



**SIXTH FRAMEWORK PROGRAMME
PRIORITY 3-NMP**

Nanotechnologies and nanosciences knowledge-based multifunctional materials and new production processes and devices



INTEGRATED PROJECT

Publishable Executive Summary

Period: 1ST December 2004 to 30th November 2005

Project acronym: **NACBO**

Project full title: **Novel and Improved Nanomaterials, Chemistries and Apparatus for Nano-Biotechnology**

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Publishable Executive Summary

The Project

NACBO is an EU FP6 integrated project funded from the NMP (nanotechnology) thematic priority and concerns the innovation and development of novel nanomaterials, materials chemistries, synthetic organic chemistries and associated integrated hardware systems for their application in nanobiotechnology. It is one of a number of new projects to be funded in Europe for the establishment and maintenance of 'centres of excellence' in research and development related to specific areas of nanotechnology. The project started on 1st December 2004.

It combines key European industries, service providers and academic researchers from the fields of nanoparticle manufacture, characterisation and application, modification chemistries, synthetic nucleic acid chemistries, molecular diagnostics methods development, diagnostic kit manufacture and integrated hardware systems and will deliver platform technologies, composed of component parts drawn from each area indicated below.

The project brings together 3 leading and innovative European industries; Philips, Savyon and Prologo and a leading world chemical industry, the Sigma Aldrich Corporation, six leading European and world universities/research institutes: Kent, Urbino, East China University of Science and Technology, the Hebrew University at Jerusalem, Shemyakin Ovchinikov Institute of Bioorganic Chemistry, Bar Ilan University and 3 major European governmental agencies responsible for public safety, and health and food quality and animal welfare; the Health Protection Agency, Criminalpol and an Istituto Zooprofilattico Sperimentale. Seven different nation states are involved in the project representing Northern Europe (UK, Netherlands and Germany), Southern Europe (Italy), an EU associated state, Israel, China and Russia. The total project funding is 12 million Euro of which 8 million are provided by the EU, 0.5 million by the Chinese Government and 3.5 million by EU industry. The project's duration is 4/5 years.

Project Summary

NACBO proposes the research, development and commercialisation of discrete but overlapping areas of material science, materials chemistry and supporting/applying hardware systems. It will deliver novel and improved solutions to emerging and current needs in biology, health, chemistry, process engineering and the environment. Most particularly its outputs intend to address molecular diagnostics. The project will also address training of individuals, at all levels, in areas of relevance to its work and promotion of public awareness and female participation in science, engineering and technology (SET) with respect to nanotechnology and biotechnology. Finally it intends to deliver an effective web based resource for reference purposes with respect to bio/environmental compatibility of materials and chemistries involved in nanotechnology. Technologically this project concentrates on 3 main themes where existing approaches, materials or methods are either limiting or non-existent and where market opportunities exist. These are (i) tailored, characterised nano- and micro- materials including paramagnetic materials) based upon, silica, magnetite and carbon in the forms of paramagnetic nanoparticles, mesoporous molecular sieves, carbon nanotubes, nanorods and nanoporous surfaces (ii) chemistries involving; surface activation leading to improved and controllable surface functionalisation of materials via electro-oxidation and chemical polymerisation of chiral dicarbazoles and dipyrroles and diene/dienophile interactions and chemistries relating to perfluoropolymers for improvements in bioseparative processes; contrasting agents including quantum dots and electron spin traps and novel assembly chemistries for synthetic nucleic acids and related monomer synthons and (iii) new hardware platforms and associated reagents for application of the above in molecular diagnostics processes particularly forensics, public health and welfare. The project balances radical, breakthrough innovation with incremental technological development and its objectives are to technologically establish new methodologies and materials, supported by at least 5 new patents and 10 new products, within its lifetime, which will access a total market estimated to be in the order of 29 Beuro by 2005.

Project Objectives

The Consortium combines key European small and large industries, service providers and academic researchers who are experts in the fields of nanoparticles manufacture, characterisation and application, modification chemistries, synthetic nucleic acid chemistries, molecular diagnostics methods development, diagnostic kit manufacture and integrated hardware systems. It will deliver **platform technologies**, composed of component parts drawn from each area indicated. It intends to be recognised as a European/World Centre for Excellence in research and application in the area of nanobiotechnology.



The specific objectives of this IP are:

- a) **To make, characterise and compare nanocomposite materials**, based upon carbon, magnetite and silica and their combinations. These will represent multi-walled carbon nanotubes and self assembling macro molecular constructs of their activated forms, nanoporous flat surface materials, nanoparticulate silica-magnetite composites, mesoporous molecular sieves based upon silica and nanorods formed from functional organic polymers.
- b) **To innovate and improve chemistries associated with the immobilisation, activation and marking of surfaces.** Specific chemistries to be considered will be based upon chiral pyrrole and carbazole polymers, perfluorbutadien, polyanilin and dendrimerisation. Additionally, 'materials contrasting' with quantum dots and modified fluorescent nucleic acids will be investigated. Finally chemical vapour deposition of surface films on to carbon nanotubes as mediators in their subsequent activation for applications or assembly into macro-molecular structures will be investigated and optimised.
- c) **To design and fabricate biological/nonbiological composites with potential for use in drug delivery and medicine.**
- d) **To innovate and improve chemistries associated with synthesis of nucleic acids and novel classes of monomer synthons.**
- e) **To design and select ligands (protein, nucleic acids and other molecular species) for immobilisation to nanomaterials** derived from (a) and (b) above and demonstrate their utility in diagnostic monitoring strategies in health (infectious and genetic disease), forensics and public health (food quality and environmental monitoring).
- f) **To innovate, improve, produce and test integrated hardware platforms utilising combinations of the above materials and chemistries in:** *in vitro*, whole live organism and environmental diagnostic procedures based upon biosensors, biochips, bioarrays and imaging platforms such as CT, MRI, PET, OMI and EPR.
- g) **To evaluate in a toxicological context all materials and chemistries, and combinations thereof, arising from the project for their bio/environmental compatibility.**

Overview of project work

This IP is composed of 4 technical work packages (WPs) covering 46 major tasks. Each major task is split into a number of subtasks. The tasks are balanced to supply through a combination of higher risk, novel technological development and lower risk incremental development of established technologies sufficient data, materials and methods to support the development of new SNP and protein based diagnostics, drug delivery vehicles, nanomaterials and associated chemistries for bioseparation and purification, new nucleic acid assembly chemistry and monomers, new particle and flat surface materials for array fabrication and associated hardware. The project also includes a full toxicological investigation of the materials and chemistries involved.

WPs 1 to 4 (the scientific and technical WPs) run in parallel with one another and information, methods and materials are regularly exchanged between them.

Although the WPs are inter-linked as indicated, they are not completely interdependent for the success of the project. There is sufficient lower risk incremental technological development built into each WP to guarantee minimum scientific and commercial outcomes. Partners are involved in constant dialogue with one another in order that optimisation of applications (WP 4 – Integration and Application) will occur. This also contributes to the efficient management of the project and to the delivery of all necessary project reports.

- **WP1** deals with the research and development of novel nanomaterials and involves 5 project partners. Work undertaken in this WP is directed to the production of structured composite nanoparticles, fluorescent nanoparticles, modified carbon nanotubes and constructs produced from their directed self assembly and biological/inorganic composites. These novel nanomaterials form the basis of study and application in other WPs most particularly WP4. Work in WP1 can be categorized as almost exclusively basic research and runs for the full duration of the project.
- **WP2** deals with the research and development of novel chemistries and involves 5 project partners. Work undertaken in this WP is directed to the synthesis and characterisation of novel chemistries associated with synthetic nucleic acids, surface modification, electron spin resonance and polymers. These novel chemistries form the basis of study and application in other WPs most particularly WP4. Work in WP2 can be categorized as almost exclusively basic research and runs for the full duration of the project.
- **WP3** deals with the research, development and improvement of instrumentation relating to molecular diagnostics and automation. It involves a single project partner and its outputs will be applied in tasks within WP4. Work in WP3 can be categorized as both basic research and demonstration and runs for the entire duration of the project.



- **WP4** involves the most complex set of activities in the project and takes outputs from all other WPs and integrates them into applications and systems. This WP also contains the task relating to toxicological evaluation of the materials and chemistry outputs from WP1, 2 and equipment from WP3. To one extent or another all Partners (12) are involved in WP4 and most tasks are highly interactive. For simplification this WP can be themed to:- Foundation studies, Drug delivery, Spin traps and Molecular diagnostics and arrays. Work in WP4 can be categorized as both basic research and demonstration and its duration is the entire period of the project but is weighted towards its end in terms of activity.

Summary of NACBO results months 0-11

Results achieved so far (including education, training and management) from the project can be summarized as:

- Composite nanomaterials (silica and metal oxides) have been synthesized, synthetic protocols have been robusted and optimized and materials are available for partners to use in other experiments.
- Robust and reproducible protocols for the synthesis of metal oxide nanoparticles have been established using hydrothermal sol-gel methods.
- New pyrrole and carbazole derivatives (benzylated protected and COOH forms) derived from both glutamic & aspartic acids have been synthesized using a triaminated trifunctional symmetrical linker $N^1(2\text{-aminoethyl})$ ethane-1,2-diamine.
- A completely new method for the synthesis of oligonucleotides based on a new class of phosphoramidite monomers with novel properties has been established in laboratory form.
- 7 model compounds based on a dye nitroxide radical structure have been prepared and investigated in terms of their EPR-signal responsiveness.
- Novel rare earth phosphate-based luminescent nano particles have been prepared with control LED diameters and excitation and emission spectra.
- Data relating to the various nanomaterials and their abilities/efficiencies in nucleic acid binding and elution have been generated and surface modified forms of the materials have been produced bearing immobilized nucleic acids and antibodies.
- Data regarding the use of these latter materials in numerous experiments for the development of novel lateral flow and hybrid capture applications as well as being used as substrates in SELDI-MS.
- Novel forms of capped quantum dots have been prepared and are available for use in experiments by partners.
- A fully functional project management structure.
- A fully functional project committee structure.
- A fully functional project website.
- An implemented staff exchange programme.
- An implemented short course for staff training.
- An implemented senior school students course in nanotechnology.
- An information pack (brochures) at base medium and high technological knowledge levels produced and distributed.
- Project poster produced and distributed.
- Production and submission of all projects reports and cost/audit statements to schedule.
- 2 patent application submitted (3 patent applications pending).
- 12 Scientific papers/ books published (4 scientific papers submitted).
- 18 Scientific Conferences attended with oral presentations.
- 7 seminars given.

Potential Impact and use of NACBO results

NACBO mobilizes the industrial and research community in nanotechnology in a multidisciplinary project around high-risk and long term goals, permitting the collaboration of public and private research organisations on a pan European scale and support development of the European Research Area (ERA). Project outputs will improve and innovate options for public health and security through the development of advanced, nano- and micro materials, synthetic nucleic acid chemistry and surface activation chemistry for challenging biotechnological applications.



Specifically, NACBO's impact will bring advances in the following areas:

Economic

- Project outputs are of major significance to the rapidly growing €250 Billion global medical equipment, services and supplies market especially the *in vitro* diagnostics sector currently valued at over €21 Billion per annum. Project results will access this total market as well as research and it is anticipated that additional partner revenue generated as a consequence of the project will be somewhere in the order of €480 million within 2 years of project end.
- The project will generate patents which will not only be exploited by partners themselves but also licensed to 3rd parties.
- The project and its activities will ensure that European business takes and maintains a leading world position in nanoscience and technology through research and development.

Improvements to quality of life for the EU and global community

- NACBO outputs address health via disease and causative agent detection, characterization and management, preservation of food quality and animal welfare.
- The project promotes better access to, and improved methods of, health care, maintenance, monitoring and treatment.
- The project delivers improved and more cost-effective methodologies for the identification of inherited genetic diseases and tissue typing for organ transplant operations.
- The project innovates new drug treatments through a reduction in time to market and cost of new pharmaceutical products.
- Indirectly, the project will lead to environmental gains via a reduction in harmful emissions and requirements for processing wastes (e.g. organic solvents) or long term storage of hazardous materials.
- The long term project benefit will be a reduction in human suffering, physical and mental.

Improvements to security for EU and global communities.

- The project expedites and contributes to the methods and hardware involved in DNA based forensic profiling of humans.
- The long term project benefit will be a reduction in crime towards people and property.

European added value

- The project combines key European industry (including an SME), service providers (including governmental agencies), and academic researchers in four European nation states (Germany, Italy, Netherlands and U.K), an EU-affiliated state (Israel) and two major developing countries (China and Russia) and promotes European and world collaboration in nanotechnology essential for reinforcing the EU's competitive position with respect to the increasing extent of US domination of this technology.
- The project supports the development of the European Research Area (ERA)
- The project promotes links with developing nations outside the EU, China and Russia thereby ensuring the recognition of European excellence in these geographical areas and academic and commercial links with them.
- The project promotes greater European integration through contribution to standardisation activities associated with project outputs (see below)
- The project provides well qualified individuals in SET with particular respect to the new developing technology, nanotechnology.
- The project will potentiate the general improvement in awareness and acceptance of new technology particularly nanotechnology by the public.

EU standards and regulations

- NACBO represents leading edge technology and outcomes are expected in some areas with what at best currently only possess a limited degree of standardisation. The work of NACBO falls within the remit of both CEN (European Committee for Standardisation) and Cenelec (European Committee for Electrotechnical Standardisation) and most of the planned activities in terms of project outputs relate to medical devices. European legislation relating to this area is contained within the Medical Devices (93/42/EEC) Directives. Results and test procedures developed in the project have the potential to be used for the promotion, establishment and harmonisation of new European codes for standardisation.



Dissemination of knowledge

In the past scientific knowledge and discoveries have mainly been imparted through publication in scientific journals but NACBO intends to 'spread the word' about nanotechnology via numerous routes and in as broad a manner as it can to reach its goal. Therefore, the NACBO dissemination strategy will be delivered largely through its training and education activity.

Summary of NACBO Training & Education activities

- Organising workshops for individuals of all skills and knowledge levels.
- Organising research meetings on topics central to NACBO.
- Publishing scientific results in scientific journals.
- Presenting research results at meeting of learned societies, conferences and through the media.
- Raising public participation and awareness in science and technology particularly in nanobiotechnology via publicity, the project website etc.
- Specifically targeting women and women's groups to increase their knowledge about and participation in science, engineering and technology (SET).
- Contributing to the development of EU standards regulations and policies.
- Improving public awareness about the safety of nanotechnology through risk assessment.

For outputs in the 1st year of the project see summary of NACBO results months 0-11 on page 5.