Pharma News & Views

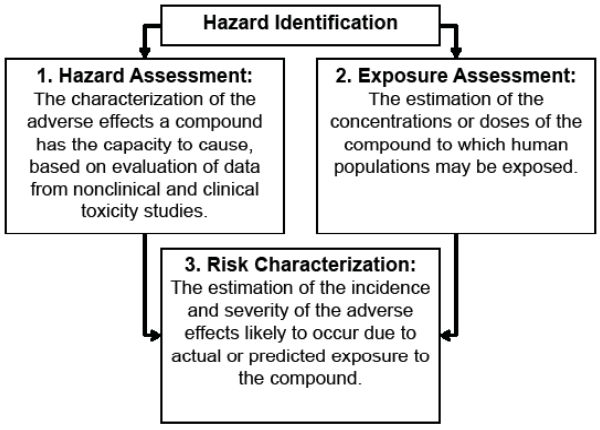
MARCH 2011 EDITION

Risk Assessment 101

Despite the precautions and safety practices that are in place, leaks from machinery, processing equipment, and medical devices, or product tampering, and contaminated ingredients from suppliers are just a few potential sources of compromised products requiring action. Without adequate evaluation and proper perspective, the consequences may include harm to consumers, loss of public confidence, and possible litigation.

A risk assessment is the process by which relevant toxicological data on a compound and the potential for exposure to this compound are brought together to produce a description of the nature and magnitude of the resultant risk (*i.e.*, determining the likelihood that an injury or adverse effect would occur; risk characterization).

The 3 main elements of a risk assessment



In instances where nonclinical or clinical data on the compound are not publicly available, a risk assessment can still be conducted using structure-activity principles. In certain cases, it may be beneficial to use structurally related substances to assess the hazardous nature of a particular compound or it may be necessary to consider combining the exposure to related compounds which are thought to possess a common mechanism of action to ensure the potential for adverse effects is not underestimated.

Risk assessment is a useful application for addressing concerns associated with leachables from medical devices, the presence of residual solvents and other processing agents in finished products, the safety of selected excipients, and other scenarios. Cantox's team includes experts with a wealth of experience in risk assessment. We can assist with risk assessment requirements necessary for product development, to meet regulatory requirements, and to assist in litigation. In addition, we can characterize realistic risks associated with inadvertent contamination of various product types to reduce uncertainty and provide a foundation for safety. Please contact us for more information on our risk assessment capabilities.

Ashuren Name Change

A few years ago, we announced that the Pharmaceutical & Healthcare Group within Cantox Health Sciences Inc.(Cantox) had changed their name and became known as Ashuren Health Sciences (Ashuren). There were no changes in our services, just a rebranding of the Pharmaceutical and Healthcare Group.

Last year, Cantox was acquired by Intertek, a worldwide leader in a diverse range of services to support global pharmaceutical, biotechnology, healthcare, and medical device industries. With the acquisition of Cantox (including Ashuren) by Intertek, it is necessary to make changes to the Ashuren name to avoid any confusion in who we are. The name change does not reflect any changes in the toxicology and regulatory consulting services offered. As always, we will continue to deliver high quality consulting services to our pharmaceutical and healthcare clients.

Our professional team of consultants and support staff look forward to serving your business needs and protecting your company's interests. If you have any questions, or would like additional information about our services, please call or email your normal contact at Ashuren/Cantox or info@cantox.com.

Ask Us!

You asked us: We submitted our product license application (PLA) more than 2 years ago, why is the Natural Health Products Directorate (NHPD) taking so long to make a decision? What is the NHPD doing to get my product reviewed in a timely manner?

The Issue

In 2004, the Natural Health Product (NHP) Regulations (NHPR) came into force stating that for the first time, all products meeting the regulatory definition of a NHP had to receive premarket approval from Health Canada through a PLA process. This created a concern for the vast majority of NHPs currently sold on the Canadian market. As the NHP industry is well aware, when the NHPR came into force there were no timelines for review and approval for PLA applications other than those claiming monograph, abbreviated labelling standard, or labelling standard compliance. This created even more frustration and uncertainty within the industry, putting applicants into a difficult position - Do they remove their marketed products from the market until they file a PLA and a decision is made (in the interim losing money)? Or do they continue to sell and run the risk of compliance action from Health Canada?

To address this problem administratively, Health Canada initially set out in its Compliance Policy that products that had obtained a submission number would not be targeted for compliance and enforcement action, except in cases where a risk is identified. **However, the National Association of Pharmacy Regulatory Authorities (NAPRA) raised concerns on this practice and through its January 2010 Position Statement advised its members not to sell any unlicensed products.** This created a potential for disruption in the market place as well as legal and credibility issues for the NHPD.

As a result, the NHPD has been forced to take a more proactive role in addressing this issue.

What is the NHPD doing?

In August 2010, the NHPD brought into effect new NHP (Unprocessed Product Licence Applications) Regulations [NHP(UPLA)R]) to allow for the legal sale of NHPs for which Health Canada has not yet issued a product licence but has completed an initial assessment of the PLA to ensure that information supporting the safety, quality and efficacy of the product has been provided, and that specific safety criteria have been met. These regulations hence allow certain NHPs to continue to be sold in Canada while they complete the full licensing process. This has brought a huge relief to the NHP industry.

How will this work?

The NHP(UPLA)R will permit the legal sale of unlicenced NHPs under certain conditions. NHPs for which PLAs have been in the submission queue for at least 180 days, will be eligible for an exemption number (allowing subsequent sale of those NHPs), provided that they do not meet certain risk criteria, in conjunction with on-market safeguards such as the filing of safety information upon request, the reporting of adverse events, the maintaining of proper labelling and the stop sale upon demand provisions in place to protect the safety of Canadians during the interim.

All products which have been assigned an exemption number will list the number on the NHP label in the form EN-XXXXXX. This number will be publicly accessible on Health Canada's website, along with the name of the product and the company name.

What do I need to do?

If you have an NHP on the market and you have not filed a PLA, you must act immediately.

If you have already filed a PLA, check the date of filing to see if it has been in the queue for 180 days to be able to opt into the NHPD program and apply for an exemption number.

Once an exemption number is assigned, the product can be sold with the exemption number on the label.

How can I take advantage of these regulations?

The NHP(UPLA)R will be repealed 30 months after they come into force (*i.e.*, February 2013); therefore, PLAs submitted less than 180 calendar days before this sunset date would not be eligible, since they could not be in queue for greater than 180 calendar days. To take advantage of these regulations for those intending to submit PLAs, timing of your submission is critical.

The Latest News–The New Compliance and Enforcement Policy

Furthermore, in August 2010, the new Compliance and Enforcement (C&E) Policy was implemented. The NHP C&E Policy describes the compliance and enforcement approach respecting NHPs under the Food and Drugs Act (FDA) and the NHPR. The implementation of this new NHP C&E Policy was followed by a 6-month compliance promotion transition period, slated to end on March 1, 2011. In December 2010, the NHPD announced to its stakeholders that the compliance promotion transition period is now being extended and the implementation of the new NHP C&E Policy will be postponed until further notice.

What does this mean?

Until such time that the C&E Policy is implemented, if manufacturers continue to market their products, they are still responsible to ensure that the products do not pose risk to the consumers.

To sell new NHPs in Canada, not only is the timing of submissions critical, but efforts should also be made to ensure that documents are complete and of high quality. Cantox encourages all companies who have not yet registered their products with the NHPD, to do so immediately. We can assist you with filing your PLA and liaise on your behalf with Health Canada. Please contact Alia Pais (apais@cantox.com) or Ratinder Brar (rbrar@cantox.com).

Regulatory Highlights

FDA

- ANDAs: Impurities in Drug Products [Nov. 2010]
- Antibacterial Drug Products: Use of Noninferiority Trials to Support Approval [Nov. 2010]
- Guidance for Industry and FDA Staff - Class II Special Controls Guidance Document: Tissue Adhesive with Adjunct Wound Closure Device Intended for the Topical Approximation of Skin [Nov. 2010]
- Guidance for Industry: Cellular Therapy for Cardiac Disease [Oct. 2010]
- Codevelopment of Two or More Unmarketed Investigational Drugs for Use in Combination [Dec. 2010]
- Investigational New Drug Applications (INDs)-Determining Whether Human Research Studies Can Be Conducted Without an IND [Oct. 2010]

Health Canada

- Notice - Submissions Seeking Changes to the Product Monograph Sections: (a) Clinical Trial Adverse Drug Reactions (3.5.2 - 3.5.3) and; (b) Post-Market Adverse Drug Reactions (3.5.5) [Dec. 2010]
- Questions and Answers for the Guidance for Industry: Preparation of Drug Submissions in the eCTD Format [Dec. 2010]
- Notice - Instructions for Submitting Drug Notification Forms (DNF) and Supporting Documents in Electronic Format [Dec. 2010]
- Mandatory Problem Reporting for Medical Devices (GUI-0059) [Jan. 2011]
- Voluntary Problem Reporting for Medical Devices (GUI-0060) [Jan. 2011]
- Guidance for the Interpretation of Significant Change of a Medical Device [Jan. 2011]

EMA

- Questions & answers on quality of herbal medicinal products/traditional herbal medicinal products [Nov. 2010]
- Guideline on the minimum quality and non-clinical data for certification of advanced therapy medicinal products [Nov. 2010]
- Practical information for sponsors during the early phase of an orphan drug application [Nov. 2010]
- Guideline on clinical investigation of medicinal products in the treatment of hypertension [Dec. 2010]
- European Medicines Agency procedural advice for users of the centralised procedure for generic/hybrid applications [Jan. 2011]
- Guidance on centrally authorised products requiring a notification of a change for update of annexes [Feb. 2011]

Contact Information...

At Cantox Health Sciences International, an Intertek Company, 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@cantox.com
or 1-877-244-4844
www.cantox.com

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
Branksomewood Road
Fleet, Hampshire, UK
GU514JS

Asia
COI Eitai Bldg. 7F.
2-31-1, Eitai Koto-Ku
Tokyo, Japan
135-0034