

A success story in these challenging times

Andrew Sandham¹ (✉) and Qingsong Ye² (✉)

¹ School of Human Sciences, University of Western Australia (UWA), Perth 6009, Australia

² Centre of Regenerative Medicine, Renmin Hospital of Wuhan University, Wuhan 430060, China

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A quantum leap in medicine often starts as a small step in research or an innovative development which leads to a greater understanding and application to previously untreatable diseases.

Nanoparticles have powers never fully appreciated a generation ago. The application in clinical medicine as a novel delivery system with powers to target therapeutic agents and deliver tailor-made diagnostic and treatment approaches, made for the individual patient, is a quantum change in the whole field of medical practice and patient management.

The ability of nanoparticles to cross tissue barriers, is changing the whole concept of the appropriate clinical management in previously untreatable diseases. The blood–brain barrier (BBB) is indeed a challenge in providing early diagnosis in preventing amyloid plaques building up in the brain, that may contribute to the devastating effects of Alzheimer's disease. Nanoparticles offer a route for the transportation and delivery of potential agents that can cross this BBB.

Enormous challenges need to be overcome to develop and refine the transition of results from the research laboratory to the clinical setting. This involves ethical issues present in human clinical trials and careful consideration by the approval agencies. These challenges require process controls, audit, and accountability, which should be a part of a quality system in any medical care.

A quality system needs clear application documentation together with methods of patient-centred evaluation during clinical trials. A clinician-centred evaluation helps the maintenance of standards through process controls and inter- and intra-centre audits of outcome and helps to identify problems when treatment is provided to the patient.

The transition from laboratory to patient of new nanoparticle therapies needs to be successful and problem-free. Many variables come into play when providing quality of clinical care for the patient, and we have to be certain that we occasion no harm and treatment is based on evidence that it will work, and in these days of finite resources it has to be cost effective.

The World Health Organisation (WHO) has a focus on quality in clinical care and on recognising new approaches to treatment of disease in human populations. It provides assistance and guidelines for implementation of new approaches to care.

National and international audit and approval pathways should be developed and streamlined to ensure this quantum change is fully regulated. There is a worldwide non-governmental Federation of National Standards Organizations representing more than 160 countries. Their standards (ISO 9000) are sets of definitions and processes to help create documents for a quality system. They are not specific to any industry. So the basic concepts of Quality Management can be applied to research, clinical trials, and therapeutic applications.

ISO 9001 has more application in the transfer of nanoparticle therapy from laboratory to the patient, as it specifies the requirements for a quality system to consistently provide services that meet patient and regulatory requirements [1]

Each stage of the transfer from the research centre to the clinic can then be documented. This produces a process and a check list which should be followed to ensure that, not only is the process well defined, but also the entire transfer can be evaluated and improved. This continuous review and evaluation can identify problems and ensure improvements are made when issues occur during the transfer from the laboratory to a clinical trial and from the clinical trial to clinical treatment.

Modern research methodology requires the development of a clear protocol with appropriate statistical evaluation and a cautious interpretation of outcome results. This is usually a requirement for the project funding required. There are occasions where projects funded by large research donors may be looking for quick results and subsequent clinical application. This is where problems can arise without strong regulatory approval and process controls in place to ensure the efficacy of the therapy and it is without significant side effects.

The WHO issued *Flexible Guidelines of Transfer of Technology in Pharmaceutical Manufacturing* in 2011 which has a role to play in the transfer of nanoparticle therapy from the laboratory to the patient [2]. This doesn't replace the Quality Control aspects played by the ISO 9001 certification but does offer some broad flexible guidelines to consider.

However, is the nanoparticle a medical device or just a therapeutic transport medium? This needs to be clarified as there are ISO certifications for the manufacture of medical devices to ensure consistency of application, but to have too many certifications and standardizations tends to be confusing.

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Address correspondence to Andrew Sandham, asandham@yahoo.com; Qingsong Ye, qingsongye@whu.edu.au

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The ISO 9001 addresses the quality of the whole process of transfer while the WHO *Flexible Guidelines on Transfer of Technology in Pharmaceutical Manufacturing* is also a useful additional publication.

This coming issue of *Nano TransMed* comprises many bright ideas in nanomedicine and transformation. Hu et al. provided insights of type-I photodynamic therapy in tumours; Wan et al. updated the advances in biomimetic nano-hydroxyapatite for bone regeneration; Mu et. al proposed the application of natural product-based nanoparticles in managing the brain injury after a stroke; Jing et al. summarized the potential of telomere biology and telomerase in stem cell-based therapy. As highlighted by Ni and Chen, there are many challenges/barriers in current applications of nano-technologies. Also, we firmly believe that

a standardised and robust system with a certain degree of flexibility may provide an optimal solution to the bench to bed transformation. Taken together, advances in nanomedicine already made are providing the basis for a whole new approach to treatment of diseases and with careful development and controlled application this is proving ‘a success story in these challenging times’.

References

- [1] ISO Standards. ISO 9001: 2015 Quality Management Systems Requirements, 2015.
- [2] World Health Organization. WHO guidelines on transfer of technology in pharmaceutical manufacturing (Annex 7), WHO Technical Report Series, No. 961, 2011.



Andrew Sandham, B.D.S. (Dunelm, UK), Ph.D. (University of Edinburgh, Scotland); FDSRCS, Royal College of Surgeons, Edinburgh, UK; Doctor of Odontology (Ministry of Education and Science, Madrid, Spain); Tandarts (The Netherlands); Fellow, Academy of Medicine Singapore; Fellow, Royal Society of Medicine London, UK.

Previously: Professor of Dento-maxillary orthopaedics, State University, Groningen, Netherlands; Professor of Dental Science and Dean of Dentistry, James Cook University, Cairns, Queensland, Australia.

Present position: Research Fellow, University of Western Australia. School of Health Sciences. Australia.



Qingsong Ye is a full professor of Orthodontics/Plastic Surgery and the Director of Center of Regenerative Medicine at Wuhan University. Prior to this, he was a visiting professor at Massachusetts General Hospital, Harvard Medical School (Boston, USA), tenured professor at School of Dentistry, University of Queensland (Brisbane, Australia), Director of UQ-WMU Institute of Stem Cell and Tissue Engineering at Wenzhou Medical University (Wenzhou, China), and Head of Orthodontic department at James Cook University (Cairns, Australia). He obtained two Ph.D. degrees (in dentistry and in medical science), his Medical Ph.D. degree is from University of Groningen (Groningen, The Netherlands), with a focus on biomaterials and regenerative medicine. He is a diplomat of Royal College of Surgeons Edinburgh, UK, a fellow of World Federation of Orthodontists, a fellow of International College of Dentists, and an elected fellow of Royal

Society of Medicine, UK. He has received numerous awards including Discovery ECR Award, Albert-Nelson Marquis Lifetime Achievement Award, etc. Professor Ye's research interests include bioactive nano-materials, dental stem cell & iPSCs, nature derived & synthetic scaffolding biomaterials, and foreign body reaction against biomaterials. His work leads to over 110 original scientific papers in high impact dental and medical journals, including *Advanced Materials*, *Nano Research*, *Biomaterials*, *Bioactive Materials*, etc. Professor Ye has a long-standing editorial experience and has served as associate editor/editor/guest editor for a dozen of biomedical journals and regular referee for over 50 SCI journals. He is the founding Editor-in-Chief of *Nano TransMed*.