NSW Government Inquiry into Nanotechnology
Responses to questions relating to submission 19 from CSIRO

(1) Your submission at page 12 notes that the goal of the Niche Manufacturing Flagship is to support the development of niche manufacturing businesses based on nanotechnology. How will the Flagship determine which businesses to support? What part can State Governments play to assist businesses from their State accessing this support?

The activities of the Flagship will provide general support to the manufacturing sector by increasing the knowledge about nanotechnologies through Flagship research projects and by contributing to international activities to understand the risks to human health and the environment from using nanomaterials.

The Flagship will perform research in specific areas which have been selected after careful market research, and analysis of CSIRO's capabilities, and are in areas where CSIRO has strong international advantage. Specific companies may collaborate with CSIRO in these selected areas, based on alignment of research interests and willingness to co-invest in high value outcomes.

State Governments may assist by supporting research in pre-competitive stages, by supporting development of facilities and technology parks which provide state-of-the-art equipment, and by supporting State-based networks of researchers and manufacturing companies.

(2) Are you able to advise why the company Ambri Ltd relocated from NSW to Queensland?

CSIRO is not in a position to answer this question.

(3) At page 7 your submission notes that what sets the Flagship initiative apart is an integrated approach to EHS research from the start. Can you expand on this integrated approach?

The Flagship plans to analyse the life cycle, "from cradle to grave", of each type of nanoparticle it uses, and incorporates into specific products. This analysis will reveal stages in the nanoparticle's life cycle which may involve intentional and/or accidental exposure to humans or release to the environment. For example, factory workers may be exposed to nanoparticles during manufacturing and packaging, especially if the nanoparticles are prepared in dry form; nanoparticles may be released to the environment during normal use of a product (eg swimmers wearing sunscreen). The consequences of exposure will depend on the toxicities of each type of nanoparticle (including the various forms in which a particular type of nanoparticle can be made (eg various sizes, shapes, surface coatings etc)), but in most cases toxicity data are not yet available. Perceived "hot spots" in the life cycles will be investigated in EHS projects in the Flagship.

We can further explain this approach to integrate EHS research with technology development by providing a specific example.

One research program within the Flagship involves the scale-up and application of spun carbon-nanotube yarns in, for example, novel textiles and biomedical applications. In the absence of precautions, it is possible that, during the process of pulling carbon nanotubes from the solid support and spinning them into yarns, some nanotubes might be dispersed into the air where they could be inhaled by the researchers or by factory workers. An EHS project

has started with a full safety audit by an independent body (NanoSafe Australia) of CSIRO's facilities and processes where the carbon nanotubes are made and spun. The project will also assess a number of available instruments, which can detect nanoparticles and quantify their numbers in air, for their ability to detect carbon nanotube fibres in the laboratory where the spinning process occurs. Once carbon nanotubes can be reliably detected and quantified, experimental procedures may be altered where necessary, and appropriate protection for workers and the environment can be put in place. In the meantime, as a precaution, workers will wear full protective gear which is extremely uncomfortable, and can be worn for only short periods.

In addition to this workplace-based project, the Flagship is looking at the effect these carbon nanotubes may have on ecosystems, should they be released into the environment.

In principle, a full EHS program would also include studies on the toxicities of these nanotubes to mammalian systems. However, as this is an active field of research internationally, the Flagship will conserve funds by not duplicating work in this area, but will establish relations with the major relevant research groups, monitor publications, and advise Flagship researchers accordingly.

The integrated approach should produce multiple benefits. Nanotechnology researchers will get a more detailed understanding of the potential safety issues surrounding their technologies and, if appropriate, early indications of any issues that might arise. Safety researchers will have direct access to nanotechnologists and therefore a better understanding of the properties of nanoparticles and nanotechnologies which will inform their studies. Potentially we will also understand more about the prospective future directions of the nanotechnology industry (i.e. second generation 'self-assembling structures' etc) and can start to consider safety implications as they arise, rather than always playing catch-up with technological developments or what is commercially available.

(4) At page 7 of the submission it argues that in the long run it is products arising from programs such as the Flagship that are more likely to be embraced by consumers and industry alike. Can you expand on this comment, and in doing so advise how consumers would be made aware that these products have been researched with safety in mind?
In general, industry takes safety very seriously, both of its workers and of the consumers who use their manufactured products. The reasons may stem from genuine concern through to financial considerations. A company is less likely to face court-cases and/or large financial payouts, such as in the asbestos-related court cases, if worker, product and environmental safety research is integrated in the development of the product.

Consumers may be made aware of the safety research associated with the development of the product if this is incorporated into the marketing strategy for the product. It is likely to provide a strong competitive advantage, particularly as consumer interest in environmental impact and health and safety concerns appear to be increasing.

(5) Your submission states at page 6 that HSE information arising from the Nanosafety research program will be made publicly available. Will this be the case for research that is supported by co-investment from companies?
At this stage, the Nanosafety research program is not financially supported by any company. However, the research required is very extensive and expensive and co-investment is being

sought from several sources including Government regulators and Departments that require HSE information on manufactured nanomaterials for their own work. CSIRO's acceptance of any external funding will be conditional on all HSE information being published without restriction; this position is not negotiable.

It is important to note that any adverse HSE information found for a nanomaterial or product can be used to guide modification of the nanomaterial or product so that it is rendered safe.

(6) At page 18 the submission notes that life cycle analyses have resulted in proposed projects studying exposure to carbon nanotubes and zinc oxide nanoparticles in the workplace and exposure to zinc oxide nanoparticles from use of sunscreens. Can you provide some details on these projects?

The project on OHS exposure to carbon nanotubes has been described above, in the answer to Question 3.

The project on OHS exposure to zinc oxide and other nanoparticles is designed to develop methods for detecting, quantifying levels, and tracking nanoparticles in the laboratory and factory. In addition, the nanoparticles will be fully characterised for their physical and chemical properties, and toxicities to mammalian cells will be determined. Bioassays will be developed to detect damage to chromosomes (genotoxicity). Whole-genome gene-expression microarray experiments will be performed to understand which gene networks may be activated upon exposure of the cells to the nanoparticles; this information will provide an understanding of the mechanisms involved in cellular response to nanoparticle exposure, and should allow biomarkers to be identified for developing bioassays (based on polymerase chain reaction (PCR)) to monitor exposure to nanoparticles. This work will be complemented by research by collaborators on changes in cellular protein levels.

The experiments with ZnO nanoparticles in sunscreens are designed to determine if the nanoparticles can penetrate skin, the impact any dermal penetration may have, and the impact of free radicals potentially generated from metal oxide nanoparticles (ZnO, TiO_2) either dermally absorbed or remaining on the surface of the skin. Skin penetration will be tested in an experiment involving humans at a Sydney beach near the end of 2008. A sunscreen containing ZnO nanoparticles with traceable zinc will be applied to the skin twice a day for a week while the volunteers go about their normal activities, and levels of the traceable zinc will be measured in samples of blood and urine taken from the volunteers during that week and in a follow-up period. The same sunscreen will be applied to the skin of mice for a week to determine if dermally absorbed ZnO nanoparticles preferentially accumulate in specific organs; any organs shown to accumulate the traceable zinc will be checked for altered structure by histological analyses, and for altered biochemistry by gene-expression micro-array experiments. Mice will also be used to assess the impact of long-term application of commercially available sunscreens containing metal oxide nanoparticles (ZnO and TiO_2) and chemical absorbers of UV radiation. These experiments will be done with and without solar exposure, to determine if free radicals, potentially generated from the metal oxide nanoparticles in the presence of visible and UV light, adversely impact the mice in an experiment lasting 2 years. The use of mice represents a "worst-case" scenario, as mouse skin is more penetrable than human skin.

An objective of the human-health nanosafety research is to develop tests for monitoring exposure of humans to nanoparticles. Some of these tests will be focussed on the detection of specific molecules which are identified to be markers of exposure. We also are investigating

more broadly-based tests for screening general health, and hence exposure to nanoparticles, where the specific bio-molecular response may not be fully known. For this work, we are focussing our investigations on a currently available, but little-known, blood test which is based on the patterns formed when a drop of blood taken from the little finger is spotted on to a glass slide and allowed to dry. Intriguingly, the varied patterns obtained appear to correlate with different disease states. This test will also be adapted to use in animals, to reduce the number of mice required for long-term experiments to monitor chronic exposure to nanoparticles.

The CSIRO Centre for Environmental Contaminants Research (CECR) has been working on the aquatic toxicology of manufactured nanomaterials, using single celled algae as model organisms, since 2006, and this research is now being transferred to the Niche Manufacturing Flagship. The CECR research addressed the central question of whether or not nanoparticles are inherently more toxic than bulk materials of the same composition. Initial studies focused on the solubility of nanoparticles, particularly zinc oxide. The results indicate that uncoated zinc oxide nanoparticles are quite soluble and their toxicity is due to their dissolution to ionic zinc which is highly toxic and already regulated in aquatic environments. However, we do not yet know how the solubility of zinc oxide nanoparticles is affected by their formulation into products, e.g. sunscreens, and further work is required.

The Flagship will conduct environmental research on additional nanoparticles, such as carbon nanotubes and silver nanoparticles. Key research areas will include: the chemical and physical transformations that occur when nanoparticles are discharged into receiving environments; the development of appropriate acute and chronic toxicity tests using a range of aquatic and terrestrial indicator organisms, and mechanistic studies to determine the causes of any observed toxicity.

The predicted outcomes of the research described above will (i) provide high quality data to contribute to the global effort to develop mechanistic models of nanotoxicity (an anticipated 10 year timeframe); (ii) contribute data to the development of regulatory guidelines for nanomaterials and (iii) allow the safe commercialisation of nanotechnology based products by providing information on hazards and risks to human health and the environment.

(7) At page 19 the submission sets out the timeframes for the impacts to be realised by the Nanosafety research theme, which runs from 2010 to 2018. The question that has to be asked is can products developed under the Flagship be commercialised prior to those milestones being met, and if so under what circumstances?
CSIRO is bound by the same legal and regulatory requirements as any other industrial organization with respect to commercialising technologies. There are currently no nano-specific regulations in NSW (or indeed anywhere globally) but this may change in the future. The aim of the integrated approach of the Niche Manufacturing Flagship is to develop products which harness the considerable benefits presented by nanotechnology and at the same time to understand and appropriately manage any potential risks posed by these technologies. This approach should enable us to address any future regulatory requirements in a timely manner.

It should be noted that research is a long-term process. It is an objective of the Flagship to accelerate the transfer of nanotechnologies to industry.

(8) At page 19 the submission notes that high level coordination of nano-safety research activities is essential. And that substantial funding is necessary to enable the integration of appropriate research programs within commercially focussed projects. Can you expand on this and perhaps suggest how and where this coordination should take place and how this funding should be sourced?

There are two aspects to Nanosafety research, and where the research is done, and the funding processes to support the work, are quite distinct.

Firstly, there is a need for information on the human and environmental toxicities of nanoparticles before they are incorporated into products. This information will be of general use to everyone, and could be resourced by public funding, and coordinated by international and national agencies. For example, the OECD is coordinating an international program on toxicity testing of manufactured nanoparticles, in which member countries are invited to sponsor, or co-sponsor, the testing of one or more of 16 identified nanoparticles. The OECD has compiled a list of end-points to be addressed, and is preparing guidelines for testing. Member countries offering to be lead sponsors are responsible for addressing all the test end-points for the nominated nanoparticle, while co-sponsors will work closely with lead sponsors and investigate a sub-set of nominated end points. Coordination of the testing at international level should identify knowledge gaps and reduce unnecessary duplication, and at the same time provide a structure through which member countries can rapidly access toxicity data for all the nanoparticles being tested.
http://www.oecd.org/department/0,3355,en_2649_37015404_1_1_1_1_1,00.html

NICNAS and CSIRO representatives participated in an OECD Workshop on the Sponsorship Program for the Testing of Manufactured Nanomaterials in Tokyo in April 2008. Based on what was learned at the workshop, they recommended to the Australian Office of Nanotechnology's HSE Working Group that an Australia consortium participate in the OECD program as co-sponsor for the testing of zinc oxide and silver nanoparticles. Plans to organise the Australian consortium are currently (July 2008) being arranged through the Australian Office of Nanotechnology with the principal coordinating role being filled by NICNAS. Funding to support the Australian consortium's activities is currently being sought from NHMRC, ARC, Government Departments and other stakeholders.

Secondly, there is a need for toxicity information of products which contain nanoparticles. The toxicity profile of a nanoparticle incorporated into a product may be quite different from that of the pristine nanoparticle before it is incorporated. Research on product toxicity is appropriately conducted by independent research laboratories (Government or commercial) with funding from the company marketing the specific product. Depending on the end use of the product, the HSE tests may be quite expensive and the creation of contestable grant programs would be helpful in assisting small companies to fast-track products for commercialisation.

Australia's regulatory agencies urgently require safety data on nanoparticles. To identify their research needs and to avoid duplication or overlapping of efforts, a Health, Safety & Environmental Working Group, consisting of representatives from Government Departments and regulatory agencies, is being coordinated at the national level by the Australian Office of Nanotechnology. CSIRO has observer status with this HSE Working Group. Nanosafety data generated by CSIRO can be communicated rapidly to all relevant regulatory agencies through this HSE Working Group. The process of communicating nanosafety data to all relevant agencies would be cumbersome and much slower without coordination at the national level.

(9) At page 24 the submission states that CSIRO is currently discussing a number of models of community engagement on the issue of nanotechnology. Can you provide some detail on the different models being considered?

The Niche Manufacturing Flagship is in discussion with the University of Western Sydney to understand the nature of its Nanotechnology Network which has been successfully engaging with the public, schools, and manufacturers in the Campbelltown area since 2006. The Flagship and UWS are exploring ways in which CSIRO may support the expansion of the UWS Nanotechnology Network to include manufacturers and public engagement beyond south-western Sydney. UWS and CSIRO would warmly welcome involvement by the NSW Government in this endeavour.

Other ideas are under development and are not yet appropriate for release.

In 2007-2008, the Australian Office of Nanotechnology organised a public forum in every capital city to raise awareness of nanotechnology. CSIRO has participated in six of these fora.

(10) Your submission notes that credible sources to inform the public about developments in science and technology are vital. What makes a source credible in the eyes of the public?
A source is regarded as credible if it is independent (particularly financially independent) from issues associated with the information and is able to provide disinterested, impartial analysis of the science relevant to the topic under consideration. This means being open about scientific disagreement and, whenever possible, provide on the uncertainty of the conclusions. While some CSIRO research is funded by companies, CSIRO researchers personally do not gain financially from their research. This situation does not necessarily exist in other research institutions where, for example, staff may retain a percentage of ownership on patents arising from their research.

In public surveys, CSIRO consistently is reported to be a credible source on developments in science and technologies.

(11) Your submission provides some very good information on the benefits and risks of nanotechnology applications and on the potential nanotoxicity. This information does not discuss nanotechnology or even nanoparticles in a generic way but make some distinctions on the basis of applications and on whether nanoparticles are soluble or insoluble for example. Should this type of information be made available to the public?
Yes, certainly it would be useful to move away from the generic term 'nanotechnology' and to introduce the concept that this encompasses a wide range of disparate technologies with very different properties and applications and thus different potential risks. However, it is probably too early to base these distinctions on very specific concepts (solubility would be a good example here), as we do not yet understand how these specific properties predict risk and this may be confusing to the public if our understanding changes with future research.

(12) How do we engage with the public on a meaningful scale? Should public concerns and desires be used to direct areas of research?
The answer to this question requires careful thought, considerable research, and input from all stakeholders.

CSIRO recently hosted a workshop with members of ASSA (Academy of the Social Sciences in Australia) to discuss the integration of social science research in Flagships. Contributions from social science research projects within Flagships potentially could guide research directions within Flagships.

Parliamentary inquiries are an important form of public engagement, providing a mechanism for distributing views from a wide variety of stakeholders and for facilitating community debate.

Media involvement is essential, provided the reporting is informed. Informed media reporting requires scientists to be prepared to talk about their work and free to discuss its implications. CSIRO participates in public debate by providing accurate and impartial information free of bias.