



March 2, 2014

Current issues with nanomedicines

By Adeline Siew, PhD

Raj Bawa, PhD, shares insight on the unresolved issues in nanomedicine development.

Current issues with Nanomedicines The global market for nanomedicines has been experiencing a strong growth and is expected to reach a value of \$177.60 billion within the next five years according to a report by Transparency Market Research (1).

Advances in nanotechnology have seen a number of nanomedicines successfully progress from the laboratory bench to the clinic with the majority of applications focused on drug delivery, such as solubility/ bioavailability enhancement and better drug targeting. Despite that, there are several issues in nanomedicine development and commercialization that remain unresolved, for example, imprecise patent classification, patent proliferation and the lack of a universal nano-nomenclature among others. To gain further insight on these interrelated issues, *Pharmaceutical Technology* spoke with Raj Bawa, PhD, patent agent at Bawa Biotech LLC (Ashburn, VA, USA), scientific advisor at Teva (Israel) and adjunct professor at Rensselaer Polytechnic Institute (Troy, NY, USA).

PharmTech: Can you talk about the current issues with nanomedicines primarily from a patent and regulatory perspective?

Bawa: Securing valid, defensible patent protection from the US Patent & Trademark Office (PTO) along with clearer regulatory/ safety guidelines from FDA are crucial to the commercialization of nanomedicines. Since the early 1990s, in light of inadequate search systems and exploding 'prior art,' the PTO has issued duplicate nanotech patents and/or patents of questionable validity to entities often called 'patent prospectors,' and a kind of 'nanopatent land grab' has continued ever since. Another problem is that the PTO continues to classify US nanopatents into Class 977 where they currently number less than 10,000. These numbers and classification system, however, are clearly inadequate because they are based on the ill-conceived National Nanotechnology Initiative (NNI) definition of nanotechnology that limits all nanostructures and nanoproducts to a subnanometer range (i.e., 1–100 nm). The shortfalls with this definition, especially for nanomedicine, are well documented. As a result, these numbers are an under-estimate and, therefore, miss the majority of patents (out of approximately 8 million US patents issued) that are nanotech-related. In fact, the confusion and ambiguity surrounding the definition of nanotechnology and nanomedicine continues to be one of the most significant problems shared by regulators, policymakers, researchers, and patent practitioners.

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Another major issue is the lack of a universal nano-nomenclature whereby distinct terms frequently refer to identical or similar nanostructures or nanomaterials. As a result, in certain sectors of nanotech, 'patent thickets' exists today that could stifle commercialization efforts in future. It is time to seriously consider governmental action under the Bayh-Dole Act of 1980 whereby an imposition of compulsory licensing or

exercise of march-in rights needs to be considered. Even the creation of an open-source type process to rectify the erroneous issuance of some of these basic, upstream nanopatents should be contemplated so that downstream development of nanomedical products is not stifled.

Advances in nanomedicine and the FDA system for governing nanomedicines are inevitably intertwined. The 'baby steps' that FDA has undertaken during the past decade have, however, led to regulatory uncertainty. At the moment, only draft FDA guidelines exist. Whether FDA eventually creates entirely new regulations or tweaks existing ones, the FDA Commissioner should officially announce that it will review nanomedical products on a sciencebased, case-by-case basis.

The toxicity of many nanoscale materials is not fully apparent. Premarket testing of nanomedicines will not detect all adverse reactions and it is crucial that long-term safety testing be conducted. Therefore, postmarket tracking or a surveillance system must be adopted to assist in recalls. Toxicity data specific to nanomaterial need to be collected and an effective risk research strategy devised. FDA should seriously contemplate nano ingredient labeling on a case-by-case basis since there are few to no reliable means for a consumer to identify marketed 'nano-containing' products. The agency has data on liposomal drugs that dates back to the 1950s. Perhaps data that pertains to 'nanoliposomes' can be compiled and released into the public domain as such data will be invaluable to a potential sponsor developing nanoliposomal medicines (which the majority of current nanomedicines are).

PharmTech: What is the future outlook for nanomedicines especially now that the pharmaceutical industry is moving away from the blockbuster model towards more targeted therapies such as personalized medicines?

Bawa: With the demise of pharma's blockbuster model, in future, novel 'multifunctional/ multicomponent' nanomedicines will be designed as new generations of drug-delivery systems to target specific organs, specific tissues, or even specific organelles.

As we rapidly enter the age of nanotheranostics, these novel 'combination drugs' will present additional challenges for FDA because the agency's current 'primary mode of action' (PMOA) regulatory paradigm may prove ineffective. Furthermore, some of these complex nanomedicines can be classified as NBCDs (e.g., Copaxone), which could present additional issues for FDA as it reviews generic versions of these NBCDs. NBCD generics will almost always lack bioequivalence to their referenced NBCD, thereby, prompting submission of clinical data from the generic drug developer. In any case, as various manufacturing and toxicology bottlenecks are overcome, the long-term development of nanomedicines will hinge on effective nanogovernance and patent reforms requiring the full commitment of various governmental entities (e.g., FDA, Congress, PTO, EPA) as well as the regulated community (i.e., big pharma and the manufacturing sector).

Reference

3. Transparency Market Research, *Nanomedicine Market (Neurology, Cardiovascular, Anti-inflammatory, Anti-infective, and Oncology Applications)—Global Industry Analysis, Size, Share, Growth, Trends and Forecas^{4t}, 2013–2019*, accessed Feb. 7, 2014.

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