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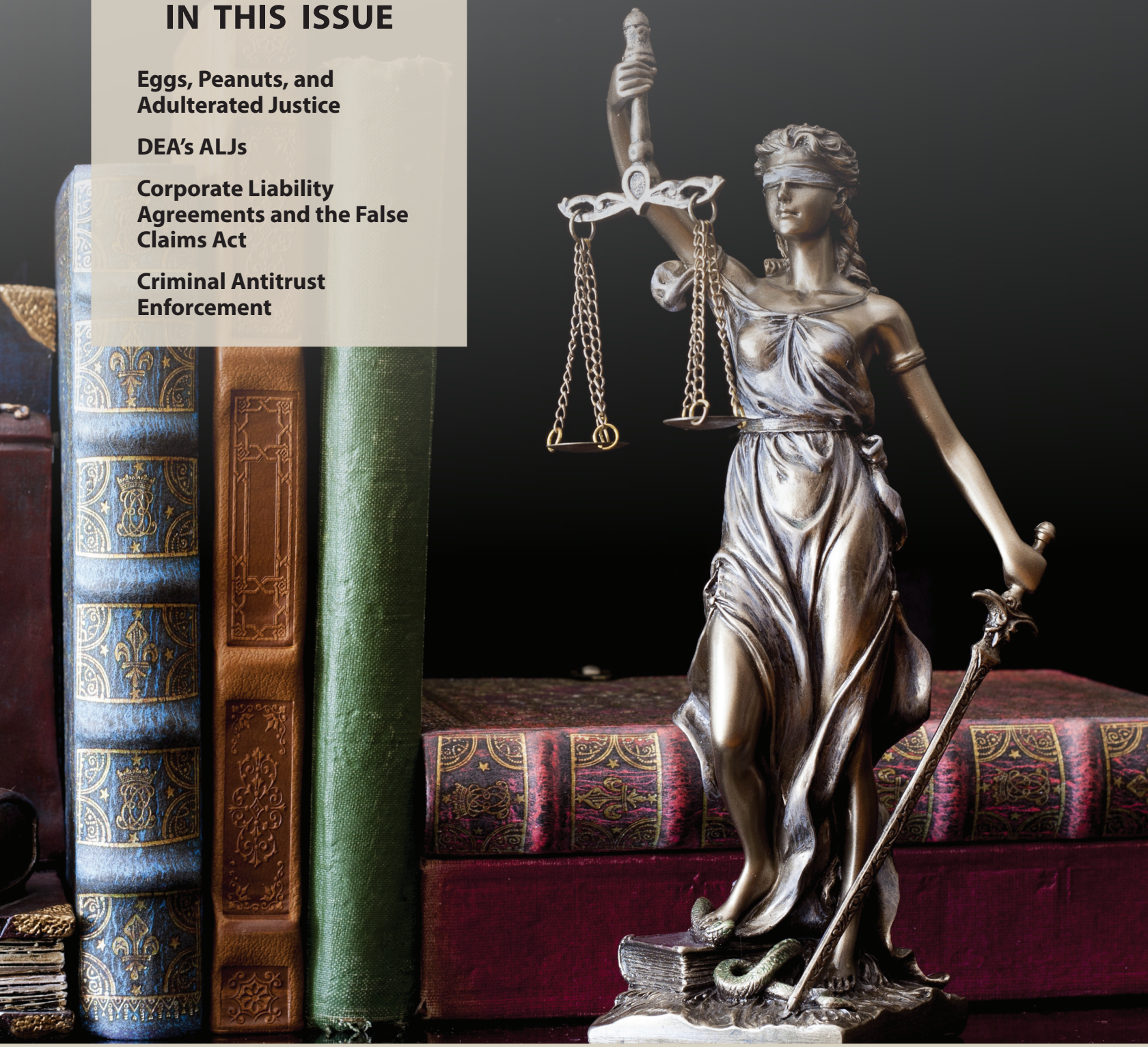

Year in Review—Top 10 Issues for Drugs and Devices in Canada in 2015

By Albert Chan, Yolande Dufresne, Eileen McMahon, and Teresa Reguly

There have been many changes to the Canadian regulatory landscape in 2015, including the implementation of Health Canada's regulatory transparency and openness framework. The initiative has introduced changes to Canada's *Food and Drugs Act*, plain language labeling requirements, as well as the publication of advertising complaints, regulatory decision summaries, and regulatory submissions under review. Below is our survey of 10 of the hottest topics for regulation of drugs and devices, including what to watch for as 2016 approaches.

Canadian Food and Drug Law Amendments 50 Years in the Making

One of the greatest changes to Canadian drug and device regulatory law this past year is Bill C-17 *Protecting Canadians from Unsafe Drugs Act (Vanessa's Law)*. Passed in November 2014, the bill amends Canada's *Food and Drugs Act*, and represents the first substantial amendment to the country's core drug and device legislation in 50 years. The amendments affect prescription and over-the-counter drugs (except for natural health products (NHPs)) and medical devices ("therapeutic products"), but does not extend to other regulated products (food, cosmetics, or NHPs). These amendments strengthen Health Canada's powers to:

a. disclose confidential business information in its possession, without the consent of the party to whose business the information relates;
b. order a postmarket label or package change;
c. issue a product recall; and
d. require that a third party provide information to help determine whether a product presents a risk to health and safety.

The maximum fine for contravening the *Food and Drugs Act* or its regulations was also increased from C$5,000 to C$5,000,000 per day, which is a significant increase, although it is yet to be seen how these increased fines will be enforced.

Thus far, the industry has expressed most concern with Health Canada's new statutory power to compel confidential business information to be disclosed without notice or permission if Health Canada believes that a therapeutic product presents a serious risk of injury to human health.

Key Takeaways: It is yet to be seen how Health Canada will exercise its new powers. However, the agency has published a "Guide to New Authorities (power to require

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and disclose information, power to order a label change and power to order a recall)." The Guide defines the principles that Health Canada will follow when exercising its newly legislated powers. Specifically, the Guide discusses applicable thresholds and considerations, as well as the scope of each particular power. It also provides insight into Health Canada's position on matters such as the meaning of "serious risk" of injury, procedural fairness, "sufficient notice" of an intention to issue an order against an affected party, as well as the content of an order.

Regulating Reprocessed Medical Devices

As a cost reduction measure, many medical devices labeled for single use are reprocessed by hospitals and other health care facilities for reuse. Historically, reprocessing would take place within the hospital; however, in recent years commercial providers have begun to offer reprocessing services—without oversight from Health Canada.

Early this year, Health Canada announced a change to its approach to regulating these devices, indicating that reprocessors will be held to the same standards as "original" manufacturers with respect to licensing, quality system management, labeling, record keeping, and reporting. This means that facilities where single-use devices are cleaned, sterilized, and packaged will require an establishment license and reprocessed devices will require premarket approval (for class II, III and IV devices) and label review. Medical device reprocessing that occurs on-site at a Canadian hospital will not be subject to oversight or enforcement by Health Canada.[2]

Key Takeaways: The industry has been given an 18-month transition period to apply for these medical device and establishment licenses with the expectation that all reprocessed devices will be in compliance with the *Medical Device Regulations* by September 1, 2016. Manufacturers, importers, and distributors that are non-compliant after that time may be subject to risk-based enforcement.

The Canadian Biosimilar Landscape Continues to Evolve

Biosimilars, or Subsequent Entry Biologics (SEBs) as they are known in Canada, are approved via the New Drug Submission (NDS) pathway under the *Food and Drug Regulations,* the same pathway that is used for "original" innovative drugs. However, through reliance on a demonstration of similarity to a comparator biologic drug, the application for approval of a biosimilar includes fewer safety and efficacy studies than a typical NDS.

The first biosimilar, Omnitrophe, a biosimilar of Genotropin (somatropin), was approved in Canada in 2009. Subsequently, two additional biosimilars of Remicade (infliximab), named INFLECTRA (infliximab) and REMSIMA (infliximab), were approved in 2014. Multiple other products are expected to enter the market in the next few years. Health Canada's reasons for approving these biosimilars, called "Summary Basis for Decisions," were published in 2015.[3]

Reimbursement remains a topic to watch, as public and private payors consider whether and with what conditions biologic products will be listed on drug formularies. The situation can be complex when a biosimilar is not approved by Health Canada for all of the same indications as its comparator product. As an example, INFLECTRA is approved for four of the same indications as Remicade; Remicade is approved for two additional indications. In the province of Quebec, both products are listed on the public formulary, but if infliximab is prescribed for an indication that is covered by both Remicade and INFLECTRA, the government will only reimburse the lowest price—i.e., up to the INFLECTRA price—except in limited situations where the prescribing physician can justify a therapeutic concern with use of the biosimilar over the comparator brand product.

Key Takeaway: As more biosimilar products are approved, with varying degrees of "similarity" to their comparator products, it is unclear whether Health Canada will approve these products using the same name for the "active ingredient" as the comparator product and how payors will treat these products for substitution/interchangeability decisions.

Look before You Tweet in Canada

Generally, the same rules apply for social media advertising as with more conventional media—which means that, in Canada, drug- and device-related social media content is subject to a high level of regulation. If a manufacturer has some degree of control over its Canadian social media content (either through a sponsorship relationship with an athlete, celebrity, or other public figure, or through social media content posted to the manufacturer's own website

feeds or social media accounts), that manufacturer could be liable if any of the content contravenes the *Food and Drugs Act* and other applicable legislation.

Furthermore, in Canada, where consumer advertising of prescription drugs is strictly limited to the name, price and quantity of the drug, social media content referencing prescription drugs carries with it a high degree of risk. Even for non-prescription drugs, NHPs, and medical devices, manufacturers must carefully monitor any social media content to ensure that it complies with the terms of market authorization for the products (for example, with respect to dosage, duration of use, instructions for use, or warnings). It is easy to see how a social media message—often constrained by character limits, unintended image content, or unsolicited user-generated content, such as "likes" or "reposts"—can quickly move from compliant to non-compliant.

Key Takeaway: As social media continues to evolve, manufacturers will want to be vigilant in monitoring social media under their control having ties to Canada, and to have policies in place for deleting posts and correcting for inaccuracies in user comments and posts.

Software and Medical Devices—Where Is the Line Drawn North of the Border?

To ensure compliance with Canadian drug and device regulatory laws, software manufacturers will want to determine whether their health-related software products are classified as medical devices (or simply as non-regulated software) in Canada. That distinction has proven to be somewhat gray in 2015 as Health Canada continues to develop its position on software regulated as medical devices.

Software is considered to be a medical device by Health Canada if it: (1) provides the only means and opportunity to capture or acquire data from a medical device for aiding directly in diagnosis or treatment of a patient; or (2) replaces a diagnostic or treatment decision made by a physician. Health Canada has published guidance to help distinguish between Class I and Class II software medical devices.[4] Some examples of health-related software that Health Canada does not typically consider to be medical devices are patient management software, the Wii Fit, pedometer software, and Body Mass Index calculators.

Key Takeaway: If a health-related software product does not neatly fit within one of the above-noted categories, the intended use of the product (including statements made on the labeling, packaging and marketing materials) and the software's operational use of patient data, if any, may help to resolve how the product will be classified. At this stage, manufacturers will want to continue to monitor Health Canada's position on software and medical devices through publications, guidance documents and policies. At a time when mobile devices and an abundance of health-related applications are becoming increasingly commonplace, we expect to see more from Health Canada on this topic in the coming months and years.

Drug Inspection Database Now Public

In 2015, Health Canada launched its new searchable drug inspection database providing public access to detailed report cards of Health Canada's drug and health product site inspections.[5] Three separate Health Canada drug inspection lists are viewable on the site: (i) drug inspections of Canadian sites, by date; (ii) drug inspections of Canadian sites that received non-compliant ratings, by date; and (iii) drug inspections of foreign sites, by date. Additionally, the database can be searched by fields including establishment name, rating, license status, and terms and conditions on license. Health Canada has uploaded details on the latest inspections as well as those conducted since 2012.

Key Takeaways: Some members of the industry have noticed growing scrutiny for drug inspections in 2015, particularly with respect to transparency, data integrity, and the strengthening of Health Canada's oversight of foreign sites. Although manufacturers have previously asserted that inspection data is confidential business information, the decision to publish this information is in line with the regulator's ongoing efforts to improve transparency. Health Canada's new practice of publicizing this information makes the management of inspection results an increasingly delicate exercise for manufacturers in the face of media or news outlets seeking to leverage this information.

Gatekeeping, Product Liability, and Class Actions

The management of class action product liability claims continues

to be an important legal topic for drug and device manufacturers in Canada. Class action proceedings have been building in frequency, and all but one of Canada's 10 provinces now have class action legislation. To certify a class action, the following criteria must typically be satisfied (although they may vary somewhat from province to province): (1) the representative plaintiff must have a valid cause of action; (2) there must be an identifiable class of two or more persons; (3) the claims of the class members must raise common issues; (4) a class proceeding would be the preferable procedure for the resolution of the common issues; and (5) the representative plaintiff seeking certification can fairly and adequately represent the interests of the class, has a litigation plan for advancing the proceeding on behalf of the class members and does not have, on the common issues for the class, an interest that conflicts with the interests of other class members.

The industry is generally of the view that, when applied to drugs and medical device product liability, class action certification requirements historically have been broadly interpreted and applied by Canadian courts. However in 2015, the British Columbia Court of Appeal overturned the B.C. Supreme Court's class certification in *Charlton vs. Abbott Laboratories*,[6] which may suggest a possible move towards more rigorous standards in certifying class actions against pharmaceutical companies. In *Charlton*, certification was refused on the basis that the representative plaintiffs were unsuccessful in demonstrating a methodology to establish causation on a class-wide basis.

Key Takeaway: Although *Charlton* represents the court's application of its "gatekeeping" role, it is yet to be seen whether this decision will be followed or adopted by other provinces.

Summary Basis of Health Canada Decisions for Medical Devices

When a medical device manufacturer applies for a Canadian license for their U.S.-marketed device, one of the first questions to be asked is, "what indications for use, safety

data, or efficacy evidence did Health Canada accept for similar comparator products in Canada?" Unlike in the U.S., where the FDA publishes device summaries in its online database, this licensing information has been largely unavailable in Canada where only basic administrative details on device licenses are available online.

Health Canada's Summary Basis of Decision (SBD) initiative is intended to overcome this limitation by enhancing the transparency of the medical device review process. Health Canada has now begun publishing select SBD documents that outline the scientific and benefit/risk-based considerations that factor into Health Canada's decision to grant market authorization for a medical device. A limitation of the current SBD process, however, is that SBDs are not drafted for all medical device applications. In fact, as of 2015, Health Canada's target is to publish five to seven SBDs per year for newly licensed Class III and IV medical devices with novel technology.

Key Takeaways: Manufacturers, particularly those integrating relatively new medical device technologies, should consult SBDs for possible insights into Health Canada's safety and efficacy requirements. Health Canada's SBD for Medical Devices can be accessed at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/md-im/index-eng.php.

Defining "Medicinal Ingredient" and Pharmaceutical Equivalence

Until now, the term "medicinal ingredient" had been undefined in Canadian regulations, and subject to ad hoc interpretation depending on the applicable context. This position was successfully challenged in the 2013 court decision *Apotex Inc. v. Canada (Health)*,[7] where the Federal Court required Health Canada to apply a consistent interpretation of the *Food and Drug Regulations*, including the interpretation of "medicinal ingredient." As a result, this past June, Health Canada clarified that the term "medicinal ingredient" in the *Food and Drugs Act* and the *Food and Drug Regulations* refers to the active pharmaceutical ingredient (API), which constitutes the raw material used in the manufacture of a finished drug product.[8]

Key Takeaways: This policy benefits innovator pharmaceutical manufacturers in making it more difficult for a generic drug product to receive marketing approval where a medicinal ingredient diverges into different chemical forms during manufacturing. For the purposes of generic drug submissions (ANDSs), Health Canada may require a generic drug manufacturer to submit additional evidence of safety or bioequivalence to a Canadian reference product, if the proposed generic involves different processing of the API, such that the "medicinal ingredient" is present in different chemical forms at the finished dosage stage. For example, if a generic manufacturer uses the same API as a raw material in the manufacturing, but the manufacturing process results in a different salt form in the finished product as compared to the innovator product (as occurred in the *Apotex* case, which brought about this interim policy), then Health Canada may ask the generic manufacturer to submit additional evidence that the two products are bioequivalent.

Medical Devices – Mandatory Problem Reporting

In view of recent enforcement efforts regarding compliance with medical device mandatory problem reporting (i.e., adverse event reporting), medical device manufacturers should keep in mind that reporting standards in Canada differ slightly from those in the US. Manufacturers must report any incident occurring in Canada that (i) relates to a failure or deterioration of a medical device, or to a defect or inadequacy in the device labeling, and (ii) has led to the death or serious deterioration of health of a patient, or could do so if the incident recurs. Further, manufacturers must notify Health Canada of any such incidents occurring outside of Canada, if those incidents (iii) lead to a corrective action either taken voluntarily by the manufacturer or mandated by a foreign regulatory authority. Health Canada takes a broad view of what constitutes a "corrective action," which may include recalls, refurbishing or upgrading devices, updates or addendums to device labels or instructions for use, or some communications with customers.

Key Takeaways: Medical device manufacturers will want to bear in mind that devices that do not require product licensing in Canada (i.e., Class I medical devices) are also subject to mandatory problem reporting, including the reporting of incidents occurring outside of Canada. In view of Health Canada's broad view on "corrective actions," medical device manufacturers should maintain

detailed records of adverse incidents and any actions taken in response.

Conclusion

The wide range of regulatory changes affecting the Canadian drug and device landscape has given both regulators and the industry much to consider in 2015. As many of our key takeaways suggest, stakeholders in the industry will want to keep a close eye on how these issues will play out in the coming year.

1. This is the first of two regulatory updates on Canada from Torys LLP covering the regulation of food, drug, device, and other regulated products.
2. For more information, please see: http://www.hc-sc.gc.ca/dhp-mps/md-im/activit/announce-annonce/md_notice_sud_uu_avis_im-eng.php.
3. The Summary Basis for Decision for Inflectra may be found at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/sbd_smd_2014_inflectra_159493-eng.php, and for REMSIMA at http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/sbd_smd_2014_remsima_160195-eng.php.
4. http://www.hc-sc.gc.ca/dhp-mps/md-im/activit/announce-annonce/md_notice_software_im_avis_logicels-eng.php.
5. The database can be accessed at: http://healthycanadians.gc.ca/apps/inspections/index-en.html.
6. 2015 BCCA 26.
7. 2013 FC 1217.
8. The interim policy is posted at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/pol/notice_im_pol_mi_avis-eng.php.