram is subjected to the evaluation by various experts from the area.

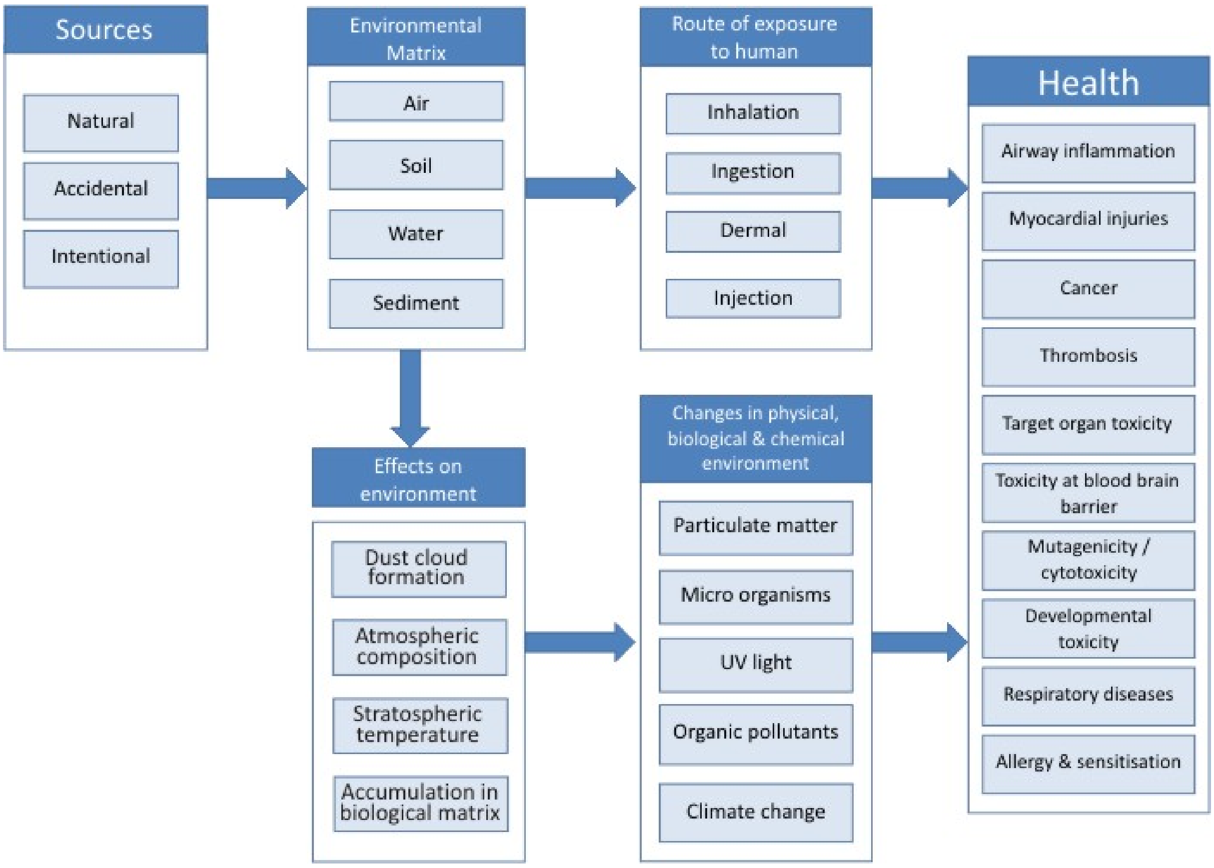

Figure 1: Generalized causal effect diagram showing the impact of ENP on human health.

Figure 1 illustrates a generalized causal effect diagram showing the impact of ENP released in the environment and their impact on human health. Bulk of the nanoparticles released in the environment through various natural and accidental processes although in many industrial settings, ENP knowingly released in the environment. These ENP may impact human health either by direct exposure or by change in the various environmental processes.

Evaluate the completeness of the diagram by answering the following questions.

1. Does the diagram take into account all of the important environmental processes affected by the release of NPs from various sources? If no, please explain.

2. Are the different causal relationships in the diagram adequately structured? If no, please explain.

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3. Are there any unnecessary parameters shown in the diagram that could be deleted? If yes, please explain.

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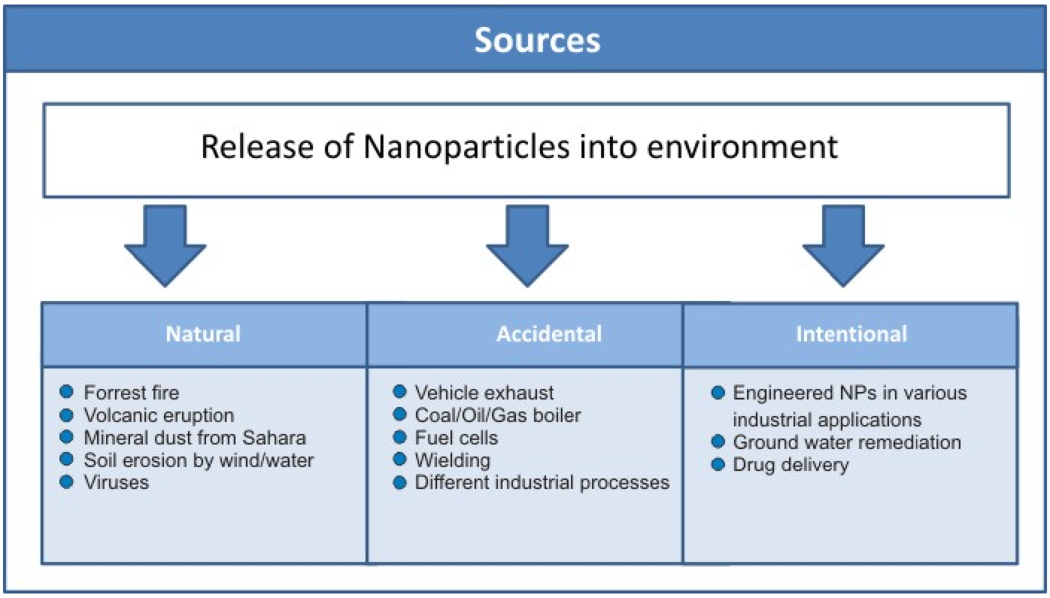
PART – B: Evaluation of individual model parameters

B1. Sources of Nanoparticles in the Environment



Nanoparticles have existed in the environment since the beginning of earth's history. Natural NPs are formed during forest fire, volcanic eruptions, in most natural water, soil and sediments etc. These natural NPs are generated by wide variety of geological and biological processes.

NPs are unknowingly released in the environment during various anthropogenic processes, mostly industrial and mechanical. These NPs are hetrogenous in nature and therefore it is difficult to measure the impact on human health in a simple way. Vehicle exhaust is the major source of anthropogenic accidental nanoparticles in the environment. The unfiltered exhaust gases from diesel engines contain large quantities of potentially harmful nanoparticles from the incomplete combustion of fuel. Even in the fireplace at home, fullerenes like Buckyballs

or Buckytubes are formed when wood is burned. In industrial process coal, oil, gas boilers releases tones of nanoparticles unintentionally (Oberdörster et al. 2005).
In various industrial settings, engineered nanoparticles are intentionally released in the environment and thus causing serious threats to environment and human health. ENP are homogenous in nature and are broadly categorized based on their chemical composition or morphological characteristics. Among metal oxides TiO2, Fe-oxides, SiO2, ZnO are few (Powell and Kanarek 2006). Use of metal oxides nanoclay, nanotubes and nanospheres are well known to all of us. Some of the areas where ENP are intentionally used are ground water remediation; biomedical uses; energy production; cosmetics; textiles; electronics etc.

Evaluate the completeness of the diagram by answering the following questions.

1. Does the diagram take into account all of the important sources of nanoparticles in the environment? If no, please explain.

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2. Are the categories of NPs present in the environment adequately structured in the diagram? If no, please explain.

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3. What is your level of confidence in the current ability of scientists to quantify emissions from the natural sources of ENP into the environment, represented in the above diagram?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

4. What is your level of confidence in the current ability of scientists to quantify accidental release of ENP into the environment, represented in the above diagram?

(Insert a checkmark in the appropriate box)

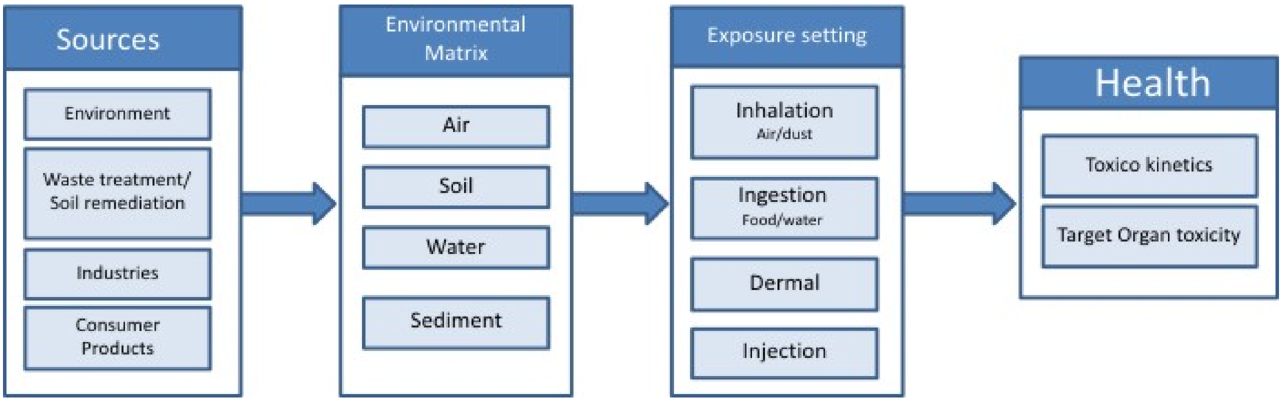
Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

5. What is your level of confidence in the current ability of scientists to quantify intentional release of ENP in the environment, represented in the above diagram?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

B2. Effect of ENP on Human – Part 1



NPs are likely to enter the environment for several reasons. They are produced by tons, and any material produced in such mass quantities is likely to reach the environment from manufacturing effluent or from spillage during shipping and handling. They are being used in personal-care products such as cosmetics and sunscreens and can therefore enter the environment on a continual basis from washing off of consumer products. They are being used in electronics, tires, fuel cells, and many other products, and it is unknown whether some of these materials may leak out or be worn off over the period of use. They are also being used in disposable materials such as filters and electronics and may therefore reach the environment through landfills and other methods of disposal.

Evaluate the completeness of the diagram by answering the following questions.

1. Does the diagram adequately describe the main pathways of exposures of humans to ENP? If no, please explain.

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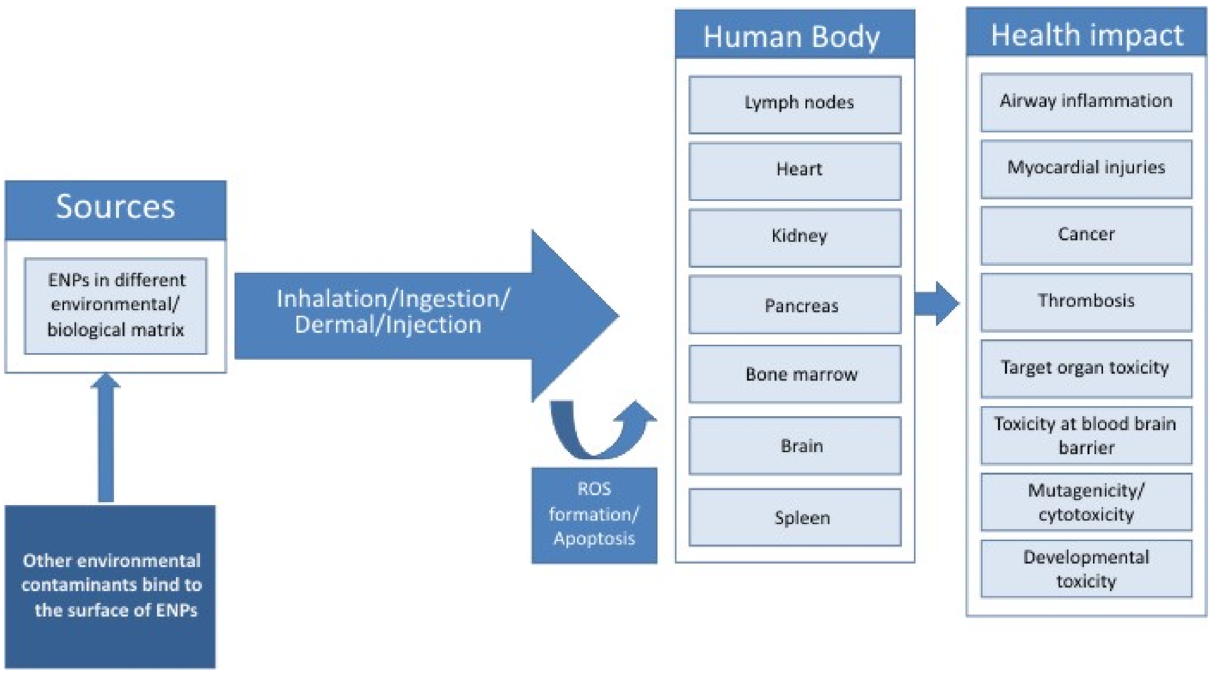
2. What is your level of confidence in the current ability of scientists to predict the sources and route of exposure of ENP to human, represented in the above diagram?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

B3. Effect of ENP on Human – Part 2



It has been suggested that inhaled nanoparticles are likely to evade phagocytosis, penetrate lung tissue, reaching interstitial spaces and to blood circulation. At the end ENPs reach sensitive target sites such as lymph nodes, spleen, heart, kidney, liver, pancreas, bone marrow and brain. Then cell membrane penetration and particle accumulation in diverse cellular organelles (e.g. mitochondria) can finally lead to injurious responses within the crucial target organs. Many injurious responses are attributed to particle-associated oxidative stress causing inflammation, cytotoxicity, malignancy etc.

Evaluate the completeness of the diagram by answering the following questions.

1. Does the diagram cover the main mechanisms of toxicity of NPs in human body? If no, please explain.

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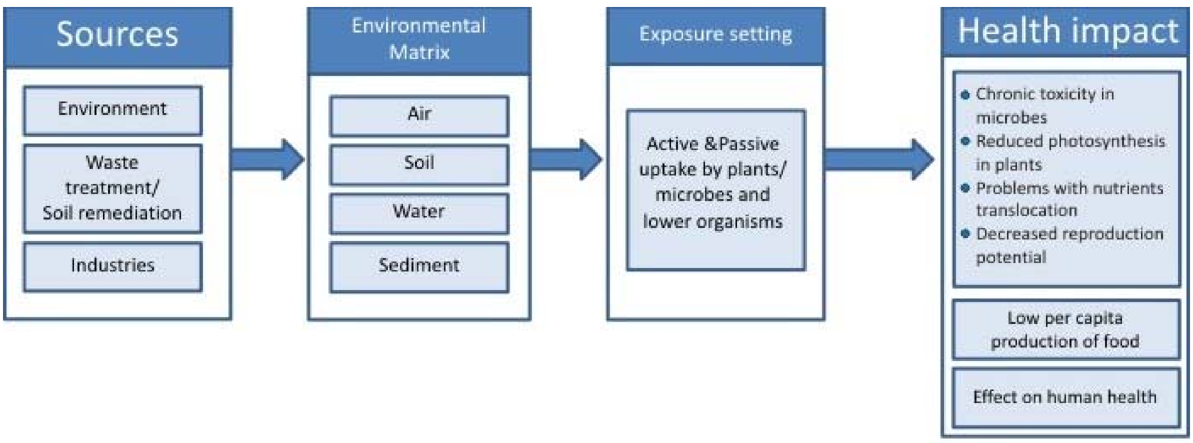
2. What is your level of confidence in the current ability of scientists to predict changes in endpoint toxicity by increase exposure to nanoparticles from various routes?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

B4. Effect of ENP on plants, microbes and other lower organism



It is inevitable that, during their use, engineered NPs will be released into the soil and waters and increase the load of NPs in different environmental matrixes. It is therefore increasing

concern over the potential impact of ENP in the environment on aquatic and terrestrial organism. Once released in the environment ENP entered in the plants and other microorganism by active or passive uptakes. Number of reports already been published where the ecotoxicological effects of variety of ENP are shown. In the work carried out by Hoecke *et al.,* 2009, Cerium dioxide nanoparticles (CeO2 NPs) shows chronic toxicity in unicellular green alga *Pseudokirchneriella subcapitata* (EC10s between 2.6 and 5.4 mg/L) and interestingly, chronic toxicity increases with the decrease in the size of nanoparticles.
Silver nanoparticles are shown to exert considerable toxicity in *C. elegans* and resulted in decreasing reproduction potential. Roh *et al.,* 2009, also showed the increased expression of the superoxide dismutase-3 (sod-3) and abnormal dauer formation protein (daf-12) with 0.1 and 0.5 mg/L of Ag NPs exposures.

In many report on plant toxicity, ENP are shown to affect photosynthesis and respiration. Studies have revealed relationships between high concentrations of some ENP and reduced plant growth. Navarro *et al*. (2008) reported that indirect toxic effects due to ENP accumulations include increased cell weight (affecting algae's ability to float) and reduced fertility of seaweeds.

Nanomaterials could impair the function or reproductive cycles of earthworms which play a key role in nutrient cycling that underpins ecosystem function (Scott-Fordsmand et al. 2008). Recent reports show the impact of naonomaterials on crops also. Carbon nanomaterials diminish rice yields and make wheat more vulnerable to other pollutants. (Lin *et al.* 2009, Wild and Jones 2009). Thus nanoparticles are one of the major concern of low per capita food production that may affect human health.

Evaluate the completeness of the diagram by answering the following questions.

1. What is your level of confidence in the current ability of scientists to predict changes in photosynthesis rate in plants as a consequence of changes in NP exposures?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

2. Does the diagram properly link the major consequences in changes in exposure to NPs and changes in plants/microbes and lower organisms? If no, please explain.

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3. What is your level of confidence in the current ability of scientists to predict the role of ENP in ecotoxicity, represented in the above diagram?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

4. What is your level of confidence in the current ability of scientists to predict the role of ENP in nutrient translocation?

(Insert a checkmark in the appropriate box)

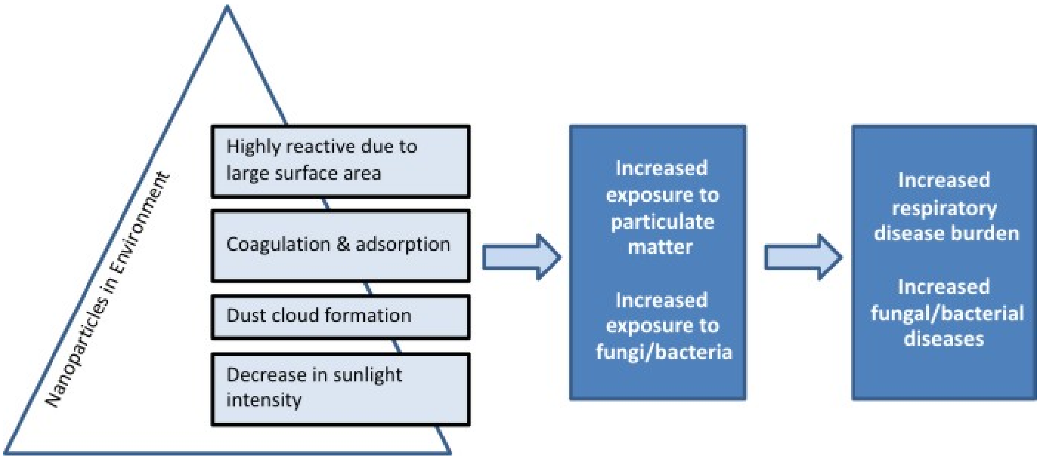
Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

5. What is your level of confidence in the current ability of scientists to predict role of ENP in decrease in per capita food production?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

B5. Effect of ENP on Dust clouds formation and Decrease in sun light intensity



Nanoparticles are thought to play important role in dust-clouds formation. Nanoparticles released in the environment coagulate to form dust cloud.

The regional haze, known as atmospheric brown clouds, contributes to glacial melting, reduces sunlight, and helps create extreme weather conditions that impact agricultural production, according to the report commissioned by the U.N. Environment Program. The pollution clouds also reduced the monsoon season in India. The weather extremes may have also played a part in reduced production of key crops such as rice, wheat and soybean.

Researchers led by Dr Orjan Gustafsson from the University of Stockholm in Sweden announced in Science that 70 percent of the brown clouds over South Asia are made up of soot from the burning of biomasses, largely wood and animal dung used for cooking and mainly contain particulate matters from unprocessed fuel and carbon nanoparticles (Gustaffson *et al.* 2009).

Impact on Himalayan Glaciers
The Himalayan glaciers provide the source of many of Asia's great rivers, with millions of people depending on them for food and water. Because Asian brown clouds increase atmospheric heating these glaciers are in retreat for the past number of decades. Asian brown clouds carry large amounts of soot and black carbon which are deposited on the glaciers, allowing them to absorb more of the sun's heat and melt quicker.

Asian brown clouds impact on Agriculture
Dimming induced by atmospheric brown clouds is considered the major cause of the changing pattern of rainfall in Asia, with decreasing rainfall in some parts while other parts experience intense floods. Asian brown clouds are interfering with centuries old monsoon patterns with disastrous consequences for food production. The large concentration of ozone in atmospheric brown clouds could decrease crop yields by as much as 20%.

Health Effects of Asian Brown Cloud
According to the UNEP report a large part of the aerosol particulars that make up atmospheric brown clouds are the result of incomplete combustion of fossil fuels and biofuels. The health impact of these particles is an increase in cardiovascular effects, pulmonary illnesses and

chronic respiratory problems. The report estimates that in India and China alone, Asian brown clouds result in over 330,000 excess deaths per year.

Evaluate the completeness of the diagram by answering the following questions.

1. Does the diagram adequately capture the role of Nanoparticles in dust clouds formation? If no, please explain.

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2. What is your level of confidence in the current ability of scientists to predict formation of dust clouds in relation to releases of bulk ENP in the environment?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

3. What is your level of confidence in the current ability of scientists to correlate the effect of brown clouds on Himalayan glaciers?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

4. What is your level of confidence in the current ability of scientists to correlate the effect of brown clouds on agriculture?
(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

5. What is your level of confidence in the current ability of scientists to correlate the effect of brown clouds on human health?
(Insert a checkmark in the appropriate box)

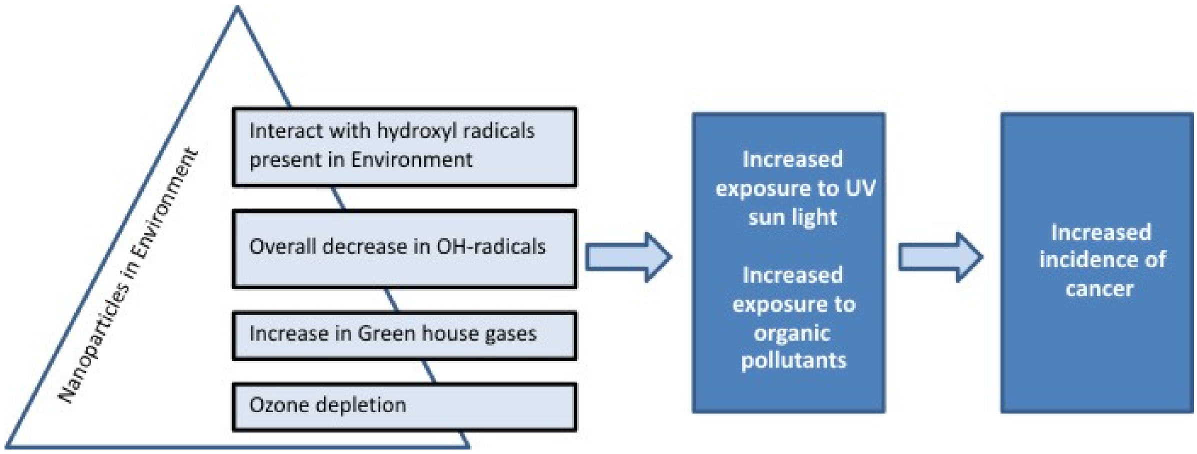
Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

6. What is your level of confidence in the current ability of scientists to predict changes in dust clouds formation and sun light intensity, with changes in ENP releases?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

B6. Effect of ENP on environmental hydroxyl radicals concentration and Ozone depletion



The hydroxyl radical, which is one of the most reactive free radicals in the environment, plays an important role in the photochemical degradation of natural organic matter and organic pollutants. Nanoparticles, being very reactive immediately bind with hydroxyl radicals and ultimately result in the overall reduction of hydroxyl radicals in the environment. As hydroxyl radical is strong oxidant and cleanup environment by degrading pollutant, its reduction is responsible for increase in green house gases which are ultimately responsible for ozone layer depletion and cause severe environmental damage that is responsible for various type of cancer in human and animals.

Evaluate the completeness of the diagram by answering the following questions.

1. Are there all important mechanisms of the effect of ENP on decrease OH radicals concentration listed? If no, please explain.

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2. Are there all important processes of how ENP influences the ozone depletion correctly depicted in the diagram? If no, please explain.

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3. What is your level of confidence in the current ability of scientists to predict the changes in ozone depletion with release of natural ENP?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

4. What is your level of confidence in the current ability of scientists to predict the changes in ozone depletion with the accidental release of ENP?

(Insert a checkmark in the appropriate box)

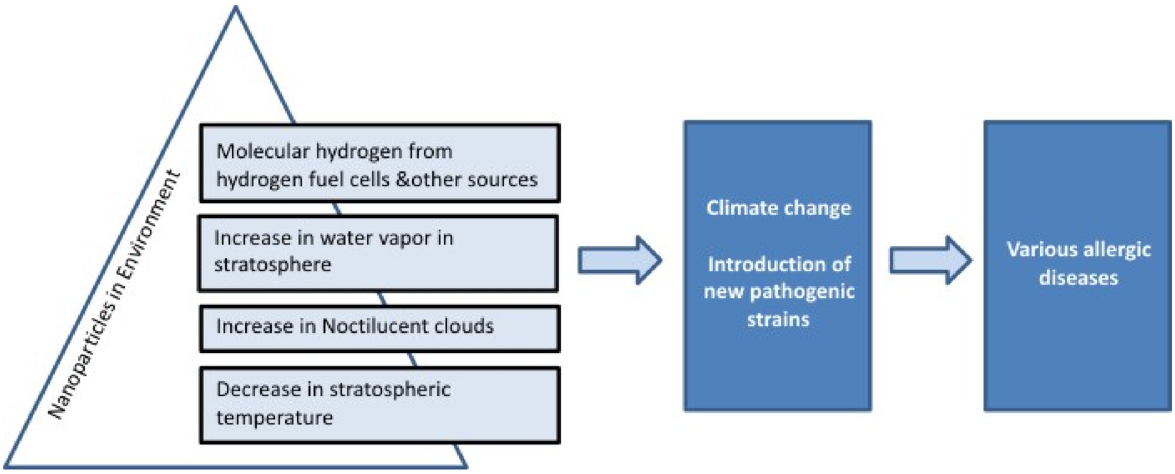
Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

5. What is your level of confidence in the current ability of scientists to predict the changes in ozone depletion with the release of engineered ENP?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

B7. Effect of ENP on increase in moisture content and decrease in environmental stratospheric temperature



Nanoparticles in the troposphere interact with molecular hydrogen accidentally released from hydrogen fuel cells and other resources. Molecular hydrogen along with nanoparticles moves to stratosphere and resulting in the abundance of water vapor in the stratosphere. This would cause stratospheric cooling, enhancement of the heterogeneous chemistry that destroys ozone, an increase in noctilucent clouds, and changes in tropospheric chemistry and atmosphere-biosphere interactions.

Noctilucent clouds are composed of tiny crystals of water ice 40 to 100 nanometers in diameter and exist at a height of about 76 to 85 kilometers, higher than any other clouds in Earth's atmosphere. Much like the more familiar lower altitude clouds, the noctilucent clouds are formed from water collecting on the surface of nano sized dust particles. The sources of both the dust and the water vapor in the upper atmosphere are not known with certainty. The dust is believed to come from micrometeors, although volcanoes and dust from the troposphere are also possibilities. The moisture could be lifted through gaps in the tropopause, as well as forming from the reaction of methane with hydroxyl radicals in the stratosphere. There is evidence that the relatively recent appearance of noctilucent clouds, and their gradual increase, may be linked to climate change. New pathogenic strains are supposed to come up in the environment because of the climate change that may cause serious threat to human health.

Evaluate the completeness of the diagram by answering the following questions.

1. Does the diagram adequately represent mechanisms of how ENP influence stratospheric temperature? If no, please explain.

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2. What is your level of confidence in the current ability of scientists to predict changes in Noctilucent cloud formation with changes in ENP releases?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

3. What is your level of confidence in the current ability of scientists to predict changes in stratoshpheric temperature as a result of Noctilucent cloud formation?

(Insert a checkmark in the appropriate box)

Very high confidence. At least a 9 out of 10 chance of being correct.	High confidence. At least an 8 out of 10 chance of being correct.	Medium confidence. At least a 5 out of 10 chance of being correct.	Low confidence. At least a 2 out of 10 chance of being correct.	Very low confidence. Less than a 1 out of 10 chance of being correct.

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NILU Norwegian Institute for Air Research

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P.O. Box 100, N-2027 Kjeller, Norway
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ABSTRACT
The HENVINET consortium has developed a questionnaire to identify knowledge gaps in the state of the art in scientific knowledge. Literature reviews covered all elements that compose the causal chain of the different environmental health issues from emissions to exposures, to effects and to health impacts. Ultimately, the aim is to discuss the implications of these for policy and research.

In this evaluation we focus on effect of nanoparticles on various environmental processes and their impact on human health. The questionnaire consists of two separate parts. In Part A, you will be asked to comments on the completeness and structure of a diagram illustrating our current understanding of the cause-effect relationship of intentional and unintentional nanoparticles on environment and their subsequent impact on human health. In Part B, you will be asked to express your level of confidence in the scientists' ability to predict the magnitude of a disease burden that is expected to occur as a result of release of nanoparticles in the environment.

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