Post-marketing surveillance of cosmetic products across the globe

SCC ONTARIO CHAPTER MEETING
May 22nd, 2014

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## COSMETOVIGILANCE

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<td>Skills &amp; capabilities</td>
<td>Dermatology, allergy, linguistic coverage, regulatory... Extensive network of health prof.</td>
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<tr>
<td>Clients’ profiles</td>
<td>Industry (Resp. Person and Distributors)</td>
</tr>
<tr>
<td>Coverage</td>
<td>EU + a few countries worldwide</td>
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* Undesirable Effect and ** Serious Undesirable Effect as defined by Regulation (EC) 1223/2009

## CONSUMER STUDIES

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CONTENT

I. Scope of the presentation
II. Americas (USA, Canada, Mercosur)
III. Asia (Japan, China, ASEAN)
IV. Europe (28 Member States (EU) and EEA)
Scope of the presentation

This presentation has a focus on **Cosmetic products**

Depending on the country, a same product can be classified differently: cosmetic, Natural Health Product (NHP), quasi-drug or drug.

Will not be covered in this presentation:

- **The requirements from the European General Product Safety Directive 2001/95/EC**
Basically Cosmetics Vigilance can be defined worldwide as the surveillance of cosmetics after the products are placed on the market.

This monitoring relies on the spontaneous reportings (voluntary or mandatory) of adverse reactions suspected to be related to the use of cosmetics.

Definition from the “Serious Undesirable Effects (SUE) Reporting Guidelines”:

“Cosmetovigilance is defined by the collection, evaluation and monitoring of spontaneous reports of undesirable events observed during or after normal or reasonably foreseeable use of a cosmetic product. Together with other tools, cosmetovigilance contributes to post market surveillance”
Main reference texts

- Food and Drugs Act, modified
- Cosmetic Regulations, modified
- Natural Health Products Regulations (NHPs) and the corresponding modifications

Current situation

1) Consumers

- Should report unwanted side effects (adverse reactions) following the use of a NHP;
- Are encouraged to report adverse reactions to cosmetics (Cosmetic or Consumer Product Incident Report; Form for Consumer)
Cosmetic or Consumer Product Incident Report; Form for Consumer


Form for Consumer

Fields marked with an asterisk (*) must be filled in.
No format required for answers unless otherwise specified. For date field, enter the date using this format: YYYY-MMM-DD or the calendar tool.

Report - Section 1

Report Type: * New
Product Type: 

Who is reporting - Section 2

Relationship to injured / involved person: 
Name: *
Address (number and street): 
Country: Province / Region: 
City: Postal Code: 
Email: Telephone: Fax: 

Privacy Notice

I authorize Health Canada to release my personal information to a person or a government that carries out functions relating to the protection of human health or safety and/or to the supplier of the product so that they may evaluate this incident. Select Yes or No.*
2) Manufacturers / Licensees

<table>
<thead>
<tr>
<th>Cosmetic products considered as drugs in Canada</th>
<th>Serious Adverse Reactions</th>
<th>Serious and Unexpected Adverse Reactions</th>
<th>Annual Summary Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occurring inside Canada: obligation to report within 15 days</td>
<td>Occurring outside Canada: obligation to report within 15 days</td>
<td>Required</td>
<td></td>
</tr>
</tbody>
</table>

| Natural Health Products | Occurring inside Canada: obligation to report within 15 days | Occurring inside & outside Canada: obligation to report within 15 days | Required |

| Cosmetic Products | Encouraged to report any incident (Consumer Product Incident Report ; Form for Industry) | | |
Fields marked with an asterisk (*) must be filled in.
No format required for answers unless otherwise specified. For date field, enter the date using this format: YYYY-MM-DD or the calendar tool.

### Report - Section 1

<table>
<thead>
<tr>
<th>Report Type: *</th>
<th>New</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal Number:</td>
<td></td>
</tr>
<tr>
<td>Product Type:</td>
<td></td>
</tr>
</tbody>
</table>

**Purpose of report:**
- [ ] 14(2) - Information regarding incident (Section 7 not required)
- [ ] 14(3) - Manufacturer/Importer report (Section 7 required)
- [ ] Notification - evaluated as not an incident

**NOTE:** If you have received this report from a customer, you will find your information in Section 6. If you want to report to Health Canada with no changes to the content of the report, go to Where you got the product - Section 6 and click the Confirmation Report button.

### Who is reporting - Section 2

<table>
<thead>
<tr>
<th>Business Name (Full legal name - no abbreviations):</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Address (number and street):</td>
<td></td>
</tr>
<tr>
<td>Country:</td>
<td></td>
</tr>
<tr>
<td>City:</td>
<td></td>
</tr>
<tr>
<td>Postal Code:</td>
<td></td>
</tr>
<tr>
<td>Website:</td>
<td></td>
</tr>
</tbody>
</table>
Main reference texts

- Federal Food, Drug and Cosmetic (FD&C) Act
- Dietary Supplement and Nonprescription Drug Consumer Protection Act (Public Law 109-462)
- Guidance for Industry Postmarketing Adverse Event Reporting for Nonprescription Human Drug Products Marketed Without an Approved Application (July 2009)

Current situation

1) Consumers

Are encouraged to report adverse reactions and quality defects...

- Through the MedWatch Web site “Bad reactions to cosmetics? Tell FDA” (FDA Form 3500 - Voluntary reporting)
- Through the MedWatch Hotline
- By contacting the FDA Consumer Complaint Coordinator of their state
2) Healthcare Professionals

Are encouraged to report adverse reactions and quality defects through the *MedWatch web pages* (FDA Form 3500 - Voluntary reporting) or by calling the *MedWatch hotline*

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**Instructions for Completing Form FDA 3500**

Form FDA 3500 may be used by health professionals or consumers (see NOTE below) for VOLUNTARY reporting of adverse events, product use errors, product quality problems and therapeutic failures for:

- drugs (prescription and over-the-counter)
- biologics, (including blood components, blood derivatives, allergenics, human cells, tissues, and cellular and tissue-based products (HCT/Ps))
- medical devices (including *in vitro* diagnostic products)
- combination products
- special nutritional products (dietary supplements, infant formulas, medical foods)
- cosmetics
- foods/beverages (including reports of serious allergic reactions)
3) Industry (manufacturers, packers and distributors)

A. OTC drug products

In case of Serious Adverse Reaction, and ICSR (Individual Case Safety Report) is to be completed using the FDA Form 3500A - Mandatory reporting within 15 calendar days of initial receipt.

B. Cosmetic products

The 2 most recent bills presented in House of Representatives “Cosmetic Safety Amendment Act of 2012” & “Safe Cosmetics and Personal Care Products Act of 2013” include:

- Mandatory report for the “Serious and Unexpected” adverse events (Cf. bill of 2012) and “Serious” adverse events (bill of 2013)
- Within 15 business days
- To the “Secretary of Health and Human Services”
SEC. 5. SERIOUS AND UNEXPECTED ADVERSE EVENT REPORTING FOR COSMETICS.

Chapter VI, as amended by sections 3 and 4, is amended by adding at the end the following:

"SEC. 606. SERIOUS AND UNEXPECTED ADVERSE EVENT REPORTING FOR COSMETICS.

(a) In General.—The Secretary shall by regulation require that a domestic or foreign manufacturer, packer, or distributor whose name appears on the label pursuant to section 602(b)(1) of a cosmetic marketed in the United States submit to the Secretary under subsection (b) a report containing information received concerning a serious and unexpected adverse event in the United States allegedly associated with the use of the product.

(b) Submission of Reports.—A serious and unexpected adverse event report shall be submitted to the Secretary no later than 15 business days after information
Extract From the Safe Cosmetics and Personal Care Products Act of 2013

(not enacted)

Introduced in House on March 21, 2013

``
SEC. 622. MANDATORY REPORTING OF SERIOUS ADVERSE EVENTS.

(a) Submission of Report on Serious Adverse Events.--The Secretary shall require that the brand owner of a cosmetic whose name appears on the label of a cosmetic marketed in the United States submit to the Secretary a report containing information received concerning any serious adverse event associated with the use of the cosmetic.

(b) Timing of Report.--A report under subsection (a) shall be submitted to the Secretary not later than 15 business days after information concerning the serious adverse event is received at the place of business of the brand owner.

(c) Content of Report.--A report under subsection (a) shall include the following information, to the extent to which the brand owner submitting the report has been able to verify the information:

(1) The identity of the individual experiencing the adverse health event.

(2) An identifiable report of such effect.

(3) The name of the cosmetic suspected of causing such effect.

(4) A description of the adverse health event.

(d) Public Availability and Privacy.--

(1) Public availability.--Subject to paragraph (2), the serious adverse event reports collected by the Secretary under this section shall be submitted electronically and shall be made accessible to the public.

(2) Privacy.--

(A) Personally identifiable information.--
Permanent Members:

Argentina
Brazil
Paraguay
Uruguay
Venezuela (5th member since July 2012)
Main reference texts

- Resolution GMC n°19/05 « Programa de cosmetovigilancia en el area de productos de higiene personal, cosméticos y perfumes » - 9/VI/05 (transposed into each country national law, except Venezuela to date)
- Manual de cosmetovigilancia - Para a Industria de Higiene Pessoal, Perfumaria e Cosméticos (Brazil)

Current situation

1) Importers, manufacturers and/or company responsible for placing a cosmetic product on the market are requested to...

- Have a cosmetovigilance system
- Evaluate and keep cosmetovigilance reports
- Report the relevant country National Authority any situation which could pose a health risk for the consumer (adverse reactions and quality defects)
2) Consumers & Healthcare Professionals

Voluntary reporting, using specific forms

Example: ANVISA website (Brazil)

http://www.anvisa.gov.br/hotsite/notivisa/apresenta.htm
Main reference texts

- Pharmaceutical Affairs Laws (PAL), Article 77-(4)-2-1; Law No.145 August 10, 1960; Final Revision: Law No.84, June 21, 2006
- Enforcement Regulations of the Pharmaceutical Affairs Law (ERoPAL), Article 253-(3); MHLW Ordinance n°1, February 1961 and MHLW Ordinance n° 114, May 2009 (Final Revision)

Current situation

1) Companies responsible for placing a cosmetic product on the market...

- A license to market cosmetics have to be obtained from the MHLW (Ministry of Health Labour and Welfare). Compliance with the GVP (Good Vigilance Practices) standards specified by the MHLW Ordinances in terms of Quality Control and Post Marketing safety management is required.

2. Revised adverse reaction reporting system for quasi-drugs and cosmetics

When MAHs of drugs, quasi-drugs, cosmetics, and medical devices become aware of any occurrence of adverse reactions/malfunctions caused by their products or research reports, it is mandatory for such MAHs to report them to the MHLW in accordance with the Pharmaceutical Affairs Law Article 77-4-2, Paragraph 1. The scope of reportable information is defined in the Enforcement Ordinance of Pharmaceutical Affairs Law. As shown in Table 1, reportable information for cosmetics, etc., was limited to research reports compared to that for drugs and medical devices.

Meanwhile, given the fact that cases of significant adverse reactions caused by medicinal cosmetics, etc., have been reported in recent years, it was determined to revise the Enforcement Ordinance of Pharmaceutical Affairs Law to require reporting of individual cases for any serious adverse reactions caused by cosmetics, etc., as with drugs, in order to identify any similar cases early and immediately take necessary measures if such cases occur in the future (shaded parts in Table 1).

**Table 1. Description of safety information that MAHs should report**
(time frame for reporting is shown in brackets)

<table>
<thead>
<tr>
<th></th>
<th>Serious adverse reaction reports</th>
<th>Unknown/ non-serious reports</th>
<th>Report of safety measures taken in overseas</th>
<th>Research reports</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drugs, medical devices</strong></td>
<td>Death or unknown</td>
<td>Known</td>
<td>Yes (Annual periodic report)</td>
<td>Yes (Within 30 days)</td>
</tr>
<tr>
<td></td>
<td><strong>(Within 15 days)</strong></td>
<td><strong>(Within 30 days)</strong></td>
<td><strong>(Within 15 days)</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Quasi-drugs, cosmetics</strong></td>
<td>Changed from no to yes*</td>
<td>Changed from no to yes*</td>
<td><strong>No</strong></td>
<td>Yes (Within 30 days)</td>
</tr>
<tr>
<td></td>
<td><strong>(within 15 days)</strong></td>
<td><strong>(within 30 days)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Including cases that require at least 30 days for treatment as well as serious adverse reactions
Therefore, it was determined only for cosmetics, etc., to include "Cases that require at least 30 days for treatment" (seriousness criteria 8 in Table 2), as well as serious adverse reactions, in the scope of individual case reporting.

### Table 2: Adverse reactions caused by quasi-drugs and cosmetics that require individual reporting

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Death</td>
</tr>
<tr>
<td>2.</td>
<td>Disability</td>
</tr>
<tr>
<td>3.</td>
<td>Events that may result in death</td>
</tr>
<tr>
<td>4.</td>
<td>Events that may result in disability</td>
</tr>
<tr>
<td>5.</td>
<td>Requiring hospital admission or prolonged hospitalization for treatment</td>
</tr>
<tr>
<td>6.</td>
<td>Severe events corresponding to those shown above</td>
</tr>
<tr>
<td>7.</td>
<td>Congenital disease or anomaly in next generations</td>
</tr>
<tr>
<td>8.</td>
<td>Cases that require at least 30 days for treatment</td>
</tr>
</tbody>
</table>

In connection with the enhancement of adverse reaction reporting system, the scope of information that MAHs of cosmetics, etc., are required to collect was also revised to include information from healthcare professionals and government agencies.

2) Healthcare Professionals

Have been encouraged to directly report to the MHLW adverse reactions caused by cosmetics, as well as adverse reactions caused by drugs.
Main reference texts

- Hygiene Supervision Over Cosmetics regulations
- Guiding Opinions on Accelerating the Construction of the Monitoring System of Cosmetic Adverse Reactions - 24th October 2011

Current situation

Ongoing process of implementing a Monitoring System of Cosmetic Adverse Reactions by CFDA

Pilot phase (2011 - 2013)

- Designation/creation of the relevant authorities (control) at provincial and national levels (1st in Shanghai)
- Team-building process
- Progressive deployment of the system

1- Pilot phase at provincial level
2- Gradual implementation at national level

- Voluntary reports are encouraged
- Promotion of the system

What should be reported?

- Adverse reactions affecting the skin and its appendages.
- Exclusion of the cases Occurring during pregnancy (1); Of occupational diseases (2); Linked with the use of counterfeit raw materials or product (3).

Who and How?

- A consumer can report an Undesirable Effect to a hospital structure, on a voluntary basis
- The structure forwards, on a monthly basis, all the reports collected to the designated provincial control authority
- The industry is encouraged to report Undesirable Effect to the designated provincial control authority
- CFDA is informed about the totality of the reports collected at provincial level
Association of South-East Asian Nations (10 Member States)

- Brunei
- Burma/Myanmar
- Cambodia
- Indonesia
- Laos
- Malaysia
- Philippines
- Singapore
- Thailand
- Vietnam
Main reference texts

- ASEAN Cosmetic Directive
- Discussion Paper on Post Marketing Surveillance/Product Safety (June 2004)
- General Information Booklet on ASEAN Harmonized Cosmetic Regulatory Scheme

Current situation

Who and How?

Companies responsible for placing a cosmetic product on the market shall report to the regulatory authority of the ASEAN Member State, all Serious Adverse Reactions within 7 calendar days if “death” or “immediate vital risk”, or within 15 calendar days if “hospitalisation” or “persistent or significant disability/incapacity”, regardless of the source of the report (Consumer, Healthcare Professional...).
28 Member States + 3 EEA countries + Monaco

Austria
Belgium
Bulgaria
Croatia
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Ireland

Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Poland
Portugal
Romania
Slovakia
Slovenia
Spain
Sweden
United Kingdom

Iceland
Norway
Principality of Liechtenstein

Principality of Monaco
(EU agreement signed)

All these countries follow Regulation (EC) No 1223/2009 on cosmetic products
The regulatory framework for placing a cosmetic product on the marketplace is specific:

• No marketing authorization approval is requested.

• Different obligations are demanded to those responsible for placing a product on the market, among which:
  • Only cosmetic products for which a legal or natural person is designated within the Community as ‘Responsible Person’ shall be placed on the market
  • Carry out a safety assessment on the product prior to its placement on the marketplace
  • Ensure the product composition is compliant with the different lists of substances that are regulated
  • Ensure the product labelling is in compliance with the requirements
  • Make the Product Information File readily accessible to the authorities

⇒ Post-marketing Surveillance +++
Main reference texts

- Serious Undesirable Effects (SUE) Reporting Guidelines

Current situation

What to report and who has to report?

Responsible Persons AND Distributors have the obligation to notify Serious Undesirable Effects (SUE) to the Competent Authority of the country where the SUE occurred “without delay” (*in practice, recommendation to notify within 20 calendar days as from the date when the RP or Distributor -any employee- becomes aware of the SUE)*.

How to report? Specific reporting form (SUE Form A)
Notification of a SUE (Article 23 of Reg. (EC) 1223/2009)

- Responsible Person
- Distributor

Competent Authority of the Member State In which the SUE occurred

Serious Undesirable Effect (SUE)

- 20 calendar days
- ...and corrective measures, if any

Other Member States Competent Authorities

Healthcare Professionals / End users (cf. Whereas 55)
3.9. Undesirable effects and serious undesirable effects

The aim of this section is to monitor the safety of the product after it has been placed on the market and to take corrective action, if necessary. To this end, the responsible person (in collaboration with the distributors) should set up a system to collect, document, establish the causality of and manage the undesirable effects caused by the product after its use in the EU. When the undesirable effects are serious, the responsible person (and the distributors) must notify the competent authority of the EU Member State where the effects occurred. Information on undesirable effects and serious undesirable effects must be included in the Cosmetic Product Safety Report, kept up-to-date and made available to the safety assessor, who may revise his or her assessment and/or take the information into account when assessing similar products.
Seriousness criteria

Seriousness criteria (in descending order of frequency as per what is observed):

- Temporary or permanent functional incapacity
- Hospitalisation
- Immediate vital risk
- Disability
- Congenital anomalies
- Death

No precise definition available to date regarding these criteria
The challenges to take into account to comply with a full EU post-marketing surveillance

- 32 countries (including the principalities) and 23 different languages (collecting relevant information on cases can rapidly become very complicated)

- Cosmetovigilance cases (Serious and Non-serious) have to be assessed using a standardized causality assessment method

- Whereas 55 of the Regulation: Some EU countries can directly receive Serious cases from other sources than the industry (End-users, Health Professionals)

- Each Member State lays down the penalties if failure, by the RP or the Distributor, to notify a SUE to the Competent Authority

- Personal Data protection rules (Directive 95/46/EC on the protection of personal data)
THANK YOU!