European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Ad hoc CHMP Expert Group Meeting on "Nanomedicines"

29th April 2009

European Medicines Agency

Executive summary

Nanoscale materials are used in medicinal products for many purposes including drug delivery systems, modified release formulations, carriers, diagnostics, and structures in regenerative medicine.
Several nano-size medicinal products have been authorized in the European Union either following the centralized procedure for the scientific evaluation of the Agency (http://www.emea.europa.eu/pdfs/human/genetherapy/7976906en.pdf)[i] or at national level, indicating the availability in the EU of experience in the regulatory evaluation network (Fig. 1).

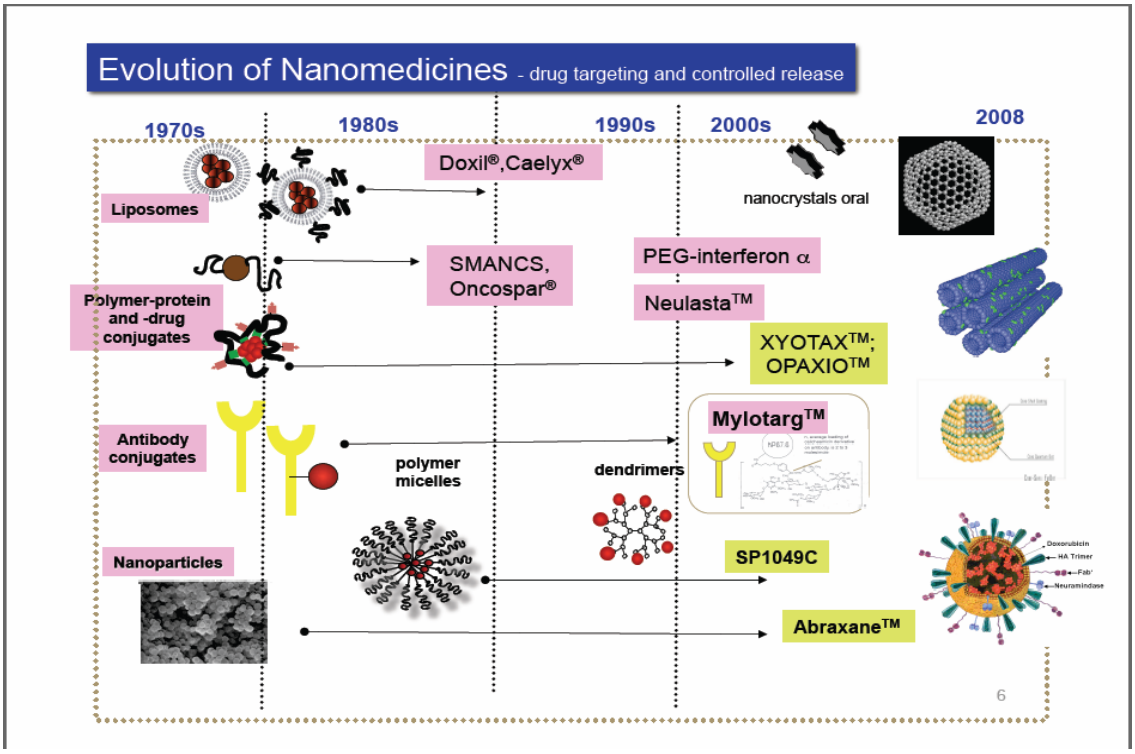


Figure 1: Evolution of nanomedicines
From R Duncan (2009)

Growing activities in the field are well represented by the sharp increase worldwide in patents especially since 2000[ii] (Fig 2).

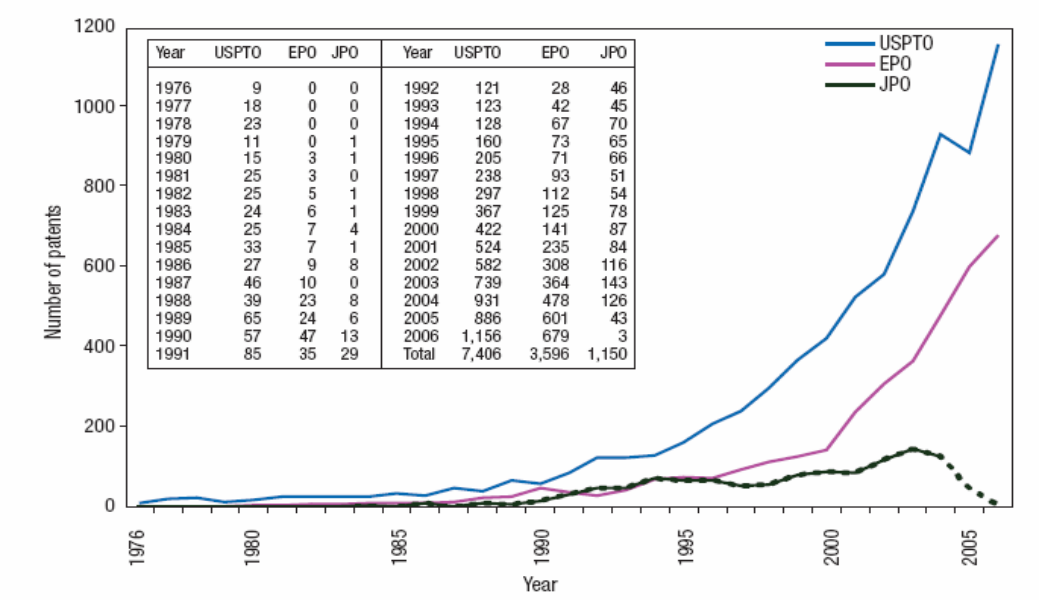


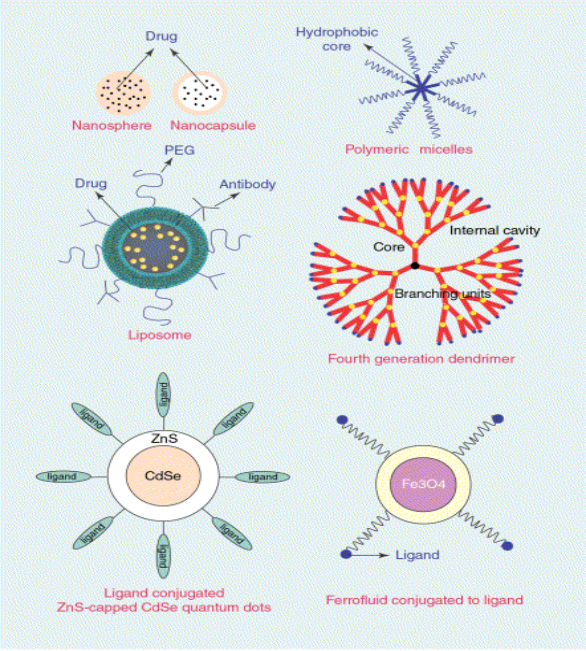
Figure 2: Trend in nanotechnologies patents
From H. Chen et al [ii]

Regulatory challenges are similar to those posed by other emerging technologies in terms of: adequacy of existing guidelines, acceptability of new testing methods, and availability of ex-parts in the network.

An additional challenge of emerging nanotechnologies in pharmaceuticals is represented by the wide spectrum of their applicability and the very diverse characteristics of resulting "nanomedicines" (Fig. 3).

The Agency's think-tank group on innovative medicines development http://www.emea.europa.eu/pdfs/human/itf/12731807en.pdf [iv] recommended that "the ongoing activities at the level of the Agency in support of the development of emerging therapies and technologies should be reinforced" as "there are particular challenges related to the introduction of these therapies [including medicines based on nanotechnology etc.] into the market". In addition DG SANCO (Directorate General for 'Health and Consumers'), in the report from their second meeting on nano-safety held in November 2008, recommended "regulators to provide clear guidance on how to interpret regulatory frameworks and clear indications to the public about action being taken in cases where relevant risk data is limited or uncertain".
Initiatives are being taken to better inform the Agency, the experts network and the industry about what is known, needed, and expected for nanomedicines: the establishment of the ad-hoc expert group in 2009 and the planning of a main conference in 2010, intend to reinforce the EMEA activities in this technology area.

The Agency held the first meeting of the ad-hoc "nanomedicines" expert group on the 29th of April 2009, set up with the objective of reviewing technical and regulatory experience on "nano-medicines" evaluation and identifying gaps and further needs. The group is composed of academic experts and competences gathered in the EMEA network, supported by the EMEA Innovation Task Force (ITF):
http://www.emea.europa.eu/pdfs/human/itf/itfmandate.pdf



- ✓ Polymeric biodegradable nanoparticles
- ✓ Ceramic (inorganic) nanoparticles
- ✓ Polymer systems and polymeric micelles - (amphililic block copolymers)
- ✓ Liposomes
- ✓ Dendrimers
- ✓ Nanocrystals (Quantum dots)
- ✓ Magnetic nanoparticles (e.g. iron oxide for MRI)
- ✓ Transdermal delivery (e.g. Nanoneedles etc.)

Figure 3: Nanoscale materials of potential use in medicinal products
From Sahoo S.K. – Labhasetwar V. (modified) [iii]

The experts presented an independent view on the main emerging aspects to be considered in the evaluation of medicines based on nanotechnologies. Scientific and technical topics were discussed as interconnected elements of the necessary holistic approach to nano-pharmaceuticals' regulatory evaluation: terminology, key aspects in manufacturing and characterization, specific issues associated with cellular biology and biological testing, non-clinical pharmacology and toxicology models, pharmacokinetics and target delivery, and clinical considerations (see experts' presentations).
The experience gained by the Agency, derived from data of nanomedicines submitted to the Agency will further be discussed with the expert group in relation to current guidelines to identify and address any significant gaps in this area.

Conclusion

There is, in the EU, long-standing experience both at research and at regulators' level for a number of established approaches (e.g. some "traditional liposome" formulations). It is now useful to take stock of what requirements and methods have been considered acceptable for these nano-pharmaceuticals in order to complement the relevant guidelines.

On the other hand, in view of the limited regulatory experience with other new and emerging nano-pharmaceuticals, the dialogue at an early stage with the Agency, sponsors and stakeholders is essential.

For this purpose, formal and informal dialogue opportunities are available at the Agency and are advertised on the EMEA webpage on Medicines and Emerging Science: http://www.emea.europa.eu/htms/human/mes/support.htm.
In addition the experience gathered at the Agency will form the basis for the agenda of the Agency's first international workshop on nanotechnologies planned for 26-27 April 2010.
For future information on the workshop, please go to our "Events" webpage:
http://www.emea.europa.eu/meetings/conference.htm

Acknowledgements for editorial work to Martine van Rooyen

References

[i] Reflection Paper on Nanotechnology-based Medicinal Products for Human Use | EMEA/CHMP/79769/2006 | June 2006

[ii] Trends in nanotechnology patents | H. Chen et al | Nature Nanotechnology | VOL 3 | March 2008

[iii] Sahoo SK – Labhasetwar V | Nanotech Approaches to Drug Delivery and Imaging | Drug Discov Today | 2003 Dec 15;8(24):1112-20 Review

[iv] Final Report from the EMEA/CHMP-Think-Tank Group on Innovative Drug Development | Doc. Ref. EMEA/127318/2007 | March 2007