

The Big Deal About Nanotechnology

Most people are aware of nanotechnology and the anticipated impact that it will have on our daily lives. News stories focused on various aspects of nanotechnology are becoming more common, and worldwide government funding of this burgeoning field is in the range of billions of dollars per year. Stain-resistant clothing, increased computing power and speed, lighter and stronger building materials, and new tools for the diagnosis and treatment of disease are among the predicted outcomes of research at the nanoscale. But what exactly is the nanoscale anyway, and why is there so much hype over it?

The definition of a nanoparticle is generally considered to be a particle with at least one dimension of 100 nm or less (for reference, the width of a human hair is approximately 80,000 nm). As a result of their small size and unique physicochemical properties, the biological effects of nanoparticles may differ considerably from those of larger particles composed of the same materials. While these properties present unique opportunities to tailor nanomaterials for specific therapeutic uses, they also present new challenges with regard to determining potential adverse effects of nanomaterials that may be due to the same properties.

Nanotechnology is being developed and applied in diverse ways in the pharmaceutical and healthcare fields. Examples include increasing the relative surface area of drug substances by nanosizing them to increase their water solubility and improve oral delivery; encapsulating drug substances in a nanoscale carrier to prolong their circulation time and achieve more desirable pharmacokinetic profiles; employing targeted nanosized therapeutics and imaging agents to minimize off-target effects and allow for enhanced pictures of diseased tissue; and using nano-based "lab-on-a-chip" diagnostics

to allow for more samples/targets to be processed per unit of tissue or time. An ultimate goal of many researchers is to develop multi-functional nano-based products that can chaperone and release drugs to a specific tissue or cell type, sense and signal molecular responses to therapeutic agents, image biomolecular processes, and possibly guide surgical procedures *via* enhanced imaging. This sounds great, doesn't it? But how do regulatory agencies view a product such as this, never mind a simpler nano-based therapeutic agent with only one desired function?

Regulatory agencies regulate products, not technologies. Consistent with this, Health Canada, the United States (U.S.) Food and Drug Administration, and the European Medicines Agency have indicated that existing regulatory requirements and procedures likely will suffice for most nano-based products that they will regulate, but acknowledge that new approaches may be required as more knowledge is gained. A common challenge is to define the appropriate regulatory route for nano-based products, particularly those that are multi-functional. Issues related to chemistry, manufacturing, and controls also are common. For example, how do you define purity (and deviation from purity) for a nano-based drug that may be composed of multiple entities, have a distribution profile for its primary particle size, may aggregate, and may also have a surface coating? Questions such as this are tricky to answer, but will need to be answered more frequently as more and more nano-based therapies are brought before the regulators.

There is no question that the "nanotechnology revolution" is upon us. While it is predicted to be enormous, only time will tell how much impact this revolution will have on the pharmaceutical and healthcare industries.

UPDATE: Ashuren has been acquired by Intertek

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Are You Ready for E-Working?

Although the electronic Common Technical Document (eCTD) is widely accepted across many regions, many smaller companies may still be reluctant to take the leap.

The hesitation in changing business practices are easy to see; lack of in-house expertise, costs of implementing an e-working environment, eCTD publishing, but also the understanding by senior executives to go electronic, are often the main stumbling blocks. In addition, if the change is not mandatory, why bother implementing eCTD? However, these concerns should not stop you in moving your organization forward into the realm of e-working.

Health Canada, the Food Drug and Administration (FDA), and Member States in the European Union (EU) all agree that the benefits of moving from paper to electronic submissions will reduce administrative overheads and minimize delays in routing and tracking, reduce archiving space and costs, and most importantly, will increase review efficiency.

The advantages of switching early from paper to electronic is not just for the big pharma companies, but can save time and money for the smaller companies:

- Gives personnel time to learn, understand and prepare pilot systems before going full scale.
- Investment can be minimised with a considered approach and what works best with in-house support and what can be out-sourced.
- Creates time to develop in-house expertise and knowledge.

Currently, Health Canada accepts hybrid submissions (full submission in eCTD filing format that is accompanied by Modules 1 and 2 in paper-based CTD format) for New Drug Submission (NDS), Abbreviated NDS (ANDS), Supplemental NDS (SNDS), Supplemental ANDS (SANDS), and Notifiable Changes (NC). Effective January 2010, Health Canada no longer accepts co-submissions (a submission in eCTD format that accompanies a complete paper-based submission in CTD format). In addition, Health Canada will accept selected submission types in eCTD electronic-only filing format: Periodic Safety Update Reports (PSUR); Risk Management Plans (RMP); Yearly Biologic Product Reports (YBPR); and Drug Notification Forms (DNF) and Forms summarizing the Post Notice of Compliance (NOC): Notices of Change (Level III) if related to a previously filed submission for a drug product in eCTD format. Reviewers prefer electronic as it allows easy access to the files as well as allowing for multiple review teams to have access at the same time.

Although the FDA currently accepts both paper and electronic submissions, electronic review will eventually become standard practice. FDA has been accepting electronic-only submissions for a vast range of submission types for

some time now, such as marketing applications [New Drug Applications (NDAs), Abbreviated NDAs (ANDAs), Biologic License Applications (BLAs)], Investigational New Drug (IND) applications, and related submissions (master files, advertising material, and promotional labeling).

It is evident that these two major players in the pharmaceutical regulatory affairs industry, are well on their way to one day making it mandatory to submit submissions in electronic-only format. Submissions to The European Medicines Agency (EMA) are now only accepted in electronic format. Paper submissions are not an option.

So the time for procrastination is over and the time to take the first step towards e-working is right now. Here are some key features of switching from paper to eCTD to take back to your organization:

- **Environmentally friendly** – Eliminates the need to waste paper and thus saving trees;
- **Time** – Routing paper both internally and at the Agency takes time and causes delays. An electronic submission is uploaded and available immediately;
- **Space** – Significantly reduce physical storage costs (no need for fireproof document cabinets) for both company and agency;
- **Savings** – Reduces costs for paper, printing, and shipping;
- **Automation** – Eliminates compiling and managing paper submissions. No need to take over entire conference rooms to put together multiple copies of massive 100 volume submissions. The entire submission can be available on the company network, allowing employees easy access from any location 24/7;
- **Communication** – Easily update during review process, reducing response time to queries which ultimately leads to reduced review time and faster approval by the Agency;
- **Reuse** – Reuse, rather than having to recreate submission components that will be used in other indications, or doses or submitted to other Agencies;
- **Efficiency** – Improves accuracy of the submission cross referencing and links, reduces time to filing, increases efficiency of Agency review and thereby reduces time-to-market;
- **Lifecycle management** – Helps in tracking creation, review and updates to submissions, amendments, licenses, queries, and product status; and lastly
- **Happy Reviewers** – Most reviewers prefer electronic over paper. Pulling up a 3-year old submission and being able to see a historical view in just a few clicks of the mouse, is far better than spending hours in a file room or looking through boxes, pulling out volume after volume to find what you are looking for.

So don't waste any more time, take that first step, it may not be as painful as you think. Or call us if you need new shoes!

Regulatory Highlights

FDA

- [Organ-Specific Warnings: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use—Small Entity Compliance Guide](#) [2010-08-17]
- [Label Comprehension Studies for Nonprescription Drug Products](#) [2010-08-03]
- [The Radioactive Drug Research Committee: Human Research Without An Investigational New Drug Application](#) [7/30/2010]
- [Bioequivalence Recommendations for Specific Products](#) [2010-06-10]
- [Q8, Q9, and Q10 Questions and Answers International Conference on Harmonisation - Quality](#) [2010-05-05]
- [Information Sheet Guidance for Sponsors, Clinical Investigators, and IRBs Frequently Asked Questions – Statement of Investigator \(Form FDA 1572\)](#) [2010-06-04]

Health Canada

- [Notice - Increased Scope of Submissions being accepted in Electronic Common Technical Document \(eCTD\) Format and acceptance of electronic-only submissions](#) [2010-08-20]
- [Management of Product Licence Applications \(PLA\) for Natural Health Products](#) [2010-08-19]
- [Notice - Health Canada 3011: Drug Submission Application Form for Human, Veterinary, Disinfectant Drugs and Clinical Trial Application/Attestation](#) [2010-06-15]
- [Food and Drug Regulations - Project 743 - Non-medicinal Ingredients Labelling \(NMI\) \(SOR/2010-105\)](#) [2010-06-04]
- [Release of the finalized Guidance Document: Non-Clinical Laboratory Study Data Supporting Drug Product](#)

[Applications and Submissions: Adherence to Good Laboratory Practice](#) [2010-04-30]

- [Release of Frequently Asked Questions related to Health Canada's Guidance Document: Disinfectant Drugs](#) [2010-04-27]

EMA

- Scientific guideline: [Guideline on quality, non-clinical and clinical aspects of live recombinant viral vectored vaccines, adopted](#) [2010-08-10]
- Scientific guideline: [Guideline on the clinical investigation of human normal immunoglobulin for intravenous administration \(IVIg\), adopted](#) [2010-08-02]
- [Clinical efficacy and safety: Radiopharmaceuticals and Diagnostic Agents](#) [2010-08-29]
- [European Medicines Agency communication on \(emerging\) safety related issues for medicines for human use](#) [2010-07-20]
- Scientific guideline: [Guideline on declaration of herbal substances and herbal preparations in herbal medicinal products/traditional herbal medicinal products in the SPC, adopted](#) [2010-04-28]
- [Enhancing quality assurance of API manufacture](#) [2010-04-14]
- Regulatory and procedural guideline: [Conduct of inspections of pharmaceutical manufacturers or importers, adopted](#) [2010-04-06]

ICH

- [E7: Studies in Support of Special Populations: Geriatrics Questions & Answers Status: Step 5](#) [2010-07]



At Ashuren, we are a team of experienced professionals that specialize in scientific and regulatory consultancy. Our focused team of consultants provides strategic advice on:

- Regulatory Affairs
- Product Development Programs
- Submission Preparation and Review
- Toxicology
- GLP Monitoring and Compliance
- Clinical Planning

If you have any questions, comments, or require further information in regards to any information provided in this document, please do not hesitate to contact:

Ratinder Brar
at rbrar@ashuren.com
or 1-877-244-4844
www.ashuren.com

Contact Information...

United States

1319 Lake Forest Circle
Hoover, Alabama
35244

1011 US Highway 22
Suite 200
Bridgewater, New Jersey
08807-2950

Canada

2233 Argentia Road
Suite 308
Mississauga, Ontario
L5N 2X7

Europe

Branksome Chambers
Branksonewood Road
Fleet, Hampshire, UK
GU514JS

Asia

160-0002
Matsuda Bld. Finesis
6-29-20, Shinjuku
Shinjuku-ku, Tokyo