Briefing Note

Mutual Recognition Agreement for pharmaceutical good manufacturing practices between Canada and the US

(For Information only)

Summary:

- While both Canada and the US have established Mutual Recognition Agreements (MRAs) with the European Union (EU), in 2014 the Canada-US Regulatory Cooperation Council (RCC) stepped away from its own commitment to pursue an MRA as part of its original 2012 work plan.
- Between 2015 and 2016, this lack of an MRA has cost both governments as much as $17.3 million in unnecessary, duplicative inspections, diverting finite inspection resources away from areas of the world that may pose a much higher risk.
- The renewed commitment in the Canada-US RCC provides the ideal opportunity to gain a formal commitment from the Canadian and US governments to establish an MRA and to immediately enter the “Mutual Reliance” phase, allowing Health Canada and FDA drug inspectors to rely upon information from drug inspections conducted within each other’s boarders.

Background

Consumer Health Products Industry:

Consumer health products are items that are used every day to maintain health and manage minor ailments. These products include over-the-counter drugs such as pain relievers and allergy medications, and natural health products such as vitamins and supplements.

The Consumer Healthcare Products Association (CHPA) is the 136-year old trade association representing the leading manufacturers and marketers of over-the-counter (OTC) medicines and dietary supplements in the United States. Consumer Health Products Canada (CHP Canada) is the Canadian national industry association representing manufacturers of evidence-based non-prescription medicines (OTCs) and natural health products (NHPs).

In the US, the OTC industry has grown over 160% in the last 10 years and is estimated to generate $40 billion in sales. Research has shown that every dollar spent by consumers on OTC medicines saves the U.S. healthcare system $6-$7, contributing a total of $102 billion in savings each year. In Canada, domestic and international sales of consumer health products have also increased rapidly over the last decade, compared to overall retail sales. From 2004 to 2014, total retail sales across the country grew at an average annual pace of 3.8 per cent while consumer health products sales increased by 4.2 per cent per year. In 2014, domestic retail sales of consumer health products were valued at $5.6 billion, while exports were estimated at $1.5 billion. Between 2004 and 2014, exports of these products nearly doubled - an increase of almost three-and-a-half times the growth in overall exports. Overall, the Canadian industry makes a $5.8 billion contribution to GDP and supports almost 57,000 jobs.

Many of CHPA's and CHP Canada's and members are global multi-national companies based in the US who are seeking better global alignment and regulatory harmonization regarding manufacturing processes.

Mutual Recognition Agreements (MRAs):

The role of an MRA for good manufacturing practice (GMP) inspections is to encourage greater international harmonization, make more efficient use of inspection capacity and reduce duplication. Canada has an MRA with the EU for drug GMP inspections, which for some EU states began in 2003. This allows both regulators to rely on each other's inspections, reduces duplications, lowers costs and allows resources to be focused on areas of the world the may pose greater risk.

The 2012 Canada-US Regulatory Cooperation Council (RCC) Work Plan committed Health Canada and the US FDA to increase mutual reliance on each other's routine surveillance of GMP inspection reports of manufacturing facilities for drugs and personal products, rather than having to conduct duplicative inspections in each country. However, in the 2014 RCC Work Plan, Health Canada and the US FDA backed away significantly from this commitment and instead decided to simply continue to engage in existing multi-lateral forums on drug GMP inspections.

At the same time as the RCC was downgrading its joint commitment, the US FDA and the EU were engaged in a mutual reliance initiative collaborating to evaluate the way they each inspect drug manufacturers and assess the risk and benefits of an MRA. In March 2017, the US FDA and the EU announced the MRA for drug GMP inspections.

Current Status

Despite the fact that OTCs are manufactured in Canada and the US to similar GMP requirements and similar protections, and despite the fact that both Canada and the US have entered into MRAs with the EU, the lack of an MRA between Canada and the US means that both regulators need to inspect the same facility making products destined for each country. Not only are facilities being inspected twice, when products cross the boarder, the same confirmatory testing needs to be repeated, adding costs, discouraging trade and creating delays for consumers to access new products.

Currently, the RCC work plans only commit Health Canada and the FDA to continue participation in existing multi-lateral forum such as the Pharmaceutical Inspection Co-operation Scheme (PIC/S), International Conference on Harmonization (ICH), the International Pharmaceutical Regulators Forum (IPRF), and the International Coalition of Medicines Regulatory Authorities (ICMRA) to achieve closer cooperation with other jurisdictions. While this commitment is important, not addressing specific areas for cooperation between Canada and the US undermines the attainment of the RCC objectives to produce tangible benefits to trade between Canada and the US.

Considerations

Policy Alignment:

- Pursuing an MRA for GMP inspections between Canada and the US aligns directly with the objectives of the RCC. These objectives continue to be a commitment from President Donald J. Trump and Prime Minister Justin Trudeau as evidenced in a recent joint statement, as well as the US government direction to reduce regulatory burden and control regulatory costs.

- Aligning inspection decisions is one of the most important initiatives to avoid unnecessary differences between Canada and the US. It would create a shared, tangible regulatory outcomes that are business-friendly, reduce costs, and increase economic efficiency without compromising health, safety and standards.

In 2012, the US Congress passed the *Food and Drug Administration Safety and Innovation Act* giving the FDA authority to enter into agreements with foreign regulators to recognize drug inspections that are capable of meeting US requirements.

In the 2011 *Special Report: Pathway to Global Product Safety and Quality*, the FDA outlined their vision for the next decade recognizing that product safety and quality no longer begin or end at the border. This report stated that it is not feasible for the US FDA to inspect every high risk international pharmaceutical facility and that there is a need to partner closely with foreign regulators to share information, effectively allocate resources based on risk, and leverage efforts of other government coalition members, industry and third parties. Health Canada committed a similar approach to collaborate with international regulatory partners in a 2015 *Annual Inspection Summary Report.* Over 80% of health products are imported into Canada, and as the global supply chain continues to expand with companies producing more products around the world, Canadians are exposed to greater risks products manufactured in countries with little regulatory oversight.

Resource Implications:

- A MRA for drug GMP inspections between Canada and the US would result in cost savings for both regulators, without compromising health and safety. This would allow both governments to more appropriately reallocate limited inspection resources to international jurisdictions where there isn't the same level of confidence, which would result in the biggest payoffs for regulators, mitigating the greatest potential risks to Canadian and US consumers.

Savings to regulators and industry due to elimination of duplicative inspections

- The FDA inspected 26 Canadian facilities in 2016 and 35 in 2015 that were already licensed and inspected by Health Canada.
    - Based on the annual generic pharmaceutical user fees for foreign finished dosage form facilities, (which cover 56% of the recovery costs for personnel and a premium for foreign inspections) we estimate the cost of one inspection and administrative licensing can range from $59,000- $273,000 USD.
    - We estimate the inspections carried out over the last two years cost the FDA and the industry each: $1.5M- $7M USD in 2016 and $2M-$9.5M USD in 2015.
    - In 2015-2016, out of the 28 EU countries that the US has just established an MRA with, Canada ranks third for most FDA inspections behind Germany (120 FDA inspections) and Italy (77 FDA inspections) during that same time, indicating an MRA with Canada would provide value compared to EU countries. If these resources for 61 foreign FDA inspections were instead spent in India or China during that same time period, it would represent a 31% and 24% increase in inspection capabilities within these counties, where oversight is most needed.

- Health Canada inspected 5 US facilities in 2016 and 2 in 2015.
    - Based on the annual 2016 fees for Drug Establishment Licenses (which cover the review of an application, annual reviews, amendments and domestic and foreign inspections) and domestic inspections occur every 3 years, we estimate the cost of one inspection and administrative licensing can range from $25,000-$120,000 CDN, which represent 61% of the recovery costs for Health Canada.
    - We estimate the inspections conducted over the last two years cost Health Canada and the industry each: $125,000-600,000 CDN in 2016 and $50,000-$240,000 CDN in 2015. This represents approximately 18% of Health Canada's limited resources for foreign inspections, as a total of 11 and 28 inspections took place in 2016 and 2015 respectively.

- Although industry would need to continue to pay the above licensing fees for foreign facilities regardless if the site is in an MRA country, tangible savings would result due to the elimination of duplicate inspections. Preparation for and conducting an inspection represents investment of 660-1040 extra person hours, beyond daily responsibilities.

Savings to industry due to elimination of duplicative confirmatory testing

- With an MRA, it would no longer be necessary to quarantine and immediately retest products that are coming from a licensed facility in the other country. The costs of retesting products can range from $150,000-$190,000 per product per shipment annually, depending on the type of testing required. As a result of these costs, some products are never launched in Canada due to limited availability of Canadian testing labs that have completed verification of the required test methods. Eliminating duplicative testing will also shorten release times, enabling consumers on both sides of the boarder faster access to new treatment options.

Review Resource efficiencies

- With an MRA, only a valid Certificate of Compliance from the other regular is required to show compliance of a site, which requires minimal review. This would eliminate the need to review large files, including Exit Inspection Reports, responses, SOPs and Site Master Files.
    - Annually, Health Canada receives over 400 Certificates of Compliance from it's MRA partners and reviews close to 500 inspection reports for foreign sites not in MRA countries.

Recommendation:

- CHP Canada and CHPA's recommendation (which is supported by the prescription drug industry, generic drug industry, and cosmetics industry) is that, under the Canada-US RCC, both governments formally commit to establishing an MRA for drug GMP inspections.
- We further recommend that the RCC formally recognize the past years' work together as being part of the "mutual reliance phase" and therefore expedite the transition time necessary to establish such an MRA.