EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Human Medicines Development and Evaluation

1st International Workshop on Nanomedicines 2010

Summary Report

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1. Foreword

On 2-3 September 2010, the European Medicines Agency (EMA) hosted the first international scientific workshop on nanomedicines. Some 200 European and international participants from 27 countries including Australia, Canada, India, Japan and the United States discussed the benefits and challenges arising from the application of nanotechnologies to medicines. Participants included representatives from patients' organisations, health care professionals' organisations, academia, regulatory authorities and pharmaceutical industry.

The participants of the workshop shared experience, reviewed existing and emerging nanomedicines and discussed a number of specific aspects, including the characterisation, biodistribution and interactions of nanomedicines with biological systems, to identify gaps in scientific knowledge and to prepare for the evaluation of future nanomedicines.

Addressing the workshop, Patrick Le Courtois, Head of Unit Human Medicines and Development at the EMA spoke of the need for regulatory bodies to be prepared for the "timely introduction of safe and efficacious nanomedicines of a high quality, as nanotechnologies bring not only opportunities to improve current treatments but also the potential to change the way we approach healthcare and diseases."

Nanotechnologies have a wide and still only partially exploited potential in the development of medicines. They provide scope for engineered nano-systems that could lead to a spectrum of useful functions such as refined drug delivery, advanced combined diagnostics/therapeutic functions, matrices and support structures for regenerative medicines. Some eighteen marketing authorisation applications for nanomedicines have been reviewed by the EMA to date. These include liposomal formulations, nanoparticles and polymers/conjugates, mainly related to anti-infectives, anti-neoplastic and immuno-modulating agents. The applications were assessed under the existing regulatory framework using established principles of benefit/risk analysis with the scientific flexibility of accepting new development models and testing methods in the evaluation of such products.
The emergence of new therapies, like nanomedicines, gives rise to questions of whether current regulatory frameworks are appropriate, whether regulators are equipped with adequate expertise. The assessment of existing nanomedicines has provided valuable experience in examining certain aspects of emerging nanomedicines.

Scientific challenges arise from the limitations of current testing methods and the unknown reliability of novel ones, because of the 'nanosize' and the unique behaviour of such nano-systems in biological structures. Further scientific research will be needed to provide a sound scientific basis for an adequate evaluation of the quality, safety and efficacy of emerging nanomedicines.

The participants agreed that the application of nanotechnologies to emerging therapies requires the pooling of knowledge and expertise at a global level and across disciplines. The EMA will continue to provide platforms for continued dialogue on emerging science, the needs of patients and expectations of stakeholders, in order to keep abreast with the scientific progress and provide a regulatory environment suitable for scientific innovation to the benefit of patients.

Notes

1. The present report includes summaries of the speakers' presentations and the discussions that took place at the workshop. Slide presentations of the speakers and podcasts of the speech from the keynote speaker can be found here.
2. Further information on activities of the Agency in the area of nanotechnologies can be found here.

Contact point & Organisational support:

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2. Agenda

The workshop focused on key features of nanomedicines[1] and the emerging scientific knowledge in the field. The objective of the workshop was to explore the science of nanomedicines and to share experience at an international level, in order to be able to anticipate future needs. This document summarises the issues identified during the workshop and the discussions on the emerging science of nanomedicines, which may assist future developments in the field and may be relevant to future regulatory considerations.

Program Chairperson

European Medicines Agency: Patrick Le Courtois

Program Committee

European Commission: Philippe Martin
European Medicines Agency: Tomas Salmonson, Jean-Louis Robert, Beatriz Silva Lima, Ruth Duncan, Rogério Gaspar, Marisa Papaluca Amati
MHLW/PMDA: Yoshikazu Hayashi
US FDA: Nakissa Sadrieh, Carlos Peña

List of speakers

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Peter Arlett
Silvia Berkner
Daan Crommelin
Kenneth Dawson
Wim de Jong
Jacques Descotes
Peter Dobson
Ruth Duncan
Rutledge Ellis-Behnke
Rogério Gaspar
Yoshikazu Hayashi
Jöns Hilborn
Simon Holland
Alexander Kabanov
Toru Kawanishi
Patrick Le Courtois
Philippe Martin
Jan Möschwitzer
Mamoun Muhammed
Marc Pallardy
Marisa Papaluca
Carlos Peña
Jan Petracek
Jean-Louis Robert
Annalisa Rubino
Kumiko Sakai-Kato
Paula Salmikangas
Duc Vu

[1] To ensure a comprehensive approach, the workshop addressed products containing materials in the submicron range.

3. Abstracts and Panel Discussions

Introduction

Welcome address and objectives of the workshop

by Patrick Le Courtois, Head of Unit, Human Medicines Development and Evaluation, European Medicines Agency

Mr. Le Courtois welcomed the audience of nearly 200 participants and explained the background to this first international scientific workshop organised in conjunction with international partners such as the European Commission, the FDA, PMDA-MHLW and Health Canada. He reminded the participants that, in 2006, regulators from the EU, US, Canada, Japan and Australia started a platform for dialogue across frameworks including food, medical devices, cosmetics and pharmaceuticals as an international observatory to share experience and understanding, not to regulate.

In June 2009, at a regulators' conference held at the FDA, it was proposed that an informal international working group on nanomedicines be established and that a scientific workshop dedicated to nanomedicines be organised (these proposals were subsequently endorsed by the European Commissioner for Health & Consumers and the US FDA Commissioner).

Nanotechnologies are integrated in a large range of applications, from aerospace materials to medicinal products. From the regulators' standpoint, preparedness is essential for understanding and anticipating how the emerging science may impact on the way health and diseases are defined and treated.

Nanotechnology applications to medicines raise several scientific challenges related to:
- The application and development of materials sciences
- The understanding of their behaviour in biological systems and living organisms
- The specificities of particular applications and borderline issues for which the development of a multidisciplinary integrated science-based approach is needed.

In bringing together regulators, academics and industry scientists with healthcare professionals and patient representatives, this workshop served as an opportunity to review the lessons learnt from nanomedicines currently on the market and in development, including issues relating to quality, non-clinical and clinical aspects, and risk management.

The objectives of the workshop were:
- To explore key emerging technologies that will provide medicines for the future
- To seek knowledge and innovation from science to inform regulatory understanding and requirements of a promising evolving field, not simply to regulate
- To identify challenges, supporting benefits for patients.

The regulatory challenges include the profound changes in the way therapeutics will be evaluated and approved to fit in the treatment offered to patients.

Regulators will have to be equipped to evaluate not only molecules but also integrated systems with additional and novel dimensions as well as properties beyond classical immunological, pharmacological and metabolic functions. It is essential that regulators are provided with up-to-date scientific information related to emerging therapies from this field to allow them to prepare for any necessary changes to existing legal and regulatory frameworks.

European Commission perspective

by Philippe Martin, Directorate General for Health and Consumers, European Commission

Were a mission statement to be drafted for nanomedicines, it would read something like: "to contribute to the delivery of effective, safe, and affordable treatments to patients, using the fundamental, flexible, and multi-functional approaches made possible by nanoscience and nanotechnologies and to contribute to sustainable economic growth directly, by improving public health and, more generally, by generating reliable revenue streams worldwide, while benefiting from a robust legislative framework and taking advantage of an environment favourable to innovation."

Even taking the above, ambitious mission statement as a starting point, while nanomedicines are not being mass-marketed just yet, we have good reasons to believe that they hold real promise.

Vision, creativity, and hard work of scientists and entrepreneurs are prerequisites for the promises of nanomedicine to come true. Still, for the vision to be translated into marketed products, for creativity to flourish, and for the hard work to pay off, there needs to be adequate funding, a robust legislative framework, appropriate methods, data and procedures for risk assessment, and a sensible governance structure.

The very high level of quality that we are aiming for demands that we learn from our successes and failures in designing nanomedicines, in financing them, in regulating them, in assessing their risks, and in addressing the aspirations of the various stakeholders. But learning requires not only the setting up of monitoring, reporting, and evaluation systems by public or private organizations, but also the establishment of a dynamic, as open as possible, and trusting learning community.

This conference should contribute directly to the realisation of the potential of nanomedicines, the creation of the required framework conditions, and the establishment of a dynamic, open, and trusting, international learning community of nanomedicines stakeholders through the exchange of information, critical discussions, and the building of personal relationships.

Keynote lecture

Way to the future: key ongoing applications in nanosciences and how they apply to pharmaceuticals

By Rutledge Ellis-Behnke, Neuroscientist in the Brain and Cognitive Sciences Department at Massachusetts Institute of Technology and Associate Professor in the Department of Anatomy at the University of Hong Kong, Faculty of Medicine

Each time in history there has been an increase in resolution by a power of ten; science and technology have leapt ahead with new discoveries, with the full impact not being felt for several decades. The nanomics revolution goes far beyond manipulating living tissue; it delves into *molecular manipulation*, enabling the creation of structures that will change what we wear and how we live.

At the nanoscale there are few distinctions between mechanical and biological processes. True nanomaterials are delivered as specific and deliberate molecular structures, or combinations of structures, designed to deliver therapeutics directly to the site, thus requiring a much lower dose. The interface of nanotechnology and healthcare forces us to completely rethink how to approach engineering in the body. Tissue engineering is no longer taking a cell, placing it in a particular scaffold, putting it back in the body and hoping that everything will reconnect and function properly. It is the

ability to *influence* an environment either by adding, subtracting or manipulating that environment to allow it to be more conducive for its purpose.

Safety of nanomedicines: One of the drawbacks is the lack of a way to measure the amount and duration of the drug delivery release of these new formulations. But with lower doses, safety will be less of an issue. By adding signalling molecules to these drugs a colour change could be sent once the drug was released and targeted properly. These response indicators in nanotherapeutics will offer control of release and function at the desired level.

The blood brain barrier (BBB) has always been the primary gating mechanism for delivering therapeutics to the brain. The use of nanotechnology eliminates this barrier because the BBB becomes invisible to the therapeutic, now small enough to travel through the normal transport mechanisms of the BBB and also pass directly through the two cell membranes before being released into the brain. Removing the BBB's gating mechanism brings both promise and concern: for drugs that have targeting issues, nanotechnology will allow drugs to find their target; but on the other side, the safety of some therapeutics is based upon having an intact BBB to prevent entrance into the brain. These changes will not only greatly impact patients, but also the pharmaceutical industry and every related manufacturer.

Challenges in translational development: There have been some recent breakthroughs in nanomedicine research in both animals and humans: reversing blindness; repairing the brain and spinal cord; stopping bleeding in less than 10 seconds; controlling the differentiation and maturation of implanted cells; preventing human prostate cancer stem cells from metastasizing; and using combination devices for detecting and identifying infectious agents. There are also several challenges slowing the movement of nanomedicines to the bedside: (1) there is the misconception that many small molecules are therapeutics; (2) multiple technologies are being combined to create drug delivery devices; and (3) new technologies are being used to evaluate efficacy and safety on materials that are orders of magnitude smaller in terms of concentration.

Bottlenecks in regulation: Typically regulation lags behind technology. We are now entering the realm of molecular medical devices. This change in size fundamentally changes how we think about PK/PD. When a molecule goes below 10nm in diameter permeability goes up to infinity, while solubility does not change. Many drugs that have failed due to solubility issues in the past may show efficacy without the side effects, if delivered in a targeted molecular form.

Nanomedicine will impact the field of medicine much like anaesthetics and antibiotics: the transformation will be so fundamental that we cannot completely comprehend how these changes will impact the future of medical care.

Session 1: Special aspects of nanomedicines - Development, Manufacturing & Characterisation

Chairperson: Jean-Louis Robert (European Medicines Agency Quality Working Party Chair)
European Medicines Agency: Evdokia Korakianiti (Quality of Medicines, Chemicals)

Nanosize does not necessarily imply novelty, and experience has been gathered as nanomedicines have already been authorised under the existing regulatory frameworks. New methods have been developed to manufacture and characterise nanomedicines. The purpose of the session is to identify the most relevant characterisation methods relevant to safety and efficacy and the factors affecting the stability *in vitro*/*in vivo* of nanomedicines.

Synthesis and characterization of Engineered Nanomaterials

by Mamoun Muhammed, Head of Functional Materials Division, and Nano Characterization Centre, Royal Institute of Technology, Stockholm

It has become abundantly clear that nanotechnology plays an important role in future technological development with very promising applications in several areas, industrially and also in the biomedical area. The merging of nanotechnology and medical science offers truly novel solutions and unprecedented approaches for treating diseases and biological disorders. The major breakthroughs in medical applications are within the areas of smart drug delivery systems, bio-diagnostics and early discovery of diseases, treatment of functional disorders, improved implants, visualization of cells, tissues, or organs, and targeting tissues and organs for regeneration and repair, etc.

Biologically relevant nanomaterials have strict requirements and are commonly prepared by solution-based techniques classified under bottom-up strategies. Among these strategies can be listed solution co-precipitation, thermolysis, sol-gel synthesis, electrochemistry, and micro-emulsion synthesis. In this lecture, some of these bottom-up strategies will be described in brief and examples will be provided for the type and application of relevant nanomaterials. Quantifying the physico-chemical properties of nanoparticles is of utmost importance for their use especially in biomedical applications. Several techniques can be applied for the characterization of nanoparticles and their surfaces.

The fabrication and characterization of several nanoparticles with different complexities was reviewed.

Viewpoint from the Industry 1

by Simon Holland, GlaxoSmithKline, Director, Process Understanding & Control within GSK Pharmaceutical Development, Ware

This presentation considered the drivers for developing sub micron or 'nano' medicines, and provided a list of nanomedicines that have been commercialised. Overall, relatively few products are available and these are usually for systemic rather than targeted delivery.

Four challenges associated with reproducible manufacturing, scale-up and stability of nanomedicines are considered: (i) optimising the manufacturing process to produce the selected drug substance particle size distribution within the drug product, (ii) scale up of the manufacturing process, (iii) establishing acceptable chemical & physical stability data to support a product shelf life, and predicting product performance *in vivo,* and (iv) establishing limits for process impurities.

The use of laser diffraction to characterise drug substance nanoparticles is discussed through a worked example of how the use of two data calculation routines, Fraunhöfer and Mie, can significantly alter particle size distributions. Of note is the variance in pharmacopoeial guidance on the use of Mie theory, and a consideration of validation standards is also provided.

An example of how a media milling manufacturing process has been optimised by the use of quality by design tools is examined, and challenges for the formulation and development of oral, parenteral and respiratory delivery of nanomedicines are considered.

Finally, ethical & public engagement considerations were highlighted.

Viewpoint from the Industry 2

by Jan Möschwitzer, Abbott, Head of Early Pharmaceutical Development, Weesp, The Netherlands

The majority of new chemical entities (NCEs) generated by modern high-throughput technologies and rational drug design suffer from undesirable physicochemical and biopharmaceutical properties, leading to erratic drug absorption, food effects and low oral bioavailability. Due to an extremely low aqueous solubility the dissolution of the compounds *in vivo* is often hindered, resulting in a low oral bioavailability. Particle size reduction is a practical method of enhancing the oral exposure of these poorly soluble drug molecules, particularly for those molecules with a dissolution rate dependent bioavailability. Nanosizing has evolved from a rescue approach for abandoned brickdust molecules to a commercially available standard formulation approach.

In the last twenty years many different particle size reduction technologies have been developed. One distinguishes several general principles to produce nanosuspensions, the liquid presentation of drug nanocrystals. Top-down technologies like wet ball milling or high pressure homogenization are currently the most advanced technologies with commercial products on the market. Both technologies utilize coarse starting material. The particle size is reduced by means of mechanical comminution caused by the shear forces, impaction forces or cavitation forces of equipment with a high power density. Another approach is based on a bottom-up principle. Here one starts with a molecular solution of the drug; particles are formed by more or less controlled precipitation processes.

A relatively new and very effective way to produce nanosuspensions is the combination of both principles. In a first step the starting material is modified using one process step (e.g. a bottom-up process) and further processed into nanosuspensions by applying another process step, a top-down process. The presentation gave an overview of the various commercially available nanosizing techniques and discussed the biopharmaceutical aspects of nanosized formulations. The process steps and considerations on the way towards a nanoformulation were explained, as well as stabilization principles and analytical characterization methods for nanosuspensions.

Panel Discussion:

Following the presentations on the special aspects of nanomedicines, further discussion took place on characterisation methods relevant to safety and efficacy and factors affecting the stability of nanomedicines *in vitro* and *in vivo*. Topics discussed included:

- Characterisation and control methods, which are essential for reproducibility and batch to batch consistency. The focus should not solely be on size, but also on surface-area, other surface chemistry and coating parameters. As for other medicinal products, it was noted that characterisation and control tests and methods (including their validation or acceptable variability), as well as management of changes during manufacturing processes would need to be considered on a case-by-case basis along the development process. The harmonisation of standard methods for the proposed tests seemed therefore inappropriate to be reflected in regulatory requirements.
- Finished product specifications: determination of quality attributes critical for manufacturing and clinical effect shall lead to the choice of the most appropriate specifications.
- Sterility issues with those compounds were also discussed which depend on methodology for size reduction and particles stabilization (e.g. conjugation which could be destroyed by some sterility methods).
- Regulatory hurdles and attrition rate for innovation are one of the objectives of this workshop: to consider the potential need for adaptation of the regulatory pathway with patient health as a first objective. Most of the hurdles identified are for science to lead regulators.

Session 2: Special aspects of nanomedicines - Non-Clinical Assessment

Chairperson: Marc Pallardy (Director of Research, School of Pharmacy, University of Paris-Sud)
European Medicines Agency: Jean-Marc Vidal (Scientific Support & Projects Section)

The speakers addressed new scientific knowledge on biological interactions of nanomedicines and existing and emerging approaches to toxicology. The limits and the possibility of extrapolating safety results from *in vitro* to *in vivo* models were also discussed.

What about safety? How do we determine risk?

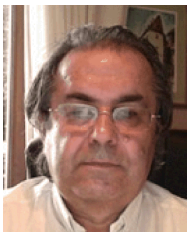
by Wim de Jong, Toxicological pathologist at the Laboratory for Health Protection Research, National Institute for Public Health and the Environment, Bilthoven

Nanotechnology is a rapidly developing technology with the potential to provide our society with a wide range of products to be used in various advanced technology applications. More specifically there is a general expectation that significant progress will be made in various medical applications for diagnostic and therapeutic purposes, including the potential for specific drug delivery in cancer therapy. However, in addition to the beneficial effects of the nanodevices being developed, the potential risks should also be taken into consideration. The small size of nanomaterials/nanoparticles results in a relatively large surface area which is accompanied by an increase in surface activity. This may or may not result in an increased reactivity towards cells and organs, leading to toxic responses. In addition, the size of nanoparticles may be similar to subcellular structures. So there is a potential for an interaction of nanoparticles with such structures. For the safety evaluation, the risk, which is a combination of the likelihood of occurrence of harm and the seriousness of that harm, has to be determined. The hazard can be evaluated by *in vitro* and *in vivo* assays of which the *in vivo* assays are, in general, more relevant for the risk assessment of a product. However, for nanoparticles there may be several complicating factors. The determination of the identity (characterization) is essential but not always easy. It is not yet known what physico-chemical properties may be associated with toxic responses. The use of the nanoparticles in assays may be difficult in view of poor dispersibility and aggregation of the particles. The quality of the preparation may vary due to low reproducibility of production and the presence of toxic residual solvents or process residues. Even the size of a nanomaterial, which is essential for its characterization, should be carefully considered, as the size determination can vary by the method used for the measurement.

When performing safety tests on Nanoparticles, one should realise that a nanoparticle does not exist only by itself. In biological systems various molecules and proteins will adhere to the nanoparticles. Although such "coatings" will increase cellular recognition of the nanoparticles, the biological effects are largely unknown. On the other hand, the application of specialised coatings offers the possibility for specific cellular targeting. In relation to toxicological evaluation there is uncertainty about the dose metric that best describes the nanoparticle effect. Traditionally the dose is expressed in mass, but for nanoparticles the surface area or particle number might be more appropriate. What is quite clear is that the particulate nature and size has an implication for the toxicokinetics of nanoformulations. In addition, as exemplified by carbon nanotubes, shape also affects the biological responses to nanomaterials.

In conclusion, our knowledge of how to evaluate the safety of nanomaterials/nanoparticles is slowly growing. There are still uncertainties which need to be addressed including issues concerning characterization, quality and reproducibility, dose metric, effect of adherence of molecules on nanoparticles, and the potential for chronic effects.

Immunology and immuno-toxicity of nanomedicines



by Jacques Descotes, Professor and Head, Poison Center and Pharmacovigilance Department, Lyon University Hospitals

Nanomedicines consist of a large variety of nanostructures with variable characteristics including size, shape, and surface properties. Therefore, immunotoxicological heterogeneity is likely to be a hallmark of nanomedicines, and therefore a critical hurdle for immune safety evaluation. Nanoparticles/materials have been shown to exert immunological effects, such as interactions with immune cells, triggering of inflammatory responses, activation of the complement cascade, or facilitation of antigen-specific hypersensitivity reactions. However, conflicting or opposite findings have also been reported so that no definitive conclusion can be made regarding the immunological effects, or lack of, for most nanomedicines now.
Immunotoxicity evaluation should focus on the four categories of immunotoxic effects, namely immunosuppression, immunostimulation/ immunoactivation, hypersensitivity and auto-immunity. So far, only a few nanoparticles/materials have been found to be inadvertently immunosuppressive. Guidelines, such as ICH S8 or ISO TS10993-20, could serve as a starting point to propose strategies to assess the immunosuppressive potential of nanomedicines. Short-term repeat-dose toxicity studies may be suitable provided consistent quality of the tested nanomedicines can be documented. The importance of including at least one immune function assay should be highlighted due to our limited knowledge on the immunotoxicity potential of nanomedicines and the reported immunological effects of various nanoparticles/materials.

A major difficulty is the urgent need to evaluate and presumably adapt current assays to the context of nanomedicines. This hurdle is particularly critical for in vitro or ex vivo immune function assays. Available data suggest that nanomedicines may exert immunostimulatory/immunoactivating properties, e.g. cytokine release, which can presumably be evaluated with dedicated in vitro or ex vivo assays. The facilitating role of nanoparticles in hypersensitivity reactions to unrelated allergens has been repeatedly reported and this issue could be addressed in safety immunopharmacology studies. Hypersensitivity reactions may be either immune mediated or nonimmune mediated. Nanomedicines can be suspected to be immunogenic due to inadvertent adsorption or intended binding of various chemicals/proteins. However, because nanomedicines are not expected to be humanized and reactive metabolites are unlikely to be generated, predicting the immunogenicity of nanomedicines may prove to be less tricky than it is for conventional medicines or biologicals. Nonimmune-mediated hypersensitivity reactions due to complement activation have been described with liposomes, but rarely if ever with other nanoparticles/materials. It is important to stress that complement activation may not result in clinically significant adverse reactions. Assays and animal models including systemic or passive cutaneous anaphylaxis, basophil activation, histamine release or complement activation can be selected case by case.

Autoimmunity, the fourth category of immunotoxic effects, is beyond reach of preclinical prediction for the time being. Available data suggest that nanomedicines may exert immunological effects, which may result in immunotoxic clinical consequences. Therefore, a systematic preclinical evaluation of the immunological safety of nanomedicines is recommended. Most currently used assays and models are presumably applicable at least to some extent, although adaptation to nanomedicines is obviously needed. In any case, the specificities and modalities of the immunotoxicity evaluation of nanomedicines remain to be fully characterized and validated for regulatory purposes.

Nanomedicines interaction with biological systems

by Kenneth Dawson, Professor of Physical Chemistry, University College of Dublin, School of Chemistry and Chemical Biology, Dublin

The importance of understanding the interactions between nanoscale materials/nanomedicines and living matter has now been appreciated by an extraordinary range of stakeholders. As the potential to manipulate materials at the nanometer scale grows, this leads to opportunities to stipulate and study specific interactions with cells, tissue, organs and whole organisms. As well as opening new directions in nanomedicine and nanodiagnostics, it offers the chance to implement these technologies in a safe and responsible manner.
The underlying reasons are real and durable. Less than 100nm nanoparticles can enter cells, less than 40 nm they can enter cell nucleus, and less than 35 nm they can pass the blood brain barrier. These are fundamental length scales of biological relevance, partly set by endogenous trafficking processes that will ensure that engineered nanoscience will impinge on biology and medicine for many decades. Nanoparticles in a biologically relevant environment (cell media, plasma etc.) draw to themselves a number of proteins and lipids that form a sort of dynamical 'corona' in slow exchange with the environment. The exchange times can be so slow that many early biological responses are defined by the associated corona biomolecules. Even functionalized particles often have some residual long-lived protein corona and an in-depth understanding of the nano-bio interface (corona), presented to cells and barriers is likely to be the key to understanding targeting. Some new approaches and tools to achieve this will be discussed.
Another key difference between nanoparticles and more conventional drugs is that, as a consequence of their size and protein corona (amongst other factors), nanoparticles are taken up into cells by active processes and trafficked to specific sub-cellular locations utilising well-defined pathways whereas drugs partition based on quasi-equilibrium principles. Thus, clearance can occur only where an established biological pathway exists. For example, at cell level, many nanoparticles enter the lysosomal pathway, where they accumulate (without clearance) within several hours. *In vivo* bioaccumulation and clearance are also likely determined by the nature of the protein corona.

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Panel Discussion:

The possibility of mimicking *in vitro* the *in vivo* system is a very difficult task as factors such as route of administration, formulation of the material, corona effects, interactions with cell surface etc. need to be considered when evaluating the safety of the nanomedicines.
In addition, the trapping in the reticuloendothelial system (mainly spleen) which is very difficult to avoid, pharmacokinetic parameters such as release rate of the active substance from the nano-system, its biodegradability and possible tissue accumulation need also to be considered.

The experience gathered by the US Nanotechnology Characterisation Laboratory (NCL) was mentioned as necessary to assess the limitations of existing methods. Standardization of method is not desirable in this highly innovative and evolving area.

On the regulatory approach the challenge is in assessing completely new technologies, in using current and knowledge guidelines to adapt them to nano-medicines and how to approach "generic" formulations of nanomedicines. As in other sessions, participants reiterated the point that the assessment of safety results should be considered on a case-by-case basis, depending on the therapeutic indications considered.

Session 3: Nanomedicines on the market and in clinical development

Chairperson: Eric Abadie (European Medicines Agency CHMP Chair) represented by Jean-Louis Robert (European Medicines Agency CHMP member)
European Medicines Agency: Mayeul Boucaumont (Scientific Support & Projects Section)

As introduction to this session, the chair recalled the involvement of the main scientific committees of the EMA (Committee for Medicinal Products for Human use – CHMP).

In June 2006, the CHMP adopted a Reflection paper on nanotechnology-based medicinal products for human use (EMEA/CHMP/79769/2006) highlighting the paradigm for the assessment of nanomedicines: "As for any medicinal product, the EU competent authorities will evaluate any application to place a nanomedicinal product on the market, utilising established principles of benefit/risk analysis, rather than solely on the basis of the technology per se."
In 2009, the CHMP also established the ad-hoc expert group on nanomedicines. This group includes selected experts from academia and the European regulatory network, who support the Agency's activities by providing specialist input on new scientific knowledge and who help with the review of guidelines on nanomedicines. The group also helps the Agency's discussions with international partners on issues concerning nanomedicines.

Some eighteen marketing authorisation applications for nanomedicines have been reviewed by the EMA so far. These include 10 liposomal formulations, nanoparticles and over 8 polymers/conjugates mainly related to anti-infectives, anti-neoplastic and immuno-modulating agents.

The main challenges that will have to be further addressed by science or by the regulators, especially for emerging nanomedicines, include:
- Scientific challenges: with questions regarding the applicability and relevance of current methods to assess characterisation and biodistribution, the interactions with biological systems (the impact of intracellular or interstitial persistence), or the impact on the immune system.
- Regulatory challenges: with the assessment of the comparability of existing nano-formulations, the adequacy of tools for risk characterisation, and the classification of converging technologies.

Liposomal nanomedicines and innovative formulations

by Daan Crommelin, Professor of Pharmaceutics, Utrecht University, and Scientific Director, Dutch Top Institute Pharma, Leiden

Several liposomal drug products have been successfully developed and have reached the market place. Examples are doxorubicin-, daunorubicin- and amphothericin B-containing liposomes. A number of other liposomal drug formulations are presently under development both for parenteral and non-parenteral use. All these formulations have to meet the high quality criteria as defined for pharmaceutical products. To ensure proper liposome performance, the batch-to-batch reproducibility and stability of the liposome dispersions have to be established. This requires the definition of the characteristics of liposome dispersions in the preformulation stage, clinical test stage and final production stage.
As patents expire, generic versions of medicines containing liposomes are now under development. Worldwide, the regulatory status of these generic versions of liposomes is not clear. The FDA has issued draft guidances for liposome products in general and for generic versions of doxorubicin-containing liposomes. The EMA is still considering how to approach the relevant issues.
In this lecture we will present some thoughts regarding regulatory strategies.

Polymer conjugates

by Ruth Duncan, Professor Emerita and Past Director, Centre for Polymer Therapeutics, Cardiff University

There is increasing anticipation that nanotechnology, as applied to medicine, will bring significant advances in the diagnosis and treatment of disease. This has prompted many Governmental Agencies to strategically review the field of 'Nanomedicine'. The primary objectives have been to (i) ascertain the status of the field; (ii) establish a common terminology; and (iii) assess potential benefits and risks. When a field suddenly becomes fashionable, it is important to keep a perspective and most importantly, distinguish the 'science fact' from 'science fiction'. Although not widely appreciated, progress in the development of nano-sized hybrid therapeutics and nano-sized drug delivery systems has already made remarkable progress over the last 2 decades. A growing number of products have secured regulatory authority approval and in turn, there is already a healthy clinical development pipeline. Such first-generation "nano-sized medicines" are already bringing clinical benefit to thousands of patients, and provide a platform for the innovative second-generation technologies that are emerging.

Polymers (both natural and synthetic) have a long history as pharmaceutical excipients, as coatings (e.g. iron oxide imaging agents) and as biomedical materials. The versatility of synthetic polymer chemistry provides a unique opportunity to tailor synthetic, biomimetic, macromolecules of specific molecular weight, size, chemical composition, and with the advent of dendrimer chemistry, architecture. The hydrophilicity of certain polymers, such as PEG, has been widely adopted by other nano-sized carriers (e.g. liposomes and nanoparticles) to confer 'stealth' properties that enable them to avoid rapid RES clearance.

The field of "polymer therapeutics" (reviewed in [1-3]) includes polymeric drugs, polymer-protein and polymer-drug conjugates and those related block copolymer micelles to which the bioactive is covalently bound, and polymer-based vectors designed for cytosolic delivery. Typically the conjugates are multi-component nano-sized systems of size ~5-20nm, whereas the self assembled micelles and nanoparticles are larger (typically 20-200nm). A growing number of polymeric drugs (reviewed in [4]) and polymer -protein conjugates (especially, but not only, PEGylated proteins, reviewed in [5]) have been transferred in clinical development, and the first products already came to market in 1990. Additionally, a growing number of polymer-drug conjugates and block copolymer micelles have entered clinical development over the last 2 decades (especially as novel anticancer agents) in an attempt to improve the bioavailability and therapeutic index of covalently bound drugs. In the case of anticancer conjugates the rationale for design has often been to capitalise on either passive tumour targeting using either the enhanced permeability and retention (EPR) effect or receptor-mediated tumour targeting and, at the cellular level, lysosomotropic drug delivery to facilitate controlled intracellular drug release.
The lessons learnt during the preclinical and clinical development of the various families of polymer therapeutics provide a sound technical framework (analytical tools/biological models) that can help shape the development of second-generation nanopharmaceuticals. This is especially true for those hybrid liposomal and nano-sized particles that have polymer-modified surfaces. The important regulatory issues relating to 'polymer therapeutics' have recently been discussed [6].

[1] Duncan, R. The dawning era of polymer therapeutics. Nature Rev. Drug Discov. 2(5),347-360 (2003).
[2] Duncan, R. Polymer conjugates as anticancer nanomedicines. Nature Rev.Cancer, 6, 688-701 (2006).
[3] Vicent, M. J. and Duncan, R. (Eds. Theme Issue.) Polymer Therapeutics: Clinical Applications and Challenges for Development. Adv. Drug Del. Rev. 61, Issue 13 (2009).
[4] Dhal, P. K., Polomoscanik, S. C., Avila, L.Z S., Holmes-Farley, R., and Miller, R. J. Functional polymers as therapeutic agents: Concept to market place. Adv. Drug Del. Rev., 61, 1121-1130 (2009).
[5] Veronese, F.M. and Bossard M. (Eds.) 'Series-Milestones in Drug Therapy: PEGylated Protein Drugs: Basic Science and Clinical Applications, Birkhauser Verlag (2009).
[6] Gaspar, R. and Duncan, R. (2009) Polymeric carriers: preclinical safety and the regulatory implications for design and development of polymer therapeutics. Adv. Drug Del. Rev., 61, 1220-1231 (2009).

Nanoparticles

by Rogério Gaspar, Professor of Pharmaceutics, University of Lisbon

Abstract unavailable at time of publishing

Panel Discussion:

Issues related to the comparability of liposomal formulations were further discussed taking into account the publication in February 2010 of draft guidance on Doxorubicin Hydrochloride by the US FDA Office of Generic Drugs. The extent of characterisation needed to assess comparability of specific liposomal formulations and the relevance of non-clinical and clinical studies to complete this exercise were further discussed. There was controversial discussion on whether a bioequivalence study might be sufficient, with provisions that same composition, origin of starting material and manufacturing process are fulfilled. The availability of accurate methods allowing the assessment of the comparability was also questioned. Finally, the importance of the choice of the starting materials and their source was considered crucial, for example with reference to characterisation and quality such as PEG as those would impact on the manufacturing process. The multidisciplinary approach used for regulatory evaluation of biosimilars was mentioned as a possible way for comparing liposomal formulations, on a case by case basis.

Finally the Chair concluded the session by highlighting:

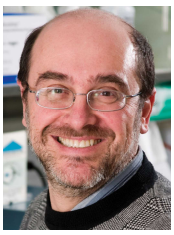
- the complexity of nanomedicines, but noting that the submitted quality, safety and efficacy data were sufficient to support the assessment of benefit-risk for those nanomedicines already on the market,
- the need to consider the optimisation of existing guidance to accommodate specific aspects of novel nanotechnologies rather than developing new requirements,
- the challenges raised by the comparability of such products, and by the determination of thresholds for acceptable differences.

Session 4: Emerging nanomedicines

Chairperson: Paula Salmikangas (European Medicines Agency, Vice-Chair of the Committee for Advanced Therapies; Chair of the Working Party on Cell-based Product) European Medicines Agency: Spiros Vamvakas (Head of Scientific Advice Section)

The speakers provided an overview of the challenges raised by the development of emerging nanomedicines in light of existing frameworks and clinical development guidelines.

Novel and innovative nanotechnology-based delivery systems



by Alexander Kabanov, Parke-Davis Professor of Pharmaceutical Sciences and Director of the Center for Drug Delivery and Nanomedicine, University of Nebraska Medical Center

A new generation of polymer therapeutics has emerged which uses self-assembling nanomaterials for delivery of drugs, genes, and imaging molecules. Examples of such materials include polymer micelles, cross-linked nanogels, and block ionomer complexes that entrap small drugs, DNA or siRNA ("polyplexes"), as well as therapeutic enzymes ("nanozymes") or antibodies ("nanobodies").

These materials are designed to improve the therapeutic index of their biologically active payloads by:
1) Protecting the payload against degradation in the body
2) Improving its pharmacokinetics and targeted bioavailability
3) Increasing its transport across cellular membranes (e.g. in cancer cells) or other biological barriers (such as the blood brain barrier (BBB))
4) Ultimately, releasing the active payload at the site of disease.

These materials are also used in combination with cell-based therapies. For example, they are loaded into immunocytes, which then carry and release the payload to the inflamed sites. Vaccination approaches using polymeric materials are also explored, such as DNA vaccination, which exploits capabilities for targeting specific immune cell populations for antigen presentation, and activation of cell signalling that favours the immune response. The studies in this field have provided observations regarding interactions of such nanomaterials with living cells and sub-cellular statures, including their cellular uptake and transport itineraries, which are sometimes remarkably specific and precise for a man-made material. Furthermore, *polymer genomics* has emerged as a field that explores the ability of synthetic polymers to affect various signal transduction mechanisms involving inflammation, differentiation, proliferation and apoptosis. The ability of the cells and organisms to respond to the effects of these polymers can be dependent on phenotype or genotype. Overall, these effects are relatively weak as they do not result in cytotoxicity or major toxicities in the body. However, when combined with biologically active agents, such as cytotoxic agents, bacterial DNA or antigens, either by mixing or covalent conjugation, the polymers can drastically alter specific genetically controlled responses to these agents. Some examples of such materials that reached clinical stage will be discussed, such as SP1049C, a polymeric micelle doxorubicin for highly resistant tumours.

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Nanosystems in regenerative medicine

by Jöns Hilborn, Professor of Polymer Chemistry and Research Coordinator on Polymer Chemistry, Uppsala University

Abstract unavailable at time of publishing

Theranostics nanoparticles (therapeutic and diagnostic)

by Peter Dobson, Academic Director, Oxford University Begbroke Science Park

The exciting new possibilities in medicine and healthcare offered by carefully designed and engineered nanoparticles are now becoming apparent. There will now be a period during which these possibilities will have to be validated in accordance with the needs of clinicians, the well-being of patients and the defining of good practice and regulation. It is possible to make almost any compound in particulate form by the appropriate choice of method. Furthermore it is also possible to tailor the size and surface properties to suit a wide range of possible applications. There is great interest in coating nanoparticle surfaces with bio-recognition molecules to enable targeting of the particles to a particular tissue or cell-type in the body. Already, there are good examples, mainly from animal experiments, that targeting can be achieved and such particles could be of great utility in image enhancement and diagnostics. It is perhaps an obvious step to combine the function of such particles with some form of therapy, for example, to destroy cancerous cells or to reduce vasculature in a tumour to reduce the flow of nutrients and produce atrophy of the malignant tissue. This might take the form of producing a local heating effect, via the properties of the nanoparticle, or the particles could be designed to carry a drug payload. Whichever route is taken, due consideration has to be given to the safety and efficacy of the approach. We are reaching the stage where it is necessary for increased dialogue to take place between the engineers, materials scientists, chemists and the clinicians and healthcare governing bodies and regulatory authorities. This talk is given largely from the perspective of a "nanoparticle engineer" and it will highlight the steps that will need to be taken before this important aspect of nanotechnology reaches clinical practice.

Panel Discussion:

Challenges raised by the development of emerging nanomedicines were further discussed as follows:
Scientific issues:

- The assessment of long-term consequences of the persistence of certain non biodegradable silica/gold nanoparticles in clinical settings was discussed, and the appropriateness of adequate non-clinical models for its assessment.
- The assessment of *in vivo* compatibility of materials was questioned depending on the mode of administration, dose and intended use (e.g. with external energy sources).
- The importance of the "purity" of polymers taking into account implications derived from the manipulations of synthetic polymers.

Regulatory issues:

- The interpretation of results from publications referring to nanoparticles for which "purity" is not necessarily known.

- The adequacy of current regulatory frameworks for borderline nanomedicines encompassing converging technologies: a case by case approach still has to be followed until science has elucidated remaining gaps. The regulatory framework will be adapted as appropriate based on science and experience.

Session 5: Nanomedicines and the application of Risk Management Principles

Management of Risks to Patients
Environmental Risk Assessment

Chairperson: Peter Arlett (European Medicines Agency Pharmacovigilance and Risk Assessment Sector)

Nanomedicines and the application of Risk Management principles including management of the risks to the patient and to the environment in the life cycle of medicinal products: What additional requirements for nanomedicines may be needed? How do we reconcile the risks from the interactions between medicines and "activating devices"? Risk Minimization: why and when? Risk communication?

Management of Risks to Patients - Safety Specification - Identification and Methodology

by Annalisa Rubino, EMA Risk Management Section

Based on the risk management cycle for centrally authorised medicines in the EU, a concept for the safety specification for medicines involving nanotechnology is drafted. The applicability of essential requirements for the safety specification according to ICH E2E and EU legislation is explored with a focus on 'nano-specific' pharmacokinetic and pharmacodynamic aspects of human medicines. Experiences with previously authorised products, falling in the scope of the current working definition of nanomedicines and their specific properties and characteristics relevant for the identification of known and unknown safety concerns, are discussed. Typically such characteristics would include, but are not limited to, areas such as biodegradability/bioaccumulation, immunogenicity, tumorgenicity, pro-inflammatory effects, protein-fibrillation, cardiovascular risks and parent-child transmission. The suitability of common in-vitro and in-vivo screening assays and other non-clinical methodologies are identified as bottlenecks due to a lack of validation. In the current guidelines for EU-Risk Management Plans, the Safety Specification is mainly built on drug-substance specific safety aspects, however new guidance would be warranted to also adequately address the risks posed by the nanotechnology itself and the inherent reactivity of associated excipients such as polymers, ligands, phospholipids or nanocarriers.

Pharmacovigilance and Risk Minimisation Plans for Nanomedicines

by Jan Petracek, CEO PharmInvent

Risk Management of medicines is already an established concept in the US and the EU. While the formats differ between regions, the principles are very similar. In the EU, a so-called Risk Management

Plan (EU-RMP) is required for all new active substances or any other "high-risk" products. For them it is particularly useful as it may improve the benefit/risk balance and allow for approval of products that would not be approvable otherwise. The use of nanotechnology in medicines itself may be seen as a risk minimisation measure, e.g. allowing for more controlled application of toxic drugs via nano delivery systems.
Nevertheless, nanomedicines are not a clearly defined group of products yet. Therefore, the discussion about risk specificities of this group is also still under development developing. Various combinations of diagnostics, medical devices and medicinal products bring wonderful opportunities for new kinds of products, and challenging regulatory questions, including how to manage the risks of these combinations. Nevertheless, pharmacovigilance planning (further post-authorisation studies), risk minimisation planning (interventions to mitigate known risks) and efficacy follow-up plans (post-authorisation planning of studies with efficacy end-points), will probably follow the same principles as for current biologics and advanced therapy medicinal products.
In conclusion, the current EU-RMP framework seems to be flexible enough to accommodate the specific risks of nanomedicines. Higher use of efficacy follow-up systems, novel designs of trials included in the pharmacovigilance plan, and a number of additional risk minimisation measures might be expected as elements of EU-RMPs for nanomedicines. In addition, closer links with Environmental Risk Assessment might be needed, most likely in the form of common instructions and trainings for users of the medicinal products.

Environmental Risk Assessment - Specific Methodological Issues and Implications for Risk Assessment

by Silvia Berkner, Risk assessor at the German Federal Environmental Agency

The current environmental risk assessment procedure for human pharmaceuticals is outlined and shortcomings concerning nanopharmaceuticals are addressed. The action limit for conducting a phase II environmental risk assessment as well as the use of mass based metrics might need adaptations. Results from ADME studies and information on the bioavailability of nanomedicines in environmental media are important prerequisites for an adequate risk assessment. Test guidelines on the fate and effects of substances in the environment have to be adapted to specific nanomaterial needs. Therefore the work of the OECD Working Party on Manufactured Nanomaterials concerning the review of relevant test guidelines is presented. The following areas were identified as needing improvement: material characterisation and metrics, test suspension preparation, test substance delivery to ensure stable and reproducible properties of the examined nanoparticles and adequate analytical detection methods. In addition ongoing work of the OECD Sponsorship Programme will be presented as a potential resource for information on environmental fate and effects of nanomedicines. The wide variety and diversity of nanoparticles used in nanomedicine applications may however require different solutions. The presentation concluded with a proposal for an interim approach for environmental risk assessment of nanomedicines.

Panel Discussion:

The application of risk management principles in the life cycle of nanomedicines raised further points for discussion. Participants were reminded that the follow-up of efficacy of nanomedicines is already foreseen as part of the marketing authorization follow-up measures, when appropriate.
As part of the genotoxicity testing of nanomedicines, some participants highlighted that the most relevant test methods would be *in vivo* models, as the relevance of *in vitro* tests is still questioned. The development of guidance/document summarizing the issues specific to nanomedicines, as has been done for medical devices, was proposed.

The assessment of biodegradability of certain nanoparticles was further discussed, and it was suggested that even in cases where only the polymer part of a nanomedicine is not biodegradable, the whole particle might need to be assessed.

The assessment of disintegration, or agglomeration in the environment was also discussed as knowledge in this field is still limited but a corona coating effect is probable and may have an impact. In the absence of further evidence, what is excreted is considered to be present in the environment. The proposed approach to be followed in those cases was to minimize volumes.
Some additional areas to further consider were suggested such as the impact at workplace, the usefulness of OECD guidelines even if intended for another scope than nanomedicines.

Session 6: International outlook for Nanomedicines

Chairperson: Yoshikazu Hayashi (MHLW/PMDA Liaison Official at the European Medicines Agency)
European Medicines Agency: Emer Cooke (International liaison officer)

An overview of the regulatory approaches and perspectives from different regulatory agencies was presented and discussed in this session.

Current initiatives in the US

By Carlos Peña, U.S. Food and Drug Administration

The U.S. Food and Drug Administration (FDA) regulates a wide range of products, including foods, cosmetics, drugs, devices, veterinary products, and tobacco products, some of which may utilize nanotechnology or contain nanoscale materials. Nanotechnology allows scientists to create, explore, and manipulate materials measured in nanometers (billionths of a meter). Such applications can have chemical, physical and biological properties that differ from those of their conventionally scaled counterparts. FDA's presentation on nanotechnology will provide interested parties with timely information about the agency's current perspective on protecting public health in this emerging science area.

Current initiatives in Japan

By Kumiko Sakai-Kato and Toru Kawanishi, Japanese National Institute of Health Sciences / Ministry of Health, Labour and Welfare

Nanomaterials often have physical, chemical, or biological properties that are different from those of materials in larger size. These properties may have potential impacts on a variety of products, and nanotechnology application to pharmaceuticals or medical devices is a typical such example. In Japan, nanomedicines have been regulated within a general framework of the Pharmaceutical Affairs Law on a product-by-product basis by the Ministry of Health, Labour and Welfare (MHLW) and the Pharmaceuticals and Medical Devices Agency (PMDA). At present, we have no specially designed regulations for nanomedicines. However, regulators and reviewers are gathering and analyzing information about the state-of-the-art technology on nanomedicines. In this presentation, MHLW/PMDA activities were introduced with respect to nanomedicines, approved nanomedicines in Japan, and the future issues on evaluation of nanomedicines.

Based on the "Science and Technology Basic Law" enacted in 1995, MHLW has been promoting applications of nanotechnology to therapeutics and diagnostics through the allocation of research grants and collaboration with other ministries. A new section was established at the National Institute of Health Sciences (NIHS) for conducting researches on evaluating and ensuring the quality of nanomedicines. Because the size-specific interaction with biological systems or biodistribution may have significant impacts on the efficacy and safety of nanomedicines, studies of the physicochemical properties, pharmacokinetics, and pharmacodynamics have been conducted. These studies would contribute to identify which quality attributes of nanomedicines are critical to efficacy and safety. Other important MHLW-supported research includes health effect evaluations of manufactured nanomaterials. These include research on methodology for health risk assessment of nanomaterials especially focusing on long-term effects.
At present, several kinds of nanomedicines have been approved in Japan, including lipid microspheres and liposomes. Because research into the application of nanotechnology to pharmaceuticals is very active in Japan, regulators, reviewers, and government researchers should keep up with the latest relevant scientific findings. Based on these findings, research outcomes at NIHS, and dialogue with industry and academia, we would envisage developing a points-to-consider document for the development and manufacturing of nanomedicines and to explore the possibility of future regulation of nanomedicines.

Current initiatives in Canada

By Duc Vu, Health Canada

Abstract unavailable at time of publishing

Panel Discussion:

Discussion started with the status of international harmonization. As mentioned in the workshop introduction from Patrick Le Courtois, in June 2009, an informal international working group on nanomedicines was established to give regulatory authorities the opportunity to share experiences, approaches and initiatives specific to nanomedicines. The current workshop is an example of outcome of such international cooperation.
Other fora were mentioned such as the WHO, ISO or OECD, providing frameworks for further international collaboration on nanotechnology. Also ICH (International conferences of harmonisation) was mentioned as possibility.

The need to engage with clinicians for the setting, and design of trials was highlighted, and the opportunity to consult regulatory agencies via scientific advice procedures was re-emphasised.

Way forward

By Marisa Papaluca, Head of Scientific Support and Projects, European Medicines Agency

The current regulatory framework based on benefit/risk approach is adequate for the development and evaluation of current "nano" applications in pharmaceuticals. New methods are accepted to complement the relevant existing guidelines and new features will be assessed as they emerge. Nanomedicines are not a homogenous group, with specialised systems engineered to a nano-scale with variable complexity

The ways we look at and act on health and disease could change due to emerging and advanced applications of nanotechnology, as might the ways we develop, approve and use medicines. Scientific understanding of the interaction between cells and nanomedicines in biological systems is rapidly evolving: immunological, metabolic and pharmacological activity is being enriched by novel and additional physical/chemical dimensions linked to how cells "see" and "respond" to "nano" properties.

Nanotechnology is developing globally, quickly and across many applications. Continued early dialogue is therefore essential for regulatory scientists to keep abreast with innovation and relevant new assessment methods. As previously unattainable effects are influencing the paradigm for future medicines, the requirements underpinning the established benefit/risk methodology need to adapt and evolve accordingly.

As orientations emerging from the workshop, the following actions were proposed:

1. Facilitate the early scientific dialogue and knowledge transfer among regulatory, academic and industrial innovators and extend the expertise available to identify risks and opportunities arising from scientific advice, qualification of novel methods, marketing authorization and new tools for risk assessment and management.

2. Dedicate international workshops to the monitoring of scientific progress in emerging nanomedicines, with the engagement of civil society, in order to anticipate patients' needs.

3. Expand multidisciplinary regulatory platforms to share experience, to learn from neighbouring frameworks, and promote convergence on requirements structuring the focus on borderline aspects, where appropriate.

4. Ensure appropriate dialogue with stakeholders to develop a common language to communicate with society on such complex scientific matters.

4. Biographies from the speakers

Dr. Patrick Le Courtois

Dr. Le Courtois is a qualified medical doctor from the University of Paris (France) and post graduate in Public Health from the University of Bordeaux (France).
After a career in Clinics and Public Health, he joined the French Regulatory Authorities in 1990, in charge of European Procedures; he has been a CPMP member.
In 1997 he joined the EMA were he had responsibilities as Head of Sector for Chemicals and for Sector Orphan Drugs and Scientific Advice. He was responsible for the implementation of the European Orphan Drug legislation for the Agency and was ICH Co-ordinator for the Agency for several years. He is Head of Unit for Human Medicines Development and Evaluation since 2001.

Dr. Philippe Martin, MBA, DEA, MS, PhD

A decision analyst, economist, and environmental physicist by training and trade, Dr. Philippe Martin provides advice on issues at the science/policy interface and, specifically, emerging risks for the Health and Consumers Directorate-General of the European Commission (SANCO). His team supports the Scientific Committee on Emerging and Newly Identified Health Risks [1].
Before joining SANCO, Dr. Martin held international posts in research policy, innovation financing, and atmosphere/biosphere research.
Dr. Martin earned an MBA from the ESSEC Graduate School of Business in Paris, a DEA from the University of Paris-Dauphine and the French Nuclear Commission, and MS and a PhD from the University of California at Berkeley (Fulbright Scholar).
[1] http://ec.europa.eu/health/scientific_committees/emerging/index_en.htm

Prof. Rutledge Ellis-Behnke

He is a Professor at Heidelberg University, Mannheim Faculty of Medicine, where he is the Director of the Nanomedicine Translational Think Tank. In addition, he is a Research Affiliate in the Brain and Cognitive Sciences department at the Massachusetts Institute of Technology. Previously he was Associate Director of the Technology Transfer Office and Associate Professor in the Faculty of Medicine at the University of Hong Kong. His primary research interest is using nanotechnology to reconnect the disconnected parts of the brain in order to restore function.
Ellis-Behnke received his PhD from MIT in Neuroscience, BSci from Rutgers University and graduated from Harvard Business School's International Senior Managers' Program (AMP/ISMP).
Prior to returning to school to pursue his PhD, Ellis-Behnke held various management positions including Senior Vice President of Huntingdon, a public company for testing and consulting services and Co-founder/CEO in 1995 of one of the first internet companies to do online commerce.
Ellis-Behnke is Associate Editor/Neurology for the journal Nanomedicine: Nanotechnology, Biology and Medicine; member of both the Executive and Scientific Advisory Boards for the Glaucoma Foundation; member of the Executive Board of the Asia Foundation for Cancer Research; member of the China Spinal Cord Clinical Trial Network, Society for Neuroscience, American Chemical Society, Association for Research in Vision and Ophthalmology and Sigma Xi, the scientific research society.
Technology Review named his "Nanohealing" discoveries one of the "Top 10 Emerging Technologies of 2007." His "Nano Neuro Knitting" and "Immediate Hemostasis" technologies have each been licensed for translation to humans.

Dr. Jean-Louis Robert

Dr Jean-Louis Robert studied chemistry at the University of Basle (CH) and obtained his Ph.D. there in 1976. He had a post-doctoral training at the Pharmaceutical Institute of the "Eidgenössische Technische Hochschule" (ETH) in Zurich (CH). He spent one year with a pharmaceutical company before joining the National Health Laboratory (LNS) in Luxembourg. In his current position he is head of the Department of Control of Medicines, an official medicines control laboratory (OMCL) at the LNS; this OMCL is a member of the European Directorate for the Quality of Medicines OMCL network (Council of Europe, Strasbourg).

He is a member of the Committee for Human Medicinal Products (CHMP) since 1995 (co-opted member since 2004) at the European Medicines Agency (EMA) in London and chairman of the CHMP/CVMP Quality Working Party since 1995.
Within the International Conference on Harmonization (ICH), he is or was involved in the following topics: Validation of Analytical Procedures (Q2) as rapporteur, Common Technical Document-Quality as rapporteur, revision of the guidelines on impurities (Q3A and Q3B) as rapporteur, Pharmaceutical Development (Q8 and Q8R1), Pharmaceutical Quality System (Q10) and currently he is rapporteur for the Implementation Working Group ICH Q8, Q9, Q10.
At the European Pharmacopoeia, he is a member of the Commission and of the group of experts 10 B (synthetic products). Currently he chairs the Steering Committee of the Certificate of Suitability of the European Pharmacopoeia.
He serves as a pharmaceutical expert at WHO. He is a "membre correspondant étranger" at the French "Académie National de Pharmacie".

Prof. Mamoun Muhammed

Mamoun Muhammed is Chair Professor and Head of the Division of Functional Materials and Director of the Nano-Characterization Centre, at the Royal Institute of Technology (KTH), Stockholm, Sweden. He received his B.Sc. from Cairo University and his Ph.D. and D.Sc. from KTH. He has published 8 books and book chapters, 200 papers and 20 patents. He has given over 250 conference and seminar presentations and more than 60 plenary, keynote and invited talks. He is the Chairman of Egypt's National Committee on Advanced Materials and has been the Chairman of the International Committee on Nanostructured Materials, Chairman of several international conferences and workshops. He has supervised over 40 graduate students.

Dr. Simon Holland

Simon has worked in the pharmaceutical industry for over 20 years. He studied chemistry at Bradford University (UK) followed by a PhD in polymer chemistry at Aston University (UK).
He joined Beecham Pharmaceuticals, Worthing (UK) in 1986 and worked on the formulation development of topical and penicillin drug products. After the merger that formed SmithKline Beecham, Simon worked on the development of neurosciences drug products and has focussed on the development of bio-enhanced formulations for the past 13 years including, with a particular emphasis, sub micron compositions. He was the R&D lead on the commercial scale nanomilling facility project that was opened at GSK Cork (Eire) in 2004.
His current position is Director, Process Understanding & Control, within GlaxoSmithKline Pharmaceutical Development at Ware (UK).

Dr. Jan Möschwitzer

Dr Jan Möschwitzer is Head of Early Pharmaceutical Development at the Sector Product Development and Support of Solvay Pharmaceuticals in Weesp (The Netherlands). Jan has studied pharmacy at the Freie Universität Berlin, Germany. He has received a Ph. D. in Pharmaceutical Technology from the same university for a work in the area of drug nanocrystals. His main research activities are focused on the development of enabling formulations for poorly soluble and poorly permeable compounds. His current responsibilities also include to align the formulation activities at the interface between Research and Development and to redesign development processes to shorten the time to market. Besides his work for Solvay he also teaches undergraduate students at the University of Berlin.

Prof. Marc Pallardy

- Vice-Dean and Director of Research, School of Pharmacy, University Paris-Sud, France.
- Head of the « Signalisation in immunopharmacology and immunotoxicology » laboratory, INSERM UMR-S 996, School of Pharmacy, University of Paris-Sud, France.
- Director PhD program "Innovative therapeutics", University Paris-Sud (250 PhD students)
- Member of the Scientific council, University Paris-Sud, France.
- Chairman "Non clinical" working group, French agency for the Evaluation of Medicinal Products.

- Vice-Chairman « Gene therapy » working groups, French agency for the Evaluation of Medicinal Products.
- Member « Cellular therapy » and "Clinical trials" working groups, French agency for the Evaluation of Medicinal Products.
- Expert to the European Medicines Agency (EMA)
- OECD expert for immunotoxic products
- President of the French society of « Cellular pharmacology and toxicology »(SPTC)
- Associate editor for Toxicological Sciences and Journal of Immunotoxicology.

Dr. Wim De Jong

Dr Wim De Jong has graduated as veterinarian in 1978, and received his PhD in veterinary science in 1985. He has a registration as Toxicological Pathologist, and has currently a position as senior researcher at the National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands. He is member of ISO TC 194 Biological Evaluation of Medical Devices, and chairman of the corresponding European CEN TC 206, member of ISO TC 229 Nanotechnology, and vice-chair of the EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR). He has a special interest in immunotoxicology and safety evaluation and risk assessment of nanomaterials and medical devices.

Dr. Jacques Descotes

Dr Descotes obtained a MD, PharmD and PhD degree. He is currently Professor of Medical Pharmacology at Claude Bernard University in Lyon, France, and head of the Poison Center and Pharmacovigilance Department at Lyon University Hospitals. He is a fellow of the US Academy of Toxicological Sciences and a Eurotox Registered Toxicologist. Dr Descotes has been in the field of immunotoxicology for more than 30 years and is the author of ten books in nonclinical and clinical toxicology, especially immunotoxicology.

Prof. Kenneth Dawson

Kenneth Dawson is Director of the Centre for BioNano Interactions (CBNI), the Irish national platform for excellence in the interaction of nanoparticles with living systems (www.cbni.eu).
Prof. Dawson is currently steering the development of this as a national core excellence facility in bionanosciences, and is the lead investigator of the Bionanoscience Activities in University College Dublin. He is Chair of Physical Chemistry, and a Director of the Complexity Centre in Rome. Prof. Dawson also has considerable experience in the management of EU projects, including multi-sectoral cross-disciplinary research projects, and currently co-ordinator of several cross EU and EU-US programs, including FP6 NanoInteract, and FP7 Neuro Nano. He has received several international prizes, including most recently the 2007 Cozzarelli prize from the National Academy of Sciences USA, as well as IBM, Packard, Canon, Sloan and Dreyfus prizes.
Prof. Dawson's professional roles include representing Ireland on the OECD and ISO working groups on standards for Nanotechnology, acting as a European representative in ICON (International Council on Nanotechnology). He is currently Editor of Current Opinion in Colloid Science, Senior Editor of Physica, and a former President of the European Colloid and Interface Society. Professor Dawson is Chairing the launch of the International Alliance on NanoEHS Harmonisation (http://nanoehsalliance.org/), a new global partnership of scientists from EU, US, and Japan to drive efforts to build consensus and standardized protocols for nanotoxicity testing. This has attracted support from governments, agencies, institutions, industry, and NGOs as a vehicle to help ensure the safe implementation of nanotechnology.

Dr. Eric Abadie

Membership in the European Medicines Agency's scientific committees:
- Chairman of the Committee for Medicinal Products for Human Use (CHMP), since 2007
- Member of the Committee for Orphan Medicinal Products (COMP), since 2001
- Member of the Committee for Proprietary Medicinal Products (CPMP) (1997 – 2004)

Membership in Agency working parties/groups:
- Chairman Pharmacogenetics Working Party, since 2001

Professional background
Current position:
- Scientific Advisor to the General Director, AFSSAPS, Paris, France

Other relevant positions:
- Director Therapeutic Evaluation, AFSSAPS, Paris, France (1994 – 2007)
- Director of Development, Laboratoires Wellcome (1992 – 1994)
- Director of Medical Affaires, SNIP (1984 – 1992)
- Adjunct Professor, Diabetology, Hopital Saint-Louis Paris (1981 – 1984)

Education
- Executive MBA, Centre Perfectionnement Affaires, Paris (1992)
- Physician, qualification in Internal Medicine, Cardiology, Diabetology

Areas of expertise and research interests
- Cardiology
- Diabetology

Prof. Daan Crommelin

Prof. Daan Crommelin is presently scientific director of the Dutch Top Institute Pharma in Leiden, a public private partnership with a €60 million annual budget aiming at bridging the gap between academic and industrial research. He is also professor at the Department of Pharmaceutics at Utrecht University. He is adjunct professor at the Department of Pharmaceutics and Pharmaceutical Chemistry at the University of Utah.
Crommelin is co-founder of OctoPlus, a Leiden based company specialized in the development of pharmaceutical product formulations and advanced drug delivery systems.
He is published extensively, was European Editor of Pharmaceutical Research, and is on the editorial board of 10 peer reviewed journals in the pharmaceutical sciences. He is on the (advisory) board of venture capital groups.
He chaired the Board of Pharmaceutical Sciences of the International Pharmaceutical Federation (F.I.P.), was chair of the organizing committee of the Pharmaceutical Sciences World Conference 2007 in Amsterdam. He was president of the European Federation of Pharmaceutical Sciences (EUFEPS) and is presently vice-chair of the scientific advisory board of the European Innovative Medicines Initiative (IMI).
He was scientific director of the Utrecht Institute for Pharmaceutical Sciences (UIPS) from its inception until 2003 and dean of the Faculty of Pharmaceutical Sciences from 2003-2006. In 2006 he was vice-dean of the Science Faculty of Utrecht University until he left for the Top Institute Pharma in Leiden.
In his career he has taught Bachelor and Master courses in biopharmacy, pharmaceutics and pharmaceutical biotechnology. He edited the textbook 'Pharmaceutical Biotechnology' which has been translated in Italian and Chinese. Three editions have appeared between 1995 and 2007. The fourth edition is in preparation. He started the successful Prestige Master programme Drug Innovation at Utrecht University. At present he is running the course Introduction in Drug Discovery and Development for Ph.D. students.

Prof. Ruth Duncan

Ruth Duncan is Professor Emerita at Cardiff University being previously Director of the Centre for Polymer Therapeutics at Keele University, and the London and Welsh Schools of Pharmacy. She also worked for Farmitalia Carlo Erba (Pharmacia) in Milan as Head of New Technologies and was Project Team Leader during the transfer of the first polymer anticancer conjugates/imaging agents into first clinical trials. She has contributed >250 scientific articles and patents, and has been the recipient many awards including; Pfizer Research Award, Young Investigator Award CRS, Interdisciplinary Award RSC UK, Berlin-Brandenberg Academy of Sciences Monika Knutzner Award for Innovative Cancer Research, GSK Intl. Achievement Award. She is a Fellow of Assoc. Pharm. Sci. and Technol. Japan (2009), and Corresponding Member of the Academy of Sciences, Mainz. Elected Co-Chair of the GRC Drug Carriers in Biology and Medicine (1998), the British Pharmaceutical Conference (2004), she also chaired the Steering Committee of the ESF's Forward Look on Nanomedicine (2003-2005). She is a member of the EMA Ad-Hoc Advisory Group for Nanomedicine and past member of MHRA CPS sub-committee.

Prof. Rogério Gaspar

Full Professor at the Faculty of Pharmacy University of Lisbon (FFUL, Portugal).
He is also a member of the Executive Committee of the European Federation for Pharmaceutical Sciences (EUFEPS) and member of the adhoc expert group in Nanomedicines of the European Medicines Agency (EMA).
Current research interests of his group (~30 researchers) are aimed at objectives including the development of new therapeutic strategies using liposomes, polymeric biodegradable nanoparticles, and polymer therapeutics. His personal main focus in research is currently oriented towards cytosolic delivery of nucleic acids and use of targeted delivery systems for combination therapy in cancer.

Dr. Paula Salmikangas

Dr. Salmikangas is a biochemist by original training, with a Ph.D. in muscle cell biology. Her main research work career has been in cell and molecular biology of various inherited diseases. Since 2006, she has been an Associate Professor of Biochemistry for the University of Helsinki.
Dr. Salmikangas has worked as a senior researcher at the Finnish Medicines Agency since 2003. Her main areas of expertise are biological medicinal products, especially cell-based medicinal products and combination products. Dr. Salmikangas has been a member of Cell Products Working Party (CPWP) in the European Medicines Agency (EMA) since 2005 and a chairperson of CPWP since 2007. She is also a member and vice-chair of the Committee for Advanced Therapies (EMA).

Prof. Alexander Kabanov

Dr. Kabanov received his Ph.D. degree in chemical kinetics and catalysis in 1987 at Moscow State University, USSR. Prior to joining the University of Nebraska Medical Center in 1994, he pioneered the use of polymeric micelles and DNA/polycation complexes for drug and gene delivery. He co-founded Supratek Pharma, Inc., Montreal, Canada, which develops therapeutics for the treatment of cancer. He leads the field of "polymer genomics" that investigates effects of polymers and nanomaterials on cellular responses to develop safe and efficient therapeutics. He has over 200 scientific papers, and over 100 patents worldwide. His work has been cited over 8,000 times (Hirsh index 51).

Dr. Jöns Hilborn

Jöns Hilborn is since 2001 the head of the Polymer Chemistry program at the Department of Materials Chemistry, Uppsala University in Sweden. His research interests are in the design, synthesis and preparation of polymers and specifically materials for tissue scaffolds and as delivery vehicles. Special focus is on cell free injectables for bone formation. Effort is also being placed on the reason for the formation of a fibrotic capsule around implants where recent findings suggest that biomechanics is one key promoter. He received his PhD from the Royal Institute of Technology in Stockholm. This was followed by seven years in industry before he joined the Swiss Federal Institute of Technology for eight years. He has published some 150 scientific papers, 25 patents and has started 4 companies.

Prof. Peter Dobson

He is currently the Director of Oxford University's Begbroke Science Park.
After a career as a lecturer in Physics at Imperial College and Senior Principal Scientist at Philips Research laboratories he was appointed to a University Lectureship and College Fellowship at the Queen's College Oxford in 1988 and a Professorship in 1996. Between1999 and 2000 he spun-off two companies, Oxonica and Oxford Biosensors and he advises several others. He was appointed to his present position in August 2002 and has created a new Science Park and developed a range of Knowledge Transfer activities. He is also currently (2009-2012) the Strategic Advisor on Nanotechnology to the Research Councils in the UK

P J Dobson, BSc, MA (Oxon), PhD, C Phys, F Inst P, Member of the ACS.

Dr. Peter Arlett

Education: Qualified in medicine from University College London (UCL) in 1991 and after specialising in hospital medicine, in 1994 became a Member of the Royal College of Physicians (MRCP) of London. In 2002 became a Member of the Faculty of Pharmaceutical Medicine (MFPM) of the Royal College of Physicians of London and in 2004 also became Honorary Senior Lecturer in the Department of Medicine at UCL. In 2007 became a Fellow of the Faculty of Pharmaceutical Medicine (FFPM) of the Royal College of Physicians of London.
Career to date: After his basic training in medicine he worked as a hospital physician in Oxford and at the Hammersmith Hospital (Imperial College). Joined the UK Medicines Control Agency (now MHRA) in 1996 where he had various responsibilities as a specialist assessor and manager. In 2001 he was appointed UK delegate to the European Committee for Human Medicinal Products (CHMP). In 2003 he joined the Pharmaceuticals Unit, DG Enterprise and Industry of the European Commission as Principal Administrator where his responsibilities included: international relations, pharmacovigilance (including lead responsibility for the revision to legislation), implementation of new pharmaceutical legislation, medicines for children (including lead responsibility for the new legislation 'the paediatric regulation'). He joined the European Medicines Agency in September 2008 as Head of Pharmacovigilance and Risk Management.

Dr. Annalisa Rubino, MSc, PhD

Annalisa Rubino is a Pharmacoepidemiologist within the Agency's Risk Management team. Dr Rubino has over 20 years of research experience in drug development within the academic and pharmaceutical environment. Before joining the EMA in February 2010, she was a Research Scientist at the Medicine and Healthcare product Regulatory Agency (MHRA) in the UK and subsequently she has been working in consultancy for the pharmaceutical industry in the arena of therapeutic risk assessment and drug safety. She has published more than 50 papers in peer reviewed clinical journals, including the British Medical Journal, Trends in Pharmaceutical Sciences, Diabetic Medicine.

Dr. Jan Petracek

Dr. Jan Petracek is executive and senior consultant at PharmInvent. His previous positions include Head of Risk Management Section of the European Medicines Agency, Head of Strategy and Development and Head of Pharmacovigilance at the National authority in the Czech Republic. He qualified as a physician from Charles University in Prague and holds an MSc with distinction in Quality and Safety in Healthcare from Imperial College London. He has 10 years of experience in pharmacovigilance and patient safety, he was a member of CHMP Pharmacovigilance Working Party, and participated in development of several national, European, ICH and CIOMS guidelines.

Dr. Silvia Berkner

Dr. Silvia Berkner studied environmental sciences at the University of Bayreuth (Germany) with the major subjects being Hydrology and Environmental Chemistry/Ecotoxicology. After graduating in 2002, she worked for a CRO company for analytical chemistry in Zirndorf (Germany). In 2003, she returned to the University of Bayreuth as a PhD student at the Department for Biochemistry. She received her PhD in Biochemistry in 2007 and continued to work at the University as PostDoc. Since January 2009 she has been employed with the German Federal Environment Agency in Dessau and works in the field of Environmental Risk Assessment of Pharmaceuticals.

Mr. Yoshikazu Hayashi

Current Position
MHLW/PMDA Liaison official at the European Medicines Agency
Professional Experience
Mr. Hayashi joined the Japanese Ministry of Health and Welfare (now the MHLW) in 1986. Since then he held a variety of positions including in the Pharmaceutical Affairs Bureau, Health Insurance Bureau, Minister's Secretariat, and Health Policy Bureau. From 1998 to 2001, he worked for the WHO/ International Programme on Chemical Safety in Geneva, Switzerland. He served as the ICH

coordinator for MHLW from 2002 to 2003. He has held his current position at the EMA since November 2009.

Dr. Carlos Peña

Dr. Carlos Peña is a Senior Scientific Policy Advisor in the Office of the Chief Scientist, within the Office of the Commissioner, at the FDA. He currently serves a lead role in the development of the agency's approach to science, policy and research needs for nanotechnology. His position involves service on the FDA Nanotechnology Task Force composed of key officials across the agency and establishing and enhancing partnerships with national and international regulatory agencies as well as other stakeholders focussed on nanotechnology.

Dr. Kumiko Sakai-Kato

Kumiko Sakai-Kato received her B.S. and M.S. degrees from the University of Tokyo. She developed her career as a research scientist at Daiichi Sankyo Co., Ltd. She received her Ph.D. degree in analytical chemistry at the University of Tokyo in 2004. After postdoctoral work at the Japan Society for Promotion of Science, she became an assistant professor at Musashino University. In 2008, she became a section head of Division of Drugs at the National Institute of Health Sciences. Her research field is analytical science for drug evaluation.

Dr. Toru Kawanishi

Dr. Toru Kawanishi graduated from the University of Tokyo, Faculty of Pharmaceutical Sciences, and joined the National Institute of Health Sciences (NIHS), the Ministry of Health, Labor, and Welfare (MHLW) in 1978. He has published about 180 scientific papers in the field of drug metabolism, chemical toxicology, biochemistry, and pharmaceutical sciences. Dr. Kawanishi is currently the Head of the Division of Drugs in the NIHS. He is a temporary member of the Pharmaceutical Affairs and Food Sanitation Council in Japan and is contributing to review quality aspects of registration applications of new drugs, and to revise the Japanese Pharmacopoeia and the Regulatory Requirements for pharmaceuticals.

Dr. Duc Vu

Dr. Duc Vu holds a MSc. in Toxicology and a PhD in Pharmacology from the University of Montreal. He also received a post-doctoral training in molecular pharmacology at the Environmental Health Research Center-Health Canada. He also received a certificate on applied epidemiology and drug development.

Since 1993, Dr. Duc Vu has been working in several organizations within Health Canada including the Pesticides Management Regulatory Agency (PMRA), the Therapeutic Products Directorate (TPP) and the Marketed Health Products Directorate (MHPD).

Prior to joining MHPD in May 2008 as the Director of the Bureau of Marketed Biologicals, Biotechnology and Natural Health Products, Dr. Vu held the position of Director of the Bureau of Cardiology, Allergy and Neurological Sciences within the Therapeutic Products Directorate of Health Canada. Dr. Vu is one of the key members working on the development and implementation of Risk Management and Pharmacovigilance planning activities in Health Canada.

Dr. Vu's scientific interests are in toxicology, pharmacology and pharmacovigilance.

Prof. Marisa Papaluca Amati

She qualified as a medical doctor in Rome in July 1978 and is a specialist in internal medicine. She did post-graduate studies in cardiology and endocrinology.

From 1978 to 1983 she was a research fellow in the State University of Rome in the area of clinical immunology, oncology and cellular immunology. From 1984 to 1994, at the Pharmaceutical Department of the Italian Ministry of Health, she was in charge as medical director of the Operative

Centre for Community Procedures and was Italian member of the former Committee for Proprietary Medicinal Products also involved in a number of ICH activities.

She joined the Agency in October 1994 where she acted as scientific secretary of the Biotechnology Working Party until December 2000. She was appointed Deputy Head of Sector for safety and efficacy of medicines in January 2001 and since then she has also been in charge of Agency activities in the field of innovation at EU and international level. She is currently Head of section for Scientific Support & Projects.

5. Overview of participation

In total over 200 experts from all over the world attended the 1st International Workshop on Nanomedicines.