**THE GMP GAZETTE™**

January 2016

<table>
<thead>
<tr>
<th>CANADA (HEALTH CANADA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HPFBI</strong></td>
</tr>
<tr>
<td>No updates</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>NNHPD</strong></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th><strong>NHPs</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Notice to Stakeholders Regarding Site Licensing Update</strong></td>
</tr>
</tbody>
</table>

**Who’s affected?** Manufacturers, packagers, labellers, importers, and distributors of natural health products (NHPs) for sale in Canada

**Summary:**
Health Canada announced the revision and finalizing of the documents entitled [Good Manufacturing Practices (GMP) guidance](#), [Site Licensing (SL) guidance](#), and [Quality Assurance Report (QAR) form](#). The key changes to the GMP guidance are:
- Terminology and interpretation of GMP requirements have been further clarified;
- Examples of evidence that would be expected to demonstrate GMP compliance have been added and/or clarified;
• Extracts of the Regulations have been reintroduced, where applicable;
• Appendix 5 - Risk Classification of NHP GMP Observations has been added.

The key changes to the Site Licensing guidance are:
• Section 2.1 Evidence of GMP compliance - clarified use of alternative standards and/or accreditations;
• Section 3.0 Submission Management - clarified processing timelines for new applications, renewals, amendments and notifications;
• Section 3.1.3 Deficiencies in the Application - revised to include reference to the Risk Classification of NHP GMP Observations and its use as a tool for NHP stakeholders;
• Extracts of the Natural Health Products Regulations (NHPR) reintroduced where applicable;
• Appendix A - Guidance on how to obtain a Foreign Site Reference Number (FSRN) added;
• Removal of Health Canada recognized third-party auditors and associated audits, in line with the update above.

The key changes to the Quality Assurance Report Form are:
• Consolidated questions relating to premises to improve clarity;
• Clarification regarding stability program requirements.

This Notice includes details regarding three specific changes:
• Implementation of Service Standards for Site Licensing
  o Revised service standards are outlined in Table 1 of the Site Licence guidance document and will apply to applications received on or after April 1, 2016.
• Licensees claiming no activity at renewal
  o To ensure that license holders are able to demonstrate compliance to the regulatory requirements, applications for renewal will be refused if no activity is claimed to have occurred in the 12 month period preceding a renewal
• Site Licence renewal reminder
  o The NNHPD will no longer be sending courtesy emails to site licence holders reminding them of their site licence expiration or obligation to submit an application for renewal as per section 36 of the Regulations

This Notice also includes an update on the revised approach to NHP Site Licensing proposal paper which was posted for consultation from January to April 2014, and the associated on-site audit pilot program.

What’s the impact? Stakeholders need to comply with these Guidances as of their effective date (December 1, 2015)
A number of Final Monographs have been posted at [What’s New](#) on December 8, 2015

**Who’s affected?** Companies preparing Product Licence Applications (PLAs) and labels for natural health product market authorization

<table>
<thead>
<tr>
<th>Listing of Final Monographs:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final Monograph for Hydrocortisone</td>
</tr>
<tr>
<td>Final Monograph for Maitake</td>
</tr>
<tr>
<td>Final Monograph for Poria</td>
</tr>
<tr>
<td>Final Monograph for Mushrooms</td>
</tr>
<tr>
<td>Final Monograph for Pygeum</td>
</tr>
<tr>
<td>Final Monograph for Aromatherapy</td>
</tr>
<tr>
<td>Final Monograph for Indole-3-carbinol</td>
</tr>
<tr>
<td>Final Monograph for 3,3'-Diindolymethane (DIM)</td>
</tr>
<tr>
<td>Final Monograph for Soy Flour</td>
</tr>
<tr>
<td>Final Monograph for Betaine/Betaine Hydrochloride</td>
</tr>
<tr>
<td>Final Monograph for Olive Leaf</td>
</tr>
</tbody>
</table>

**What’s the impact?** Stakeholders must be aware of the content of these Monographs to ensure their PLAs are accepted.
**Classification of Medicated Vapour Products - Health Canada Notice 2015-12-08**

**Who’s affected?** Companies marketing medicated vapour products, available as topical rubs, patches, plug-ins (inserts or pre-filled) and solutions for use in vapourizers or humidifiers.

**Summary:**
- The purpose of this Notice is to communicate to industry and health care professionals that medicated vapour products containing ingredients such as eucalyptus, menthol and/or camphor are classified and regulated as drugs under the *Food and Drugs Act* (FDA).
- It outlines the principles and considerations applied in determining whether or not these products are over-the-counter (OTC) drugs or natural health products (NHPs).
- To assist those medicated vapour products classified as NHPs to transition to the NHP regulatory framework, the Department has developed a Medicated Vapours monograph [Medicated Vapours](#).

**What’s the impact?** Individuals looking to market medicated vapour products have the opportunity to make representation to Health Canada on the classification of their products if required/desired. Questions regarding Medicated Vapour Products and delivery devices that are not prefilled can be sent to the contact numbers and addresses mentioned in the posting.

Posting date: December 8, 2015

**DISINFECTANTS**

No updates

**NON-PRESCRIPTION DRUGS**
**Classification of Medicated Vapour Products - Health Canada Notice 2015-12-08**

**Who's affected?** Companies marketing medicated vapour products, available as topical rubs, patches, plug-ins (inserts or pre-filled) and solutions for use in vapourizers or humidifiers.

**Summary:**
- The purpose of this Notice is to communicate to industry and health care professionals that medicated vapour products containing ingredients such as eucalyptus, menthol and/or camphor are classified and regulated as drugs under the *Food and Drugs Act* (FDA).
- It outlines the principles and considerations applied in determining whether or not these products are over-the-counter (OTC) drugs or natural health products (NHPs).
- To assist those medicated vapour products classified as NHPs to transition to the NHP regulatory framework, the Department has developed a Medicated Vapours monograph [Medicated Vapours](#).

**What’s the impact?** Individuals looking to market medicated vapour products have the opportunity to make representation to Health Canada on the classification of their products if required/desired. Questions regarding Medicated Vapour Products and delivery devices that are not prefilled can be sent to the contact numbers and addresses mentioned in the posting.

Posting date: December 8, 2015

<table>
<thead>
<tr>
<th>TPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>COSMETICS</td>
</tr>
<tr>
<td>No updates</td>
</tr>
<tr>
<td>DRUGS</td>
</tr>
</tbody>
</table>
Draft - Revised Guidance Document: Information and Submission Requirements for Subsequent Entry Biologics (SEBs)

Who's affected? Sponsors that are interested in pursuing subsequent entry versions of biologic drugs with expired patents

Summary:
Health Canada has released a draft version of the revised Guidance Document: Information and Submission Requirements for Subsequent Entry Biologics (SEB Guidance) for consultation.

Key revisions to the SEB Guidance include:
- Section 2.1.3, Reference Biologic Drug: Further guidance is provided in the selection of a reference biologic drug. Also includes revisions to Section 2.1.3.1 Considerations for the use of a non-Canadian reference biologic drug, to provide clarity on establishing a link between the non-Canadian reference and Canadian reference biologic drug.
- Section 2.3.3, Non-Clinical and Clinical Information: Additional detail is provided for performing non-clinical and clinical studies for SEBs, including discussion on immunogenicity, the use of the most sensitive population in clinical trial design and a new section on extrapolation.
- Section 2.4, Post-Market Requirements: Updated information for periodic benefit-risk evaluation reports (PBRERs) and labelling changes for product class type-specific safety information, including Health Canada's considerations in the review of a Supplemental New Drug Submission (SNDS) and use of previously demonstrated similarity provided in the original New Drug Submission (NDS) to support a change.
- Section 3.0, Consultation with the Biologics and Genetic Therapies Directorate: A new section which promotes early consultation with Health Canada, as well as the launch of three year pilot for SEB Scientific Advice Meetings to allow for discussion of an SEB with Health Canada early in the development process.

What’s the impact? This consultation is open for comment until February 15, 2016. Refer to the posting for contact numbers and addresses. For convenience, this template may be used.

Posting date: December 7, 2015

Administrative Changes: Guidance Document - Fees for the Review of Drug Submissions and Applications

Who's affected? Sponsors of new drug submissions (NDS), supplements to a new drug submission (SNDS), abbreviated new drug submissions (ANDS), supplements to an abbreviated new drug submission (SANDS) and drug identification number (DIN) applications

This document:
- Provides guidance on the interpretation of the *Fees in Respect of Drugs and Medical Devices Regulations* with a focus on how the fees for the review of a NDS, SNDS, ANDS, SANDS and DIN application contained in Part 2, Division 1 of these regulations will be administered.
- Underwent an administrative change on November 20, 2015 to Section 2.2.2. As of November 9th, 2015, the Accounts Receivable address has changed.

**What’s the impact?** Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches, supported by adequate justification, should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

Posting date: December 10, 2015

The new Government of Canada National Vaccine Storage and Handling Guidelines for Immunization Providers are now available online, at the following links:

**Who’s affected?** Immunization providers storing and handling vaccines. This is also of interest to companies manufacturing, storing and distributing vaccines.

These guidelines discuss:
- The Cold Chain and the importance of maintaining it.
- Vaccine personnel and storage and handling protocols
- Storage equipment
- Vaccine storage practices
- Temperature monitoring
- Storage troubleshooting
- Cold chain breaks
- Vaccine management (e.g. expiration dates, inventory management)
- Distribution
- Disposal
What’s the impact? Specific recommendations for vaccine storage and handling procedures may vary among public health offices and immunization programs, therefore the document is meant to supplement existing policies rather than replace them. Efficient vaccine storage and handling is a shared responsibility from the time the vaccine is manufactured until it is administered.

Publication date: December 14, 2015

MEDICAL DEVICES

Notice - Transition Plan for the Medical Device Single Audit Program (MDSAP)

Who’s affected? Medical device manufacturers

Summary:
- The Medical Device Single Audit Program (MDSAP) was initiated at the International Medical Devices Regulators Forum's (IMDRF) inaugural meeting in Singapore in 2012.
- The program was designed and developed so that a single audit, performed by an authorized Auditing Organization (AO), meets the quality management system (QMS) requirements of multiple regulatory agencies, derived from the International Organization for Standardization (ISO) 13485:2003.
- The participating agencies are Health Canada, the Australian Therapeutic Goods Administration (TGA), the Brazilian Agência Nacional de Vigilância Sanitária (ANVISA), the Japanese Ministry of Health, Labour and Welfare (MHLW), the Pharmaceuticals and Medical Devices Agency (PMDA), and the United States Food and Drug Administration (FDA).
- The MDSAP pilot was launched on January 1, 2014 and is scheduled to conclude December 31, 2016.
- MDSAP will replace the current Canadian Medical Devices Conformity Assessment System (CMDCAS) program, even in situations when a manufacturer intends to sell only in Canada.
- The implementation will begin at the conclusion of the Pilot on January 1, 2017, and will span a period of two years.
- During this two year period, Health Canada will accept certificates issued under both CMDCAS and MDSAP.

What’s the impact? Stakeholders need to be aware of the timelines for the transition to MDSAP. As of January 1, 2019, only MDSAP certificates will be accepted. Further details will be released as the transition plan is finalized.
Guidance Document - Fees for the Review of Medical Device Licence Applications

**Who’s affected?** Manufacturers submitting Class II, III and IV medical device licence applications and licence amendment applications

This document:
- Provides guidance on the interpretation of the *Fees in Respect of Drugs and Medical Devices Regulations* with a focus on how the fees for the review of medical device licence applications contained in Part 3 of these regulations will be administered.
- Underwent an administrative change on November 20, 2015 to Section 2.2.2. As of November 9th, 2015, the Accounts Receivable address has changed.

**What’s the impact?** Guidance documents are administrative instruments not having force of law and, as such, allow for flexibility in approach. Alternate approaches, supported by adequate justification, should be discussed in advance with the relevant program area to avoid the possible finding that applicable statutory or regulatory requirements have not been met.

Posting date: December 9, 2015

---

USA (FDA)

CDER

DRUGS
Draft Guidance for Industry, *Advancement of Emerging Technology Applications to Modernize the Pharmaceutical Manufacturing Base*

**Who’s affected?** Companies interested in participating in a program involving the submission of chemistry, manufacturing, and controls (CMC) information containing emerging manufacturing technology to FDA as part of an investigational new drug application (IND) or original or supplemental new drug application (NDA), abbreviated new drug application (ANDA), or biologic license application (BLA) reviewed by CDER.

This draft guidance:
- Provides recommendations regarding participation in this program
  - Modernizing manufacturing technology may lead to a more robust manufacturing process with fewer interruptions in production, fewer product failures (before or after distribution), and greater assurance that the drug products manufactured will provide the expected clinical performance
  - Pharmaceutical companies can submit pre-submission questions and proposals about the use of specific emerging technology to a group within CDER (Emerging Technology Team – ETT)
  - Through the ETT, FDA intends to encourage the adoption of innovative approaches to pharmaceutical manufacturing by facilitating the regulatory review of submissions to the Agency involving manufacturing technologies likely to improve product safety, identity, strength, quality, and purity

**What’s the impact?** For comment purposes only. Comments must be submitted either electronically or in writing to the FDA by **February 22, 2016** to ensure the Agency considers them before beginning on the final version.

Issued date: December 23, 2015
### CFSAN

#### COSMETICS

No updates

### DIETARY SUPPLEMENTS

No updates

### CDRH

#### MEDICAL DEVICES
eCopy Program for Medical Device Submissions - Guidance for Industry and Food and Drug Administration Staff

Who’s affected? Companies preparing medical device submissions

This guidance:
- Provides clarification to the processing and technical standards for eCopies based on FDA’s experience to date with the program
  - An electronic copy (eCopy) is defined as an exact duplicate of the paper submission, created and submitted on a compact disc (CD), digital video disc (DVD), or a flash drive. An eCopy is accompanied by a paper copy of the signed cover letter and the complete paper submission.

What’s the impact? For submissions to be processed and accepted for review by FDA, they must include an eCopy in accordance with the standards provided by this guidance, unless they have been identified as being exempted or waived. Submissions submitted without an eCopy, and eCopy submissions that do not meet the standards provided in this guidance will be placed on hold until a valid eCopy is submitted to FDA and verified to meet the standards, unless a waiver or exemption has been granted.

Issued date: December 3, 2015

USP (GENERAL CHAPTERS)

No updates