Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**lixisenatide + insulin glargine (Soliqua), diabetes mellitus, type 2**
Name of the Patient Group	**Diabetes Canada**
Author of the Submission	**Ann Besner**
Name of the Primary Contact for This Submission	**Seema Nagpal**
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1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

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Diabetes Canada is a national health charity representing 11 million Canadians living with diabetes or prediabetes. The priorities of our mission are diabetes prevention, care and cure. Our focus on research and policy initiatives helps us to deliver impact at a population level, and our partnerships broaden our reach in communities across the country. We drive excellence in disease management by putting practical, evidence-based tools into the hands of health-care providers. We advocate for environments that make the healthy choice the easy choice. We continue our search for a cure, as well as for better prevention and treatment strategies, by funding the work of innovative scientists. In 1921, Canada changed diabetes for the world with the discovery of insulin. By 2021, we will change the world for those affected by diabetes through healthier communities, exceptional care, and high-impact research. For more information, please visit: www.diabetes.ca.

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

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This submission contains patient input from online surveys conducted in October 2016 and April 2018. Each survey was open for two weeks to people across Canada and consisted of a self-administered questionnaire. The surveys were directed at people living with type 2 diabetes and caregivers of people with type 2 diabetes and asked questions about respondents' lived experience with diabetes and diabetes medications, and expectations for new drug therapies in Canada. Awareness about the surveys was generated through Diabetes Canada's social media channels (Twitter and Facebook); the October 2016 survey was also advertised to Diabetes Canada e-mail subscribers through e-blasts.

A total of 847 people responded to the October 2016 survey – 790 identified as living with type 2 diabetes while 57 said they were caregivers to somebody with type 2 diabetes. Of those who responded to questions about age and time since diagnosis (n=379), 70% were over the age of 55, with the largest number of respondents (56%, n=211) falling within the 55-69 year old category, and 60% had been living with diabetes for over 10 year (17% of this group reported having diabetes for over 20 years).

Fewer people (n=12) participated in the April 2018 survey – there were 11 respondents who said they live with type 2 diabetes and one caregiver to somebody with type 2 diabetes. Only two respondents disclosed their age and time since diagnosis – both people were between the ages of 25 and 55, one has had diabetes for less than a year, and the other for 6-10 years.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease impacts patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

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Diabetes is a chronic, progressive disease with no known cure. Type 1 diabetes occurs when the body produces either very little or no insulin. Type 2 diabetes occurs when the pancreas does not produce enough insulin or the body does not effectively use the insulin that is produced. Common symptoms of diabetes include extreme fatigue, unusual thirst, frequent urination and weight change (gain or loss).

Diabetes requires considerable self-management, including eating well, engaging in regular physical activity, maintaining a healthy body weight, taking medications (oral and/or injectable) as prescribed, monitoring blood glucose and managing stress. Poor glucose control is serious and problematic. Low blood glucose can precipitate an acute crisis, such as confusion, coma, and/or seizure that, in addition to being dangerous themselves, may also contribute to a motor vehicle, workplace or other type of accident causing harm. High blood glucose over time can irreversibly damage blood vessels and nerves, resulting in blindness, heart disease, kidney problems and lower limb amputations. The goal of diabetes management is to keep glucose levels within a target range to minimize symptoms and avoid or delay complications.

The majority of respondents spoke negatively of their experience being chronically ill. They said diabetes is a "horrendous experience", "manageable but a bother", an "awful disease", inconvenient and frustrating, and "isn't fun to live with". One respondent referred to it as a "terrible way of life", while another spoke about its permanence, lamenting that there is no "holiday" from diabetes.

Most people surveyed commented on the adverse effect diabetes has had on their lives. They must constantly think about and plan around their disease. It affects everything from eating and exercising to working and socializing. Overall, diabetes makes it difficult to be flexible and spontaneous. It is always top-of-mind when making decisions and can be very stressful. Daily routines end up very "regimented" and closely "controlled". Diabetes is even more difficult to treat when someone is also dealing with comorbidity or disability. Testing and visits to health care providers were described as burdensome.

Respondents shared that meal timing, intake and food choices are restricted, which takes away from the pleasure of eating, and that it is difficult to constantly be receiving direction from others (i.e. health care providers) on the items that are good to consume and those that should be avoided. They said it is challenging to be on medication all the time and to experience variability in blood sugar control. Several respondents spoke about the blame they inflict upon themselves for their disease, the shame and guilt they feel, and the stigma they experience. Some talked about how tough it is to interact with people who know very little about diabetes or who offer unsolicited advice about its management.

Many people mentioned dealing with disease symptoms, medication side effects and diabetes complications. Respondents describe being chronically in pain and feeling exhausted. They experience weight management issues, neuropathy, nephropathy, changes to circulation and increased risk of heart

attack, vision problems, and sexual changes, including erectile dysfunction. They reported incidence of depression and anxiety.

Respondents to the October 2016 survey said they experienced the following symptoms and conditions "sometimes" ("moderately"), "often" ("severely") or "very often" ("very severely") at the time of survey completion (n=691 for this question):

- hyperglycemia (75%)
- hypoglycemia (38%)
- high blood pressure (51%)
- high cholesterol (48%)
- heart problems (18%)
- mental health problems (30%)
- kidney symptoms or disease (19%)
- foot problems (45%)
- eye problems (42%)
- nerve damage (37%)
- damage to blood vessels, heart or brain (10%)
- liver disease (9%)

Other concerns cited include gastroparesis, GI issues (nausea, vomiting), bladder and bowel incontinence, yeast infections, erectile dysfunction, skin rash and weight gain.

Of those who responded to this question in the April 2018 survey (n=4), people experienced hyperglycemia, hypoglycemia, high blood pressure, high cholesterol, mental health problems and eye problems "sometimes", "often" or "very often". Additionally, bladder issues, infection control and general muscle/joint pain were reported.

People shared that diabetes has adversely affected relationships. It's made it hard for them to work, travel, and even drive – one respondent mentioned losing a driver's license because of diabetes. Diabetes decreases independence. People are fearful of complications and concerned about the long-term effects of the disease on health. They also mentioned the significant and overwhelming financial burden diabetes poses on individuals and families.

Below are some quotes from respondents of both surveys that further illustrate the degree and extent to which diabetes affects daily living and quality of life:

"It is part of every decision I make on a daily basis regarding general health, exercise, nutrition, social activities, work etc."

"Diabetes makes some activities of daily living more difficult, time consuming and dangerous."

"It forces you to me[sic] fully aware at all times of your health: your glucose levels, A1C[sic], diet, exercise, different oral medication, insulin, activity level, mood. You think about it all the time and how best to keep on top of everything."

"Managing my diabetes is a full time job and detracts from my quality of life. I have to make sure I carry insulin and some form of sugar with me everywhere I go, I have to watch what I eat and record the impact it mason[sic] my blood sugars. It is time consuming and demoralizing when you don't get the expected results even though you have done your best to manage the disease."

"It's a bit depressing to constantly have to take medication."

"I feel like my body is breaking down 25 years ahead of its time."

"Made me feel guilty whenever I eat[sic] food that tastes good plus made me worry about what's down the road for me."

"Had to carefully adapt daily routines to ensure stable blood sugars in a normal busy day. In some cases I had to inject insulin in public which occasionally embarrasses or upsets people."

"The fact that I have to consistently monitor myself and wonder if I'm going to lose my eyes is something I wouldn't wish on my worst enemy."

"I am a…mother…and hate the fact that I have developed diabetes and have to take medications for it. This disease gets in the way all the time (more trips to the doctor, more trips to the pharmacy, having to remember to take my medication and ensuring that I don't take too much medication so that I can drive my vehicle). My kids have to know what to do if I pass out, and that isn't the type of responsibility that young children should have."

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

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There were 647 respondents who reported antihyperglycemic agents being part of their past or present medication history in October 2016. The medications being taken at the time of survey completion included Metformin (371), GLP-1 receptor agonists (312), SGLT2 inhibitors (165), combination of SGLT2 inhibitors with Metformin (45), DPP-4 inhibitors (72), combination of DPP-4 inhibitors and Metformin (147), sulfonylureas (140), TZDs (10), combination of TZDs with Metformin (17), combination of TZDs with glimepiride (4), meglitinides (9) and acarbose (9). Many people reported taking insulin (309). A number of respondents indicated that they had experience with certain medications in the past as part of a clinical trial. Some reported stopping certain medications due to reasons other than the end of a clinical trial. The most commonly cited medications in this group were TZDs (97), sulfonylureas (94), GLP-1 receptor agonists (94) and DPP-4 inhibitors (92).

Over 60% respondents to the October 2016 question noted improvements in meeting target blood glucose levels (fasting, post-prandial, upon waking) and hemoglobin A1c levels after initiation on their current medication regimen, compared to before (when they were not on treatment). About 46% said they were "better" or "much better" able to avoid hypoglycemia, and 39% said their current regimen helped them maintain or lose weight more effectively than in the past. Gastrointestinal side effects were "neither better nor worse" than previously in 39% of respondents. Close to two-thirds indicated they were either "satisfied" or "very satisfied" with the medication or combination of medications they are currently taking for their diabetes management.

Respondents who answered this question (n=382) in the October 2016 survey reported the following benefits and side effects as "quite important" or "very important" when choosing pharmacotherapy for diabetes management:

- keeping blood glucose at satisfactory level during the day or after meals (98%)
- keeping blood glucose at satisfactory level upon waking or after fasting (97%)
- avoiding low blood sugar during the day (90%)
- avoiding low blood sugar overnight (90%)
- avoiding weight gain/facilitating weight loss (91%)
- reducing blood pressure (79%)
- reducing risk of heart problems (90%)
- avoiding gastrointestinal issues (nausea, vomiting, diarrhea, pain) (87%)
- avoiding urinary tract and/or yeast infections (84%)
- avoiding fluid retention (85%)

In the more recent study conducted in April 2018, the following medications were reported being currently in use in respondents (n=3): Metformin (3), GLP-1 receptor agonists (1), SGLT2 inhibitors (1), DPP-4 inhibitors (1) and sulfonylureas (1). Insulin use was reported as follows: long-acting - glargine (1) and rapid-acting (1). No respondent had used a medication in a past clinical trial or reported stopping a medication for any reason. All those who responded to the question (n=3) said they were "better" or

"much better" able to meet blood glucose targets in general, upon waking, and post-prandially on current antihyperglycemic therapy. They all also stated that their current medication(s) helped them achieve hemoglobin A1c targets and maintain or lose weight "better" or "much better" than their previous regimen. When asked what factors were important in choosing between diabetes medications, 100% of respondents (n=3) said the following were "quite important" or "very important": keeping blood glucose at satisfactory level during the day or after meal and upon waking or after fasting, avoiding low blood sugar during the day and overnight, avoiding weight gain/facilitating weight loss, reducing blood pressure and risk of heart problems, and avoiding gastrointestinal issues (nausea, vomiting, diarrhea, pain), urinary tract and/or yeast infections and fluid retention.

Below are some direct quotes from respondents to both the October 2016 and April 2018 surveys that describe what they like and dislike about current therapy:

"Generally satisfied with my current medications and blood sugar levels."
- 55 to 69 year old person with type 2 diabetes, diagnosed 6-10 years ago, taking a GLP-1 receptor agonist, a sulfonylurea, metformin and insulin

"Since starting [a GLP-1 receptor agonist] my sugar levels have improved significantly and I have sustained a continued slow weight loss."
- person over 70 years old with type 2 diabetes, diagnosed more than 20 years ago, taking a GLP-1 receptor agonist, an SGLT2 inhibitor, metformin and insulin

"Makes my life easier to maintain – especially busy at work (life can feel more normal). Diabetes does not rule under these meds."
- 55 to 69 year old person with type 2 diabetes, diagnosed 6-10 years ago, taking a GLP-1 receptor agonist and metformin

"I like that I only have to take the pills once a day and that I only require one injection before bed. I couldn't keep up with taking medications at various times throughout the day."
- 40 to 54 year old person with type 2 diabetes, diagnosed 3-5 years ago, taking a GLP-1 receptor agonist, a sulfonylurea and metformin

"[A GLP-1 receptor agonist] has made such a difference to my [blood sugar] control. I feel good, have no diabetic issues with eyes, feet, kidneys or nerve damage. All the other medicine that I had tried gave me stomach upset, highs, lows and no control. I think it is just criminal that it is not covered by seniors medical. Even through I have proved that all other meds do not work for me."
- 55 to 69 year old person with type 2 diabetes, diagnosed 11-20 years ago, taking a GLP-1 receptor agonist and insulin

"Insulin regulation is somewhat hard even though I watch what I eat, and exercise... sometimes experience hypoglycemia."
- 40 to 54 year old person with type 2 diabetes, diagnosed 3-5 years ago, taking a DPP-4 inhibitor, an SGLT2 inhibitor and insulin

"I dislike the cost of the meds. It is very disheartening to be dependent on medication that is not covered by Pharmacare."
- 40 to 54 year old person with type 2 diabetes, diagnosed 3-5 years ago, taking a GLP-1 receptor agonist, metformin and insulin

"Too many pills and times of day to remember."
- person with type 2 diabetes, age and time since diagnosis unknown, taking a DPP-4 inhibitor combined with metformin

"I prefer oral medication over injectable medication. [A GLP-1 receptor agonist] was very difficult to administer and was quite painful. It left a lump under my skin at the injection site but resolved after a couple of weeks."

- 55 to 69 year old person with type 2 diabetes, diagnosed more than 20 years ago, taking a DPP-4 inhibitor, an SGLT2 inhibitor, a sulfonylurea, metformin and insulin

"I'm not sure if they're working as well as they should be. Recently I'm having trouble keeping my blood sugar where it should be, and take high amounts of insulin to compensate."

- person over 70 years old with type 2 diabetes, diagnosed more than 20 years ago, taking a GLP-1 receptor agonist and insulin

5. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

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When asked about their expectations for new diabetes therapies, respondents to the October 2016 and April 2018 survey expressed a strong desire for medications that have been proven safe and can normalize/stabilize blood glucose levels and improve hemoglobin A1c without causing weight gain or hypoglycemia. They wish for new treatments to enhance weight loss and improve health outcomes at an affordable cost. Ideally, they'd like medications and diabetes devices to be covered in a timely manner by public and private plans. They want treatments that are easily administered, cause the least amount of disruption to lifestyle and allow for flexibility with food intake and choices. They also want medications that help avoid polypharmacy and eliminate the need for injections while minimizing risk of any short-term medication-related side effects or long-term disease-related side effects. Several respondents hope future treatments will reverse or cure diabetes.

Below, respondents provided input on desired improvements to treatment and the impact these would have on daily life and overall quality of life:

"Help with ha1c[sic], reduce weight gain, promote weight loss, supported by formulary to keep cost down."

"I want my medication minimal, and descrete[sic]."

"I am hoping that the newer drugs are approved quicker by my Insurance Company."

"Improve diabetes control and health outcomes. I hope that these medications will be covered and available for all patients living with diabetes."

"Manage diabetes effectively without needing such a large variety of medications."

"Control glucose levels, cause little or no side effects, be reasonably priced."

"I hope they get cheaper so we can afford the ones that work the best."

"Keep blood sugar at acceptable levels in order to be able to live a healthy normal life without worry of complications from high blood sugars."

"Ease of use, and low cost is very important. I am also hoping any new therapies will help reduce weight or maintain it."

"Newer drugs will hopefully demonstrate benefits beyond just sugar control. More studies will hopefully show significant reduction of cardiovascular risks as well as renal complications associated with diabetes."

6. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

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Soliqua has not yet received a Notice of Compliance from Health Canada. Consequently, few Canadians would have first-hand experience with the medication to report on. Of those who participated in the April 2018 survey and responded to the questions specific to Soliqua (n=3), none had ever taken it or could comment on the groups of people for whom it would be best suited. All respondents (n=3) said that having combination diabetes medications is “very beneficial” or “extremely beneficial”. They provided comments in support of combination medications, indicating that often times too many are prescribed, which is burdensome. Respondents implied that combination medications are easier to use which, in turn, promotes more regular use and supports adherence to a prescribed regimen. One person said “*the less medication [I] have to take, the better it is on my mental health.”* Some respondents were unsure how exactly a combination medication would affect their ability to afford diabetes therapies and injection supplies; one person said there would be no change. A few felt that combination mediations would decrease the time and effort they spend administering medication, but other respondents equally didn’t know about this.

In the October 2016 survey, some respondents commented on the advantage of having combination medications available for diabetes treatment. Several spoke about how burdensome it is to take several oral and/or injectable medications for their management and that it would make a different to their daily management and quality of life to reduce the number of agents they administer. When asked about hopes for new therapies, they explicitly said it would be beneficial to have a greater number of combination mediation options available (“*more combo meds with GLP-1”, “mixed meds for one injection”*).

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

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Soliqua does not have a companion diagnostic, therefore this question is not applicable to our submission.

8. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

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Diabetes is a disease that requires intensive self-management. Diabetes Canada's 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada highlight the importance of personalized care when it comes to the pharmacologic management of the condition. Specifically, after initiating healthy behaviour measures, the guidelines recommend selecting diabetes treatment modalities based on a patient's degree of glycemic control and various other considerations. To achieve optimal blood glucose levels, individualization of therapy is essential. This includes careful consideration of medication selection, route of administration (oral, injection, pen or pump), frequency with which someone monitors blood glucose and adjusts dosage, benefits and risks that the patient experiences and/or tolerates, and lifestyle changes the patient is willing or able to make. Our survey responses reinforce the message that different people with diabetes require different medications/treatment modalities to help effectively manage their disease. Their unique clinical profile, preferences and tolerance of therapy should direct physicians to the most appropriate choice and combination of treatments for their disease management.

Many people with diabetes hope for less dependence on insulin and medications. While current therapies have generally led to improvement for many people with diabetes in blood glucose and hemoglobin A1c control, respondents hope for even better, more affordable antihyperglycemic agents that they can access equitably and in a timely manner, and that they can take consistently, if effective, to help them lead a normal life. Lixisenatide + insulin glargine (Soliqua) may help people to achieve better glycemic control, which could potentially improve lives and save millions of dollars in direct health-care costs. For this reason, lixisenatide + insulin glargine (Soliqua) should be an option for people living with diabetes.

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   There was no assistance from outside Diabetes Canada to complete this submission.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   There was no assistance from outside Diabetes Canada to collect or analyze data used in this submission.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000

   Please find attached a list of organizations who have provided financial support to Diabetes Canada, along with the amounts provided.

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Seema Nagpal, BScPharm, MSc, PhD
Position: Epidemiologist and Senior Leader, Public Policy
Patient Group: Diabetes Canada
Date: May 10, 2018

Financial Contributions to Diabetes Canada (updated 2017)

Constituent/Name	Funder range ($)
AstraZeneca Canada Inc	350,000+
LifeScan Canada Ltd.	350,000+
Novo Nordisk Canada Inc	350,000+
Sanofi Canada	350,000+
Sun Life Financial	350,000+
Eli Lilly Canada Inc	250,000-349,999
Ascensia Diabetes Care	175,000-249,999
Janssen Inc	175,000-249,999
Medtronic Of Canada Ltd	175,000-249,999
Dairy Farmers Of Canada	100,000-174,999
Merck Canada Inc	100,000-174,999
WEIGHT WATCHERS	100,000-174,999
Abbott Diabetes Care	50,000-99,999
Canola Council Of Canada	50,000-99,999
Insulet Canada Corporation	50,000-99,999
Knight Therapeutics Inc.	50,000-99,999
Manulife Financial	50,000-99,999
Nestle Health Science	50,000-99,999
RBC Foundation	50,000-99,999
The Bank of Nova Scotia	50,000-99,999
Abbott Nutrition	25,000-49,999
BD Medical Diabetes Care	25,000-49,999
Beer Canada	25,000-49,999
Dexcom Canada	25,000-49,999
Dynacare	25,000-49,999
Heartland Food Products Group	25,000-49,999
McNeil Consumer Healthcare	25,000-49,999
Rexall Foundation	25,000-49,999
Roche Diabetes Care	25,000-49,999
SaskCanola	25,000-49,999
Auto Control Medical Inc	5,000-24,999
Bayer Pharmaceuticals	5,000-24,999
Boehringer Ingelheim (Canada) Ltd	5,000-24,999
Canadian Association of Optometrists	5,000-24,999
Canadian Produce Marketing Association	5,000-24,999
CHICKEN FARMERS OF CANADA	5,000-24,999
Edelman Canada	5,000-24,999
EOCI Pharmacomm Ltd.	5,000-24,999
Euro Harvest Bakery Wholesalers	5,000-24,999
Farleyco Marketing Inc	5,000-24,999
ForaCare Technology Canada Inc.	5,000-24,999
Holista Foods	5,000-24,999
InBody Canada	5,000-24,999
Innovative Medicines Canada	5,000-24,999
Ipsen	5,000-24,999
Jays Care Foundation	5,000-24,999
mdBriefCase Group Inc.	5,000-24,999

Montmed	5,000-24,999
Myelin & Associates	5,000-24,999
Novartis Pharmaceuticals Canada Inc	5,000-24,999
Ontario Pork Council	5,000-24,999
Original Energy Sales	5,000-24,999
Paladin Labs Inc	5,000-24,999
Pharmasave Drugs (National) Ltd	5,000-24,999
Prime Strategies Inc.	5,000-24,999
PULSE CANADA	5,000-24,999
Royal College Of Physicians And Surgeons Of Canada	5,000-24,999
Tykess Pharmaceuticals	5,000-24,999
Urban Poling Inc	5,000-24,999
Valeant Canada LP	5,000-24,999
VitalAire Canada Inc	5,000-24,999