CANADA

PROVINCE OF QUEBEC
DISTRICT OF MONTREAL

NO: 500-06-000732-152

(Class Action)
SUPERIOR COURT

DIANE GAGNON

Petitioner

-vs.-

BAYER INC.
and
(…)
BAYER CORPORATION
and
(…)
(…)
BAYER AG
and
BAYER HEALTHCARE LLC
(…)

Respondents

THIRD AMENDED APPLICATION TO AUTHORIZE THE BRINGING OF A CLASS ACTION & TO APPOINT THE PETITIONER AS CLASS REPRESENTATIVE
(Art. 574 C.C.P and following)

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TO THE HONOURABLE MR. JUSTICE GARY D.D. MORRISON OF THE SUPERIOR COURT, SITTING IN AND FOR THE DISTRICT OF MONTREAL, YOUR PETITIONER STATES AS FOLLOWS:

I. GENERAL PRESENTATION

A) The Action

1. Petitioner wishes to institute a class action on behalf of the following group, of which she is a member, namely:

    - all persons residing in Quebec who were prescribed and have ingested the drug (…) XARELTO® (rivaroxaban) since 2008, and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

2. "XARELTO" is the brand name of the anticoagulant[1] drug, Rivaroxaban, which is prescribed to patients in order to reduce the ability of the blood to clot in the arteries, veins and/or heart and/or to prevent existing blood clots from increasing in size. Specifically, the ingestion of XARELTO is used to:

    (i) Reduce the risk of stroke in patients with non-valvular atrial fibrillation (AF)[2],

    (ii) Treat deep vein thrombosis (DVT)[3] and pulmonary embolism (PE)[4] and to reduce the risk of reoccurrence, and

    (iii) Prevent or reduce venous thromboembolism (VTE)[5] after knee and hip replacement surgery;

3. Petitioner contends that Respondents represented to the medical and healthcare community, to Health Canada, to the United States Food and Drug Administration ("USFDA") and to the Class Members that they researched, designed, developed, manufactured, and tested XARELTO and that it had been

[1] Anticoagulant medicines are used to prevent the formation of blood clots.

[2] Atrial fibrillation (AF) is a common heart rhythm disorder (a cardiac arrhythmia) associated with deadly and debilitating consequences including heart failure, stroke, poor mental health, reduced quality of life and death. It accounts for approximately 15% of all strokes in Canada and this risk increases with age, so that after the age of 60, 1/3 of all strokes are caused by it.

[3] Deep vein thrombosis, or deep venous thrombosis, (DVT) is the formation of a blood clot (thrombus) within a deep vein, predominantly in the legs.

[4] Pulmonary embolism (PE) is a blockage of the main artery of the lung or one of its branches by a substance that has travelled from elsewhere in the body through the bloodstream (embolism). PE most commonly results from deep vein thrombosis (a blood clot in the deep veins of the legs or pelvis) that breaks off and migrates to the lung, a process termed venous thromboembolism (VTE).

[5] Venous thromboembolism (VTE) comprises both deep vein thrombosis (DVT) and pulmonary embolism (PE). The most serious complication of DVT occurs when the blood clot dislodges and travels to the lungs, becoming a PE.

found to be safe and/or effective for its intended use. In addition, the Respondents concealed their knowledge of XARELTO's defects from the medical and healthcare community, Health Canada and the USFDA, and from Class Members;

4. The Respondents marketed, packaged, promoted, advertised, distributed, labelled and/or sold XARELTO as a new, safe, effective, and more convenient oral treatment that was more effective than Warfarin (also known by the brand names Coumadin, Jantoven, Marevan, and Uniwarfin), a long-established safe treatment for the prevention of heart attacks, strokes, and blood clots in the veins and arteries despite a wealth of existing knowledge that the drug had dangerous side effects including, an increased risk of major life-threatening internal bleeding, among other serious and severe bleeding complications;

5. Importantly, there is no antidote to XARELTO, unlike Warfarin. Therefore, in the event of hemorrhagic complications, there is no available reversal agent and the Respondents gave inadequate warnings and/or information on the topic;

6. In addition, while the Respondents were labelling XARELTO as a drug that prevents heart attacks, strokes, and blood clots, its side effect of major internal bleeding has the potential to cause heart attacks and death. Thus, the Respondents researched, designed, developed, manufactured, tested, marketed, packaged, promoted, advertised, distributed, labelled and/or sold XARELTO as a preventative drug, without so much as mentioning that it was also a catalyst;

6.1 In short, the Respondents' liability rests on (i) inadequate warning about the risk of bleeding and inadequate warning as to the lack of a reversal agent, (ii) inadequate instruction on safe and effective use and proper monitoring, (iii) there was a design defect in that there was no reversal agent, and (iv) the weak efficacy is outweighed by the serious risks associated with the drug;

7. Respondents continue to market, package, promote, advertise, distribute, label and/or sell XARELTO throughout Canada, including within the province of Quebec, with inadequate warnings as to its serious and adverse side effect of the increased risk of major life-threatening internal bleeding and the lack of an antidote which has severe and life-threatening complications which are permanent and lasting in nature and this has caused physical pain and mental anguish, including diminished enjoyment of life, as well as the need for lifelong medical treatment, monitoring and/or medications, and fear of developing any of the above named health consequences which are described in more detail below;

B) The Respondents

8. (…)

9. (…)

10. (…)

11. (…)

12. (…)

13. (…)

14. Respondent Bayer Inc. ("Bayer Canada") is a Canadian pharmaceutical corporation with its head office in Toronto, Ontario. Bayer Canada is and was at all relevant times involved in the research, design, development, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of pharmaceutical products including XARELTO. It is a subsidiary of (…) Bayer Canadian Holdings Inc. ("Bayer Canada Holdings") and non-party Bayer Global Investments B.V., that does business throughout Canada, including within the province of Quebec, the whole as appears more fully from a copy of an extract from the *Registraire des enterprises*, produced herein as **Exhibit R-3**;

15. Respondent Bayer Canada is the Canadian manufacturer, "sponsor", and the owner of the patent for XARELTO for the "• prevention of stroke and systemic embolism in patients with atrial fibrillation, in whom anticoagulation is appropriate. • treatment of venous thromboembolic events (deep vein thrombosis [DVT], pulmonary embolism [PE]) and prevention ofrecurrent *[sic]* DVT and PE" under three (3) Drug Identification Numbers ("DIN") according to its three (3) strengths being: 10 mg (DIN: 02316986[6]), 15 mg (DIN: 02378604[7]), and 20 mg (DIN: 02378612[8]), the whole as appear more fully from a copy of Health Canada's Patent Registers for the Medicinal Ingredient "rivaroxaban" and the Brand Name "XARELTO", produced herein *en liasse* as **Exhibit R-4**;

15.1 In addition, Respondent Bayer Canada, as sponsor for XARELTO in Canada, is responsible for its Product Monographs (Exhibit R-15), which are the primary source of information for healthcare professionals and patients, setting out the uses, dosage, and risks associated with the drug;

16. (…)

[6] Associated patent numbers for DIN 2396561: 2547113, 2624310, and 2823159.
[7] Associated patent numbers for DIN 02378604: 2396561, 2547113, 2624310, and 2823159.
[8] Associated patent numbers for DIN 02378612: 2396561, 2547113, 2624310, and 2823159.

17. Respondent Bayer Corporation ("Bayer USA") is an American pharmaceutical corporation with its head office in Pittsburgh, Pennsylvania. It is a wholly-owned subsidiary of Respondent Bayer AG and it is the parent company of Respondent Bayer HealthCare LLC and Bayer HealthCare Pharmaceuticals, Inc[9]. Bayer USA is and was at all relevant times involved in the research, design, development, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of pharmaceutical products including XARELTO;

18. (…)

19. (…)

20. Respondent Bayer AG is a German chemical and pharmaceutical corporation with its head office in Germany. It is the parent company of Respondents Bayer Canada, (…) Bayer USA and Bayer HealthCare LLC, as well as, Bayer HealthCare AG, Bayer Pharma AG, and Bayer HealthCare Pharmaceuticals, Inc. It is the third largest pharmaceutical company in the world. Bayer AG is and was at all relevant times involved in the research, design, development, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of pharmaceutical products including XARELTO. It is the registrant of the trade-mark (word) XARELTO (TMA726283) which was filed on August 8, 2002, the whole as appears more fully from a copy of said trade-mark from the CIPO database, produced herein as **Exhibit R-6**;

21. In addition, Respondent Bayer AG is the applicant of the patent for XARELTO, which was filed on December 11, 2000 and issued on October 14, 2008 – the current owner is its subsidiary, non-party Bayer Intellectual Property GMBH, the whole as appears more fully from a copy of patent no. 2396561 from the CIPO database, produced herein as **Exhibit R-7**;

22. Respondent Bayer HealthCare LLC is an American pharmaceutical corporation with its head office in Whippany, New Jersey. It is a wholly-owned subsidiary of Respondent Bayer USA. Respondent Bayer Healthcare LLC is and was at all relevant times involved in the research, design, development, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of pharmaceutical products including XARELTO;

23. (…)

24. All Respondents have either directly or indirectly researched, designed, developed, manufactured, tested, marketed, packaged, promoted, advertised, distributed, labelled and/or sold XARELTO to distributors and retailers for resale

[9] Bayer USA is the parent company of Respondent Bayer HealthCare LLC, which owns 100% of non-party Schering Berlin, Inc., which owns 100% of (…) Bayer HealthCare Pharmaceuticals, Inc. (…)

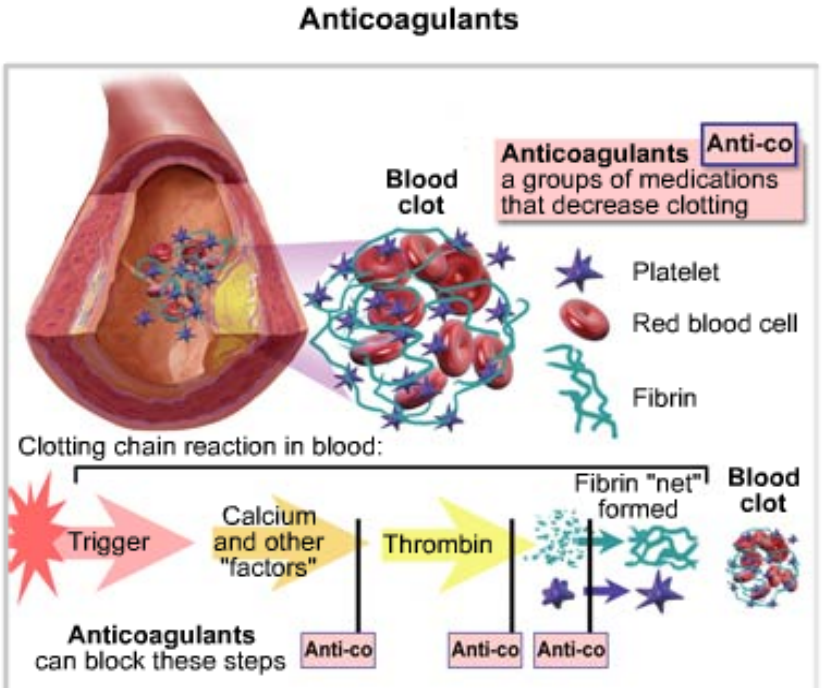
to or, directly to physicians, hospitals, medical practitioners and to the general public throughout Canada, including within the Province of Quebec;

25. Given the close ties between the Respondents and considering the preceding, all Respondents are solidarily liable for the acts and omissions of the other. Unless the context indicates otherwise, all Respondents will be referred to as "Bayer" for the purposes hereof;

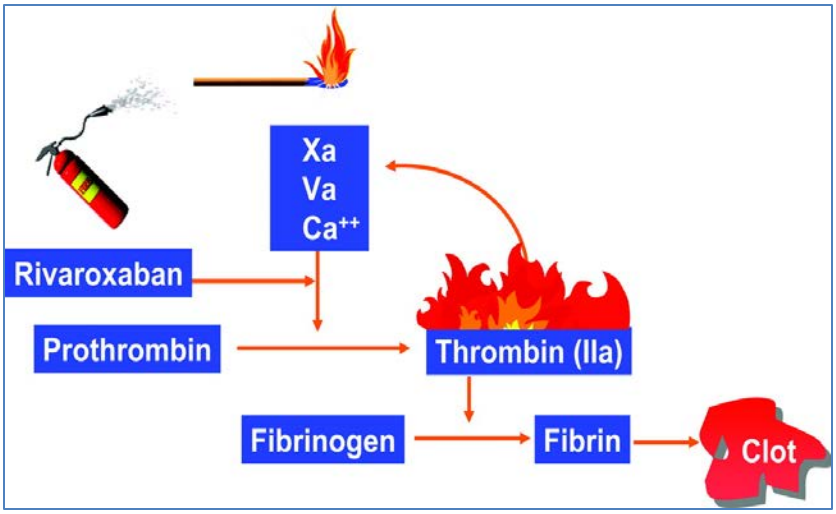
C) The Situation

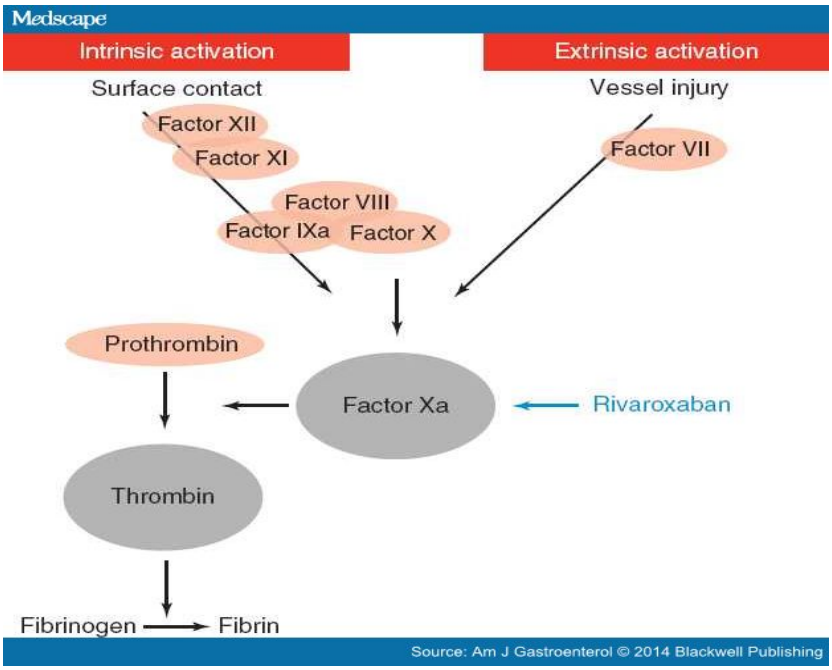
I. What is XARELTO?

26. XARELTO belongs to a group of medicines called anticoagulants. It works by directly inhibiting the blood-clotting "Factor Xa"[10] and thereby reducing the tendency of the blood to form clots. Specifically, it is an oral anticoagulant medication that is prescribed to patients to reduce the risk of stroke in patients with non-valvular atrial fibrillation (AF), to treat deep vein thrombosis (DVT) and pulmonary embolism (PE), and to reduce the risk of reoccurrence, and to prevent or reduce venous thromboembolism (VTE) after knee and hip replacement surgery;



[10] Simply put, Factor Xa, also known as Stuart-Prower factor and as prothrombinase, thrombokinase or thromboplastin, is an enzyme that participates in the coagulation or clotting of blood.





27. On September 15, 2008, Respondent Bayer Canada obtained approval for XARELTO from Health Canada in the 10 mg strength for the "prevention of venous thromboembolic events (VTE) in patients who have undergone elective total hip replacement or total knee replacement surgery". On March 19, 2009 this approval was supplemented due to "[t]he addition of new physician sample labelling". On January 16, 2012, Respondent Bayer Canada obtained approval from Health Canada to market XARELTO in Canada in the 10, 15, and 20 mg strengths as a "prevention of stroke and systemic embolism in patients with arterial fibrillation". On February 15, 2012 this approval was supplemented with the "treatment of deep vein thrombosis (DVT) without symptomatic pulmonary emoblism *[sic]* (PE)" for the 15 and 20 mg strengths. Lastly, on April 18, 2013,

Respondent Bayer Inc. obtained approval from Health Canada to market XARELTO as a "[t]reatment of pulmonary embolism (PE) and prevention of recurrent deep vein thrombosis (DVT) and PE" in the 10, 15, and 20 mg strengths, the whole as appears more fully from a copy of the five (5) Notices of Compliance obtained from Respondent Bayer Canada from Health Canada and from a copy of the Health Canada Summary Basis of Decision (SBD) for Xarelto dated February 13, 2009, produced herein *en liasse* as **Exhibit R-8**;

28. Accordingly, the Respondents launched XARELTO in Canada in 2008 in the 10mg strength as a prescription medication to prevent VTE in patients undergoing total hip replacement or total knee replacement surgery and in 2012, the Respondents launched XARELTO in all three (3) strengths, namely 10, 15, and 20 mg as a prescription medication to prevent stroke and systemic embolism in patients with atrial fibrillation. These uses increased to the present day classification as an anticoagulant medication to reduce the risk of stroke in patients with non-valvular atrial fibrillation (AF), to treat deep vein thrombosis (DVT) and pulmonary embolism (PE) and to reduce the risk of reoccurrence, and to prevent or reduce venous thromboembolism (VTE) after knee and hip replacement surgery;

29. On July 1, 2011, non-party Janssen Research & Development, LLC[11] ("Janssen R&D") obtained approval from the USFDA to market XARELTO in the United States as a "prevention (prophylaxis) of deep vein thrombosis (DVT), which may lead to a pulmonary embolism (PE) in people undergoing knee or hip replacement surgery" and on November 4, 2011, non-party Janssen R&D obtained approval from the USFDA to market XARELTO in the United States as having the ability to "reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation", the whole as appears more fully from a copy of the Press Release entitled "Johnson & Johnson Pharmaceutical Research & Development, L.L.C. submits New Drug Application to FDA for Rivaroxaban" dated July 30, 2008, from a copy of the New Release entitled "FDA Approves XARELTO® (rivaroxaban tablets) to Help Prevent Deep Vein Thrombosis in Patients Undergoing Knee or Hip Replacement Surgery" dated July 1, 2011, from a copy of the Press Release entitled "New Drug Application Submitted to FDA for Rivaroxaban for Prevention of Stroke in Patients with Atrial Fibrillation" dated January 5, 2011, and from a copy of the News Release entitled "FDA Approves XARELTO® (rivaroxaban) to Reduce the Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation" dated November 4, 2011, produced herein *en liasse* as **Exhibit R-2**;

29.1 Warfarin has been on the market for approximately 50 years; however, it requires the following of certain dietary restrictions, regular blood monitoring, and accordant dosage changes. It is therefore more cumbersome on the patient;

[11] Janssen Research & Development, LLC was formerly known as Johnson and Johnson Pharmaceutical Research and Development LLC.

30. A one-year supply of XARELTO costs approximately $3,000 as compared to the similar anticoagulant, warfarin, which costs approximately $200 per year;

II. The Scientific Studies Behind the Drug

31. The studies that follow demonstrate that ingesting XARELTO has an increased risk of serious bleeding events and/or the severity thereof;

32. Approval of XARELTO for the prophylaxis of DVT and PE in patients undergoing hip replacement or knee replacement surgeries was based on a series of clinical trials known as the Regulation of Coagulation in Orthopedic Surgery to Prevent Deep Venous Thrombosis and Pulmonary Embolism studies (the "RECORD" studies) (Exhibit R-8). The findings of the RECORD studies showed that rivaroxaban was superior to enoxaparin for thromboprophylaxis after total knee and hip arthroplasty (based on the Respondents' definition), accompanied by similar rates of bleeding. However, the studies also showed a greater incidence with XARELTO of bleeding leading to decreased hemoglobin levels and transfusion of blood, the whole as appears more fully from a copy of the New England Journal of Medicine article entitled "Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Total Knee Arthroplasty" dated June 26, 2008, from a copy of the Lancet journal article entitled "Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial" dated June 28, 2009, and from a copy of the New England Journal of Medicine article entitled "Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Hip Arthroplasty" dated June 26, 2008, produced herein *en liasse* as **Exhibit R-9**;

32.1. The RECORD studies were flawed in design. A USFDA Official Action Indicated ("OAI"), which rated inspections in 2009, disclosed rampant violations including, "systemic discarding of medical records," unauthorized unblinding, falsification, and "concerns regarding improprieties in randomization", the whole as appears more fully from a copy of the JAMA Internal Medicine article entitled "Research Misconduct Identified by US Food and Drug Administration" dated February 9, 2015, produced herein as **Exhibit R-9A**;

33. Approval of XARELTO for reducing the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation was based on a clinical trial known as the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation study ("ROCKET AF") - which set out to prove, and in fact did prove, that rivaroxaban was non-inferior to warfarin for the prevention of stroke or systemic embolism in patients with non-valvular atrial fibrillation, with a similar risk of major bleeding. However, "bleeding from gastrointestinal sites, including upper, lower, and rectal sites, occurred more frequently in the rivaroxaban group, as did bleeding that led to a drop in the hemoglobin level or bleeding that

required transfusion". Interestingly, the ROCKET AF study was sponsored by non-party Janssen R&D (then Johnson & Johnson Pharmaceutical Research and Development) and Respondent Bayer HealthCare Pharma, the whole as appears more fully from a copy of the New England Journal of Medicine article entitled "Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation" dated September 8, 2011, from a copy of the Supplementary Appendix, from a copy of the Disclosure Forms, and from a copy of the Protocol, produced herein *en liasse* as **Exhibit R-10**;

34. The ROCKET AF study was controversial as reviewers had noted that warfarin had not been well-managed or optimally used in the study and that this flaw prevented the study results from definitively proving that rivaroxaban was no worse than warfarin. This is dangerous territory as the flawed results could lead to use of a drug that could increase death and injury, the whole as appears more fully from a copy of the Institute for Safe Medication Practices' Quarter Watch entitled "Monitoring FDA MedWatch Reports - Why Reports of Serious Adverse Drug Events Continue to Grow" dated October 3, 2012, produced herein as **Exhibit R-11**;

34.1 In addition, the flaws in the ROCKET AF study were noted by the USFDA, which stated that there is a "lack of substantial evidence that [XARELTO] will have its desired effect when used as recommended", "the data comparing [Xarelto] to warfarin are not adequate to determine whether [Xarelto] is as effective for its proposed indication in comparison to warfarin when the latter is used skillfully", and that "[t]here is insufficient information about the drug to determine whether it is safe for use", the whole as appears more fully from a copy the USFDA Draft Briefing Document for the Cardiovascular and Renal Drugs Advisory Committee (CRDAC) for the meeting dated September 8, 2011, from a copy of the Forbes article entitled "FDA Reviewers Recommend Complete Response Letter for Rivaroxaban (Xarelto)" dated September 6, 2011, from a copy of an extract from Respondent Bayer's website at www.investor.bayer.de entitled "Bayer Confident in Results of ROCKET AF Study to be Reviewed by the FDA Cardiovascular and Renal Drugs Advisory Committee" dated September 6, 2011, and from a copy of the Pharmaletter article entitled "Disappointing FDA briefing papers on Bayer/J&Jâs *[sic]* Xarelto" dated September 7, 2011, produced herein *en liasse* as **Exhibit R-11A**;

34.2 Public Citizen also noted these control flaws and wrote a letter to the USFDA stating that they ""strongly oppose FDA approval... The 3 ROCKET AF trial conducted in support of the proposed indication had a suboptimal control arm...", the whole as appears more fully from a copy of the letter sent from Public Citizen to the USFDA dated October 20, 2011, produced herein as **Exhibit R-11B**;

34.3 A further issue with the ROCKET AF study was the once-a-day-dosing of XARELTO that it employed. The USFDA stated "the sponsor's rationale for evaluating only once daily dosing during Phase 3 is not strong. Most importantly, there is clinical information from Phase 2 trials ... and from clinical pharmacology studies suggesting that twice daily dosing, which would produce lower peak blood levels and higher trough blood levels of [Xarelto], might have been associated with greater efficacy and/or a better safety profile" (Exhibit R-11A);

34.4 Cardiologist Stephen Nissen stated "[m]y concern was that the dose [for Xarelto] was selected more for a marketing advantage rather than for the scientific data that was available, and that was a mistake", the whole as appears more fully from a copy of the transcript from the USFDA Center for Drug Evaluation and Research – Cardiovascular & Renal Drugs Advisory Committee conference dated September 8, 2011 and from a copy of the Summary Minutes of same, produced herein *en liasse* as **Exhibit R-11C**;

34.5 In fact, before the ROCKET AF study began, non-party Janssen Pharmaceuticals, Inc.[12] asked the USFDA if it was in agreement with the once-a-day dosing regimen and it was not; suggesting that "administering XARELTO twice a day might result in better outcomes". The worry was that once-a-day dosing could lead to "sharp fluctuations in the amount of the drug in patients' blood, sacrificing safety or efficacy", that there was "no rational basis for the … choice of the dose tested in ROCKET", and that it "probably increased the risk of bleeding". The once-a-day regimen was used anyway, the whole as appears more fully from a copy of the USFDA Center for Drug Evaluation and Research Summary Review dated November 4, 2011 and from a copy of the Project on Government Oversight article entitled "Drug Problems: Nominee to Head FDA Led Clinical Trial FDA Faulted" dated November 12, 2015, produced herein *en liasse* as **Exhibit R-11D**;

34.6 Although the USFDA concluded that a twice-daily dosing regimen "must" be studied "before this product is approved" (Exhibit R-11A), this never happened and XARELTO was approved for use;

34.7 More recently, it was reported in a German newspaper that the device[13] that was used to measure the blood clotting in the ROCKET AF trial may have been faulty and that this was being investigated by the USFDA and the European Medicines Agency. The device was only used on the warfarin test group as regular testing is not conducted with XARELTO, making it seem like patients on warfarin may have been more prone to bleeding than usual due to the

[12] Janssen Pharmaceuticals, Inc. was formerly known as Janssen Pharmaceutica Inc. and formerly known as Ortho-McNeil-Janssen Pharmaceuticals, Inc.

[13] The test devices in question are hand-held coagulation analyzers that display results of tests to determine how quickly a patient's blood clots. The longer the clotting occurs in the prescribed therapeutic range, the less the risk of bleeding or stroke.

malfunction, making it appear that XARELTO was non-inferior and/or superior, the whole as appears more fully a copy of the Handelsblatt article entitled "Authorities Target Bayer Blood Thinner" dated December 10, 2015 and from a copy of the PM Group article entitled "Bayer defends Xarelto as pivotal trial scrutinised" dated December 10, 2015, produced herein *en liasse* as **Exhibit R-11E**;

34.8 When approving XARELTO for use, the USFDA expressed desirability in monitoring XARELTO dosage based on the ROCKET studies. The clinical pharmacology in these studies demonstrated a linear correlation between rivaroxaban (XARELTO) levels and prothrombin time ("PT")[14]; and subsequently a correlation between PT and the risk of bleeding. At least at this time, the Respondents were aware of the correlation between XARELTO and bleeding risks, but had simply "not chosen to utilize this information." At all relevant times, the Respondents controlled the contents of their label as demonstrated by their decision to go forward without regard to the USFDA's suggestion to utilize this information, the whole as appears more fully from a copy of the USFDA Approval Letter dated November 4, 2011, from a copy of the USFDA Summary Review dated November 4, 2011, and from a copy of he USFDA Medical Reviews dated November 4, 2011, produced herein *en liasse* as **Exhibit R-11F**;

34.9 Most recently, it has been uncovered that a faulty blood-testing device, the INRatio, which is sold by non-party Alere, may have compromised the results of the ROCKET AF clinical trials by leading doctors to give patients the wrong dosage of warfarin, which led to additional bleeding episodes and gave an unfair advantage to XARELTO. In 2006, as the ROCKET AF trials were beginning, the INRatio was facing scrutiny by the USFDA, who claimed that the devices were generating "clinically significant" erroneous values and that complaints were not being properly investigated. In 2014, the INRatio monitors were recalled due to the fact that they might provide inaccurate results, the whole as appears more fully from a copy of the New York Times article entitled "F.D.A. Asks If Faulty Blood Monitor Tainted Xarelto Approval" dated February 22, 2016, from a copy of the USFDA recall alert entitled "Alere Recalls INRatio® and INRatio2® PT/INR Monitoring System Due to Incorrect Test Results" dated 2016, from a copy of an extract from nonparty Alere's website at www.inr-care.com containing a list of all recalled devices, from a copy of non-party Alere's recall notification entitled "URGENT: MEDICAL DEVICE RECALL – Alere INRatio®/INRatio®2 PT/INR Monitoring System" dated July 26, 2016, from a copy of the New England Journal of Medicine article entitled "Point-of-Care Warfarin Monitoring in the ROCKET AF Trial" dated February 25, 2016, and from a copy of the Medscape article entitled "BMJ: Rivaroxaban Maker Withheld INR Device Concerns From FDA in ROCKET AF" dated September 30, 2016, produced herein *en liasse* as **Exhibit R-11G**;

[14] Prothrombin time (PT) is a blood test that measures how long it takes blood to clot.

34.10 On October 11, 2016, the USFDA concluded that the Alere INRatio device had minimal effects on the Rocket AF Study;

35. Approval of XARELTO for the treatment of DVT and/or PE and the reduction in recurrence of DVT and/or PE was based on the clinical trials known as the EINSTEIN-DVT, EINSTEIN-PE, and EINSTEIN-Extension studies. The EINSTEIN-DVT study tested XARELTO versus a placebo, and merely determined that XARELTO offered an option for treatment of DVT, with obvious increased risk of bleeding events as compared to a placebo. The EINSTEIN-Extension study confirmed that result. The EINSTEIN-PE study's findings showed that a rivaroxaban regimen was non-inferior to the standard therapy for initial and long-term treatment of PE. However, the studies also demonstrated an increased risk of adverse events in users of XARELTO, including those that resulted in permanent discontinuation of XARELTO or prolonged hospitalization, the whole as appears more fully from a copy of the New England Journal of Medicine article entitled "Oral Rivaroxaban for Symptomatic Venous Thromboembolism" dated December 23, 2010, from a copy of the Expert Review of Cardiovascular Therapy Clinical Trial Report entitled "Oral rivaroxaban after symptomatic venous thromboembolism: the continued treatment study (EINSTEIN-Extension study)" dated July 2011, and from a copy of New England Journal of Medicine article entitled "Oral Rivaroxaban for the Treatment of Symptomatic Pulmonary Embolism" dated April 5, 2012, produced herein *en liasse* as **Exhibit R-12**;

36. The Respondents have used the results of the RECORD studies, the ROCKET AF study, and the EINSTEIN studies to promote XARELTO in their promotional materials, including, the XARELTO website, which tout the positive results of those studies. However, the Respondents' promotional materials fail to similarly highlight the increased risk of gastrointestinal bleeding and bleeding that required transfusion, among other serious bleeding concerns;

37. In addition, the Respondents designed their studies to under-represent the true risk of adverse bleeding events and they failed to conduct proper studies that they knew or should have known would have disclosed the true risks;

38. These studies serve to indicate the importance of informing both patients and healthcare professionals of these adverse side-effects so that they may make informed decisions regarding this medication. In addition, should the patient make an informed decision to take XARELTO in spite of the serious risks, knowledge of these risks would have led to regular blood monitoring and/or doctor follow-up to ensure proper dosage if at all;

39. The Respondents, in failing to advise doctors and patients of the increased risks associated with XARELTO, effectively usurped their ability to make informed decisions regarding its use and removed their ability to limit and/or control the risk through engaging in precautionary monitoring measures;

40. In August of 2014, the Journal of Neurosurgery published an study that showed that the use of XARELTO and other newer anticoagulant medications could lead to irreversible intracerebral hemorrhage or bleeding inside the brain, the whole as appears more fully from a copy of the Journal of Neurosurgery article entitled "Race against the clock: Overcoming challenges in the management of anticoagulant-associated intracerebral hemorrhage" dated August 2014, produced herein as **Exhibit R-13**;

40.1 On January 15, 2009, merely months after the approval of XARELTO in Canada, the first serious adverse event was reported to Health Canada, whereby a 64-year-old female suffered a life-threatening pulmonary embolism following an operation on her knee. Thereafter, there were 6 serious adverse events reported on February 18, 2009, all pulmonary embolisms. After this, there were daily and/or weekly reported serious adverse events reported until the present, with a total of 1666 serious adverse events being reported to Health Canada, the whole as appears from a copy of Health Canada's list of adverse reaction reports, produced herein as **Exhibit R-13A**;

40.2 Of these serious adverse events reported, 126 resulted in death between February 18, 2009 and September 25, 2014, the whole as appears more fully from a copy of Health Canada's list of adverse reaction reports and from a copy of the actual reports, produced herein *en liasse* as **Exhibit R-13B**;

40.3 XARELTO has been cited fairly often in reports submitted to the USFDA regarding adverse medical events in patients, according to the Institute for Safe Medical Practices ("ISMP"). In 2014 alone, XARELTO was implicated in over 3,331 "serious" adverse event reports, including 379 cases in which patients died. The USFDA received 525 reports, marking more than all other therapeutic drugs, the whole as appears more fully from a copy of the Quarter Watch report dated September 23, 2015, produced herein as **Exhibit R-13C**,

III. The Respondents' Marketing Practices

41. The Respondents marketed XARELTO as a new oral anticoagulant treatment alternative to warfarin (Coumadin), a long-established safe treatment for preventing stroke and systemic embolism. The Respondents sharply emphasized the supposed benefits of treatment with XARELTO over warfarin, which they refer to as the Xarelto Difference – namely, that XARELTO is a single daily dose pill that does not require regular monitoring of plasma levels with blood tests, that it is more convenient than warfarin, and that it does not limit a patient's diet;

42. For example, in advertising XARELTO on the Respondents' websites, they state:

> With XARELTO®, blood tests aren't typically necessary to set your starting dose, and you don't need to schedule regular blood tests throughout your treatment to have your dosage adjusted. So instead of spending time monitoring your blood, you can do more of the things you enjoy. (emphasis added)

The whole as appears more fully from a copy of an extract from the website www.xarelto.com and from a copy of the Respondent-sponsored WebMD webpage for XARELTO available at www.webmd.com, produced herein *en liasse* as **Exhibit R-14**;

43. This emphasis on convenience is dangerously misleading and it negated the already inadequate language in XARELTO's labelling concerning the serious risk of severe and irreversible bleeding;

43.1 In reality, the "XARELTO Difference" was nothing more than a marketing campaign based on unsound science;

43.2 XARELTO's clinical studies indicate that XARELTO is safer and more effective where there is regular blood monitoring, dosing adjustments and twice-a-day dosage;

43.3 Ingesting XARELTO without the necessary blood monitoring and dosage adjustments can cause major, life-threatening bleeding events. It is absolutely vital that doctors who prescribe XARELTO balance the dose of the drug to ensure that the blood is thinned enough to reduce the risk of stroke, but not thinned so much as to increase the risk of a major bleeding event. The Respondents were well-aware of this fine balance and of risk and the need for blood monitoring, but have failed to disclose this vital health information;

44. In its QuarterWatch publication for the first quarter of the 2012 fiscal year (Exhibit R-11), the Institute for Safe Medication Practices ("ISMP") noted that, even during the approval process, USFDA "[r]eviewers also questioned the convenient once-a-day dosing scheme [of XARELTO], saying blood level studies had shown peaks and troughs that could be eliminated by twice-a-day dosing";

44.1 The use of XARELTO without appropriate blood monitoring, dose adjustment and twice-a-day dosing, can cause major, life-threatening bleeding events. Physicians using XARELTO must be able to balance the dosage to ensure that the patient's blood is thinned enough to reduce the risk of stroke, but not thinned so much as to increase the risk for a major bleeding event. The Respondents were aware of this risk and the need for blood monitoring, but failed to disclose this vital health information to patients, doctors, Health Canada and the public;

45. Importantly, there is no antidote to reverse the life-threatening effects of XARELTO, unlike warfarin. Therefore, in the event of hemorrhagic complications, there is no available reversal agent;

45.1 In the year between July 1, 2011 and June 30, 2012, there were 1,080 "serious injury reports" filed with the USFDA, including 65 deaths associated with the use of XARELTO. Therefore, of the reported hemorrhagic events, approximately 6% resulted in death, which was 50% more than the risk of a hemorrhage-related death with warfarin, the whole as appears more fully from a copy of the Quarter Watch report dated January 9, 2013, produced herein as **Exhibit R-14A**;

45.2 By the end of 2012, 2,081 "serious injury reports" were filed with the USFDA, including a total of 151 deaths associated with XARELTO. Of there reported hemorrhagic events, 7.3% resulted in death. This data is derived from XARELTO's first year in the United States market, the whole as appears more fully from a copy of the Quarter Watch report dated October 17, 2013, produced herein as **Exhibit R-14B**;

45.2.1 The ISMP referred to these figures as constituting a "strong signal" regarding the safety of XARELTO, defined as "evidence of sufficient weight to justify an alert to the public and the scientific community, and to warrant further investigation" (Exhibit R-11);

45.3 In the first quarter of 2013, the number of serious adverse events associated with the use of XARELTO surpassed that of Pradaxa (another oral anticoagulant) significantly, with XARELTO numbering 680 and Pradaxa numbering 528. Previously, Pradaxa had been ranked as the number one reported drug for adverse events in 2012, the whole as appears more fully from a copy of the Quarter Watch report dated May 7, 2014, produced herein as **Exhibit R-14C**;

45.3.1. Moreover, in the first eight months of 2013, at least 968 adverse event reports involving XARELTO were reported to German health officials, including 72 deaths, as compared to a total of 750 reports and 58 deaths having been reported in 2012, indicating that the increase tracked with the rise in use of XARELTO, which had reportedly increased 240% after just 1.5 years on the market. the whole as appears more fully from a copy of the Respiratory Medicine Case Reports case report entitled "Fatal pulmonary hemorrhage after taking anticoagulation medication" dated 2015, produced herein as **Exhibit R-14D**;

45.4 In spite of the strong indication that XARELTO was causing serious bleeding events and a particularly large amount of deaths as a result, the Respondents failed to inform consumers, health care professionals, and the scientific community and they failed to perform further investigation into its safety;

46. This important information hardly present in the Product Monograph at present as it is only mentioned once in the “Overdosage” section and is unclear. The excerpt is as follows:

> A specific antidote for XARELTO is not available. The use of activated charcoal to reduce absorption in case of XARELTO overdose may be considered. Administration of activated charcoal up to 8 hours after overdose may reduce the absorption of XARELTO.

The whole as appears more fully from copies of the Product Monographs for XARELTO last revised on:

- September 10, 2008,
- September 14, 2011,
- January 11, 2012,
- February 13, 2012,
- July 18, 2012,
- April 12, 2013,
- June 5, 2013,
- August 28, 2013,
- July 10, 2014,
- February 20, 2015,
- May 22, 2015,
- July 20, 2015,
- September 1, 2016,

produced herein *en liasse* as **Exhibit R-15**;

46.1 The product monographs failed to adequately explain the following:

- That XARELTO can cause bleeding;
- That XARELTO poses a greater risk of bleeding than enoxaparin and warfarin;
- That all patients should be assessed for the risk of bleeding prior to using XARELTO;
- How to identify patients who are at an increased risk of bleeding, and who should not be prescribed XARELTO or who should take precautionary measures;
- Drug interactions that affect hemostasis and increase the risk of bleeding in XARELTO patients;

- Precautionary measures to be taken by patients at an increased risk of bleeding;
- All patients should be monitored for signs of bleeding and how to perform routine monitoring;
- How to investigate the source of bleeding that occurs in XARELTO patients; and
- That there is no effective way to reverse XARELTO bleeding;

46.2 A copy of the XARELTO product monograph dated September 20, 2019, is produced herein as **Exhibit R-15B**;

47. There are feasible alternatives to XARELTO in the form of anticoagulants for which there is an established antidote, i.e., reversal agent, and for which there is an established blood monitoring protocol. The lack of these attributes in XARELTO rendered its design defective, which was a substantial factor in causing the Plaintiff's and Class Members' injuries. Today, the Respondents are frantically searching for an antidote that they should have developed before making the business decision to release XARELTO into the marketplace;

48. Clinical collaboration agreements were entered into by the Respondents with Portola Pharmaceuticals Inc., a pharmaceutical corporation based in San Francisco, California for the development of an antidote for XARELTO. On January 9, 2015, Portola Pharmaceuticals Inc. announced positive results for the safety and efficacy of Andexanet Alfa as a suitable antidote therapy for a major bleeding episode from XARELTO in the ANNEXA-R[15] study and that it would present its findings to the American College of Cardiology on March 16, 2015, the whole as appears more fully from a copy of the Globe Newswire News Release entitled "Portola Announces Phase 3 ANNEXA-R Study of Andexanet Alfa and Factor Xa Inhibitor XARELTO(R) (rivaroxaban) Met Primary Endpoint With High Statistical Significance" dated January 9, 2015 and from a copy of the non-yet-registered trade-mark "ANNEXA" (Application Number: 1707663) which was filed on December 17, 2014, produced herein *en liasse* as **Exhibit R-16**;

48.1 On August 17, 2016, the USFDA responded to Portola Pharmaceuticals Inc.'s ("Portola") application for ANDEXXA (andexanet alfa) as a therapy for patients treated with XARELTO *inter alia* when reversal of anticoagulation is needed due to a life-threatening or uncontrolled bleeding event. On December 19, 2016, Portola Pharmaceuticals Inc. announced that it signed a $50 million loan agreement with Bristol-Myers Squibb Company and Pfizer Inc. to provide additional funding toward the development and testing of ANDEXXA, the whole as appears more fully from a copy of the Press Release entitled "Portola Pharmaceuticals Receives Complete Response Letter from FDA for Biologics

[15] Andexanet Alfa a Novel Antidote to the Anticoagulant Effects of FXa Inhibitors – Rivaroxaban.

License Application for AndexXa™ (andexanet alfa)" dated August 17, 2016 and from a copy of the Globe Newswire article entitled "Portola Pharmaceuticals Enters into $50 Million Loan Agreement with Bristol-Myers Squibb and Pfizer for Continued Development of AndexXa™ (andexanet alfa)" dated December 19, 2016, produced herein *en liasse* as **Exhibit R-16A**;

48.2 ANDEXXA was developed to address an unmet medical need for patients treated with direct FXa inhibitors when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding, the whole as appears more fully from a copy of the USFDA "Summary Basis for Regulatory Action" dated May 3, 2018, produced herein as **Exhibit R-16B**;

48.3 In May 2018, ANDEXXA was granted accelerated approval by the USFDA for patients treated with rivaroxaban when reversal of anticoagulation was needed due to life-threatening or uncontrolled bleeding and on December 31, 2018, the USFDA approved the "Prior Approval Supplement" for ANDEXXA for full commercial launch in the United States, the whole as appears more fully from a copy of the USFDA Accelerated Approval letter dated May 3, 2018, from a copy of the USFDA Supplement Approval letter dated December 31, 2018, from a copy of the Portola Pharmaceuticals press release entitled "U.S. Food and Drug Administration Approves Portola Pharmaceuticals' Prior Approval Supplement for Andexxa® Generation 2 Manufacturing Process" dated December 31, 2018, from a copy of the MPR article entitled "FDA Approval Expands Access to Factor Xa Inhibitor Antidote Andexxa" dated January 3, 2019, and from a copy of the Patented Prices Review Board Canada report entitled "Meds Entry Watch New Medicines Approved in 2018", produced herein *en liasse* as **Exhibit R-16C**;

48.3 ANDEXXA is marketed as enabling for rapid reversal of anti-FXa activity within 2 minutes following administration binding and sequestering the FXa inhibitor rivaroxaban to allow for FXa to restore thrombin generation, which is necessary for fibrin and clot formation, the whole as appears more fully from a copy of an extract from the Portola website at http://andexxa.com and from a copy of the ANDEXXA package insert, produced herein *en liasse* as **Exhibit R-16D**;

49. The Respondents have spent significant money in their promotion of XARELTO, which included at least $11,000,000.00 spent during 2013 alone on advertising in journals targeted at prescribers and consumers in the U.S. In the third quarter of the 2013 fiscal year, XARELTO was the number one pharmaceutical product advertised in professional health journals based on pages and dollars spent, the whole as appears more fully from a copy of the Drugs.com article entitled "Janssen, Forest Labs dominate top five in spent advertising" dated September 2013, produced herein as **Exhibit R-17**;

50. As a result of the Respondents' aggressive marketing efforts, XARELTO garnered approximately $122 million in global sales in 2011, $457 million in

2012 (a 274.4% increase), $1.3455 billion in 2013 (a 194.7 % increase), and $2.5252 billion in 2014[16]. Thus, in 2013, XARELTO cleared the $1 billion threshold commonly referred to as "blockbuster" status in the pharmaceutical industry. Thus, Xarelto is now considered the leading anticoagulant on a global scale in terms of sales, the whole as appears more fully from copies of four (4) Bayer Annual Reports for the years 2008, 2012, 2013, and 2014 produced herein *en liasse* as **Exhibit R-18**;

50.1 In 2013, XARELTO was ranked 42 in terms of global sales of all prescription medications and in 2014 it climbed to number 23, indicating a 212% growth from 2012 to 2013 and a 77% growth from 2013 to 2014, the whole as appears more fully from a copy of the PM Group's Top Pharma List for the years 2013 and 2014, produced herein *en liasse* as **Exhibit R-18A**;

51. The Respondents' website for XARELTO claims that over nine (9) million people worldwide have been prescribed XARELTO, the whole as appears more fully from a copy of an extract from the Respondents' website at www.xarelto.com, produced herein as **Exhibit R-19**;

52. As part of their marketing of XARELTO, the Respondents employed a "pull marketing" technique[17] whereby direct-to-consumer advertising campaigns were disseminated that were designed to influence patients, including the Petitioner, to make inquiries to their prescribing physician about XARELTO and/or request prescriptions for XARELTO;

53. In the course of these direct-to-consumer advertisements, the Respondents exaggerated the efficacy of XARELTO with respect to preventing stroke and systemic embolism, misleadingly suggested that no blood monitoring was required, failed to disclose the need for dose adjustments, failed to adequately disclose to patients that there is no antidote for XARELTO to reverse the anticoagulation effects, and that such irreversibility could have permanently disabling, life-threatening and fatal consequences;

54. It is this manner that sales of XARELTO have been steadily rising as can be clearly seen from the Bayer Annual Reports (Exhibit R-18) despite the number of serious and life-threatening side effects related to the medication. In fact, the Respondents are actually looking to expand their market size to include its use for patients with acute coronary syndrome (ACS), peripheral artery disease and embolic stroke of indeterminate source, the whole as appears more fully from a copy of the Drugwatch article entitled "Xarelto Report: Prescriptions Rise despite Hike in Bleeding Events" dated November 13, 2014 and from a copy of

[16] € 86 million is approximately $122 million Canadian, € 322 million is approximately $457 million Canadian, € 949 million is approximately $1.3455 billion Canadian, and € 1,679 million is approximately $2.5252 billion Canadian, not adjusting for currency fluctuations at the time.

[17] A "pull marketing" technique primarily targets patients by urging them to "pull" or request certain drugs from their physicians whereas a "push marketing" technique primarily targets physicians by urging them to "push" certain drugs onto their patients.

the Associated Press article entitled “FDA Rejects Wider Use of J&J’s Xarelto for 3rd Time” dated February 14, 2014, produced herein *en liasse* as **Exhibit R-20**;

55. On June 6, 2013, the Respondents received a letter from the USFDA’s Office of Prescription Drug Promotion regarding its promotional material for the atrial fibrillation indication, stating that, “the print ad is false or misleading because it minimizes the risks associated with Xarelto and makes a misleading claim” regarding dose adjustments, which was in violation of USFDA regulations. The USFDA Office of Prescription Drug Promotion thus requested that the Respondents immediately cease distribution of such promotional material[18], the whole as appears more fully from a copy of the letter sent from the USFDA’s Office of Prescription Drug Promotion to Johnson & Johnson dated June 6, 2013, produced herein as **Exhibit R-21**;

56. On the Respondents’ website it is rather difficult to find information on the side effects of XARELTO, but when the most intrepid consumer does in fact find this information, in addition to the run-on sentence of possible “undesirable effects” all that is provided is the following:

> Contraindications:
> Hypersensitivity to the active substance or any of the excipients; active clinically significant bleeding; lesion or condition if considered a significant risk for major bleeding; concomitant treatment with any other anticoagulants except under specific the circumstances of switching anticoagulant therapy to or from rivaroxaban or when unfractionated heparin is given at doses necessary to maintain an open central venous or arterial catheter; hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C; pregnancy and breast feeding.
>
> Warnings and Precautions:
> Clinical surveillance in line with anticoagulation practice is recommended throughout treatment. Xarelto should be discontinued if severe haemorrhage occurs. Increasing age may increase haemorrhagic risk.

The whole as appears more fully from a copy of an extract from the Respondents’ website at www.xarelto.com, produced herein as **Exhibit R-22**;

57. On the Respondents’ Canadian website, the following is provided in terms of warning:

[18] This letter (Exhibit R-19) indicates that the Respondents were in violation of the *Food and Drugs Act*, RSC 1985, c. F-27, namely s. 9.

> Contraindications: clinically significant active bleeding including gastrointestinal bleeding; lesions or conditions at increased risk of clinically significant bleeding, e.g., recent cerebral infarction (hemorrhagic or ischemic), active peptic ulcer disease with recent bleeding, patients with spontaneous or acquired impairment of hemostasis; concomitant systemic treatment with strong inhibitors of both CYP 3A4 and P-glycoprotein (P-gp); concomitant treatment with any other anticoagulant (including unfractionated heparin [UFH] except at doses used to maintain a patent central venous or arterial catheter; low molecular weight heparins [LMWH]; heparin derivatives; and oral anticoagulants except under circumstances of switching therapy to or from Xarelto®); hepatic disease associated with coagulopathy and having clinically relevant bleeding risk; pregnancy; nursing women; hypersensitivity to Xarelto® (rivaroxaban) or to any ingredient in the formulation.

The whole as appears more fully from a copy on an extract from the Respondents' website at www.xarelto.ca, produced herein as **Exhibit R-23**;

58. Nowhere on their websites do the Respondents indicate the crucial fact that there is no antidote for XARELTO such that in the event of hemorrhagic complications, there is no available reversal agent as there is for warfarin;

59. Despite various warning changes, the Respondents' marketing of XARELTO continues to fail to warn consumers, healthcare professionals and the public:

    a. Of the serious and significant risk of serious, severe and irreversible bleeding complications;

    b. That in the event of a bleeding complication, there is no antidote to reverse it; and

    c. That people taking XARELTO should closely and frequently monitor their blood;

IV. <u>The Respondents' Liability</u>

60. Although XARELTO is marketed, packaged, promoted, advertised, distributed, labelled and/or sold as a safe and effective prescription drug to reduce the risk of stroke in patients with non-valvular atrial fibrillation (AF), to treat deep vein thrombosis (DVT) and pulmonary embolism (PE), and to reduce the risk of reoccurrence, and to prevent or reduce venous thromboembolism (VTE) after knee and hip replacement surgery, it has the serious side effect of the increased

risk for severe and irreversible bleeding and/or hemorrhagic complications, which has no available antidote;

61. A reasonably prudent drug researcher, designer, developer, manufacturer, tester, marketer, packager, promotor, advertiser, distributer, labeller and/or seller in the Respondents' position would have adequately warned both doctors and patients of the risks associated with the use of XARELTO;

62. There have been thousands of reports of severe hemorrhagic events and death reported with federal regulators in the United States and in Europe. On a global scale, in the first eight (8) months of 2013, German regulators received XARELTO-related adverse event reports, including 72 deaths, as compared to a total of 750 reports and 58 deaths in 2012;

63. Despite a clear signal, the Respondents failed to either alert the public and the scientific and medical community or to perform further investigation into the safety of XARELTO;

64. The Respondents were negligent in the research, design, development, manufacture, testing, marketing, packaging, promotion, advertising, distribution, labelling and/or sale of XARELTO in one or more of the following respects:

    a. They knew of should have known that XARELTO increased the risk of the adverse side effect of severe and irreversible bleeding and/or hemorrhagic complications, which has no available antidote and which has severe and life-threatening complications;

    b. They failed to ensure that XARELTO was not dangerous to consumers <u>in its ordinary use</u>;

    c. They failed to conduct appropriate testing to determine whether and to what extent the ingestion of XARELTO poses serious health risks, including the bleeding complications;

    d. They failed to adequately test the product prior to placing it on the market;

    e. They failed to adequately test XARELTO in a manner that would fully disclose the side effect of severe and irreversible bleeding and/or hemorrhagic complications;

    f. They failed to use care in designing, developing and manufacturing their products so as to avoid posing unnecessary health risks to users of such products;

g. They failed to conduct adequate pre-clinical and clinical testing, post-marketing surveillance and follow-up studies to determine the safety of the drug;

h. They failed to advise that the consumption of XARELTO could result in severe and disabling side effects, including but not limited to, severe and irreversible bleeding and/or hemorrhagic complications;

i. They failed to advise the medical and scientific communities of the potential to increase the risk of severe and irreversible bleeding and/or hemorrhagic complications;

j. They failed to provide adequate and timely warnings or sufficient indications about the increased potential health risks associated with the use of XARELTO;

k. They failed to adequately warn emergency room doctors, surgeons, and other critical care medical professionals as well as Class Members and the medical and health community in general, that unlike generally-known measures taken to treat and stabilize bleeding in users of warfarin, there is no effective agent to reverse the anticoagulation effects of Xarelto, and therefore no effective means to treat and stabilize patients who experience uncontrolled bleeding while taking XARELTO;

l. They failed to provide adequate instructions on how to intervene and/or stabilize a patient who suffers a bleed while taking XARELTO;

m. They failed to provide Class Members and their physicians with adequate warnings or sufficient indications of inherent risks associated with XARELTO;

n. They failed to adequately warn Class Members and their physicians about the need to undergo regular medical monitoring to prevent the severe and irreversible bleeding and/or hemorrhagic complications;

o. They failed to provide adequate warnings regarding the need to assess renal functioning prior to starting a patient on XARELTO and to continue testing and monitoring of renal functioning periodically while the patient is on XARELTO;

p. They failed to provide adequate warnings regarding the need to assess hepatic functioning prior to starting a patient on XARELTO and to continue testing and monitoring of hepatic functioning periodically while the patient is on XARELTO;

q. They failed to instruct prescribing physicians and patients on how to determine proper dosing;

r. They failed to provide adequate updated and current information to class members and their physicians respecting the risks of XARELTO as such information became available;

s. They failed to provide prompt warnings of potential hazards of XARELTO in the products' monograph and in the products' labelling;

t. They failed to warn that class members and their physicians that the risks associated XARELTO would exceed the risks of other available anticoagulant medications;

u. After receiving actual or constructive notice of problems XARELTO, they failed to issue adequate warnings, to publicize the problem and otherwise act properly and in a timely manner to alert the public, the Class Members and their physicians, of the drugs' inherent dangers;

v. They failed to establish any adequate procedures to educate their sales representatives and prescribing physicians respecting the risks associated with the drug;

w. They falsely stated and/or implied that XARELTO was safe when they knew or ought to have known that this representation was false;

x. They disregarded reports of severe and irreversible bleeding and/or hemorrhagic complications among patients;

y. They failed to accurately and promptly disclose to Health Canada information relating severe and irreversible bleeding and/or hemorrhagic complications associated with XARELTO and to modify XARELTO product monograph and product labelling accordingly in a timely manner;

z. They failed to monitor and to initiate a timely review, evaluation and investigation of reports of severe and irreversible bleeding and/or hemorrhagic complications associated with XARELTO in Canada and around the world;

aa. They failed to properly investigate cases of severe and irreversible bleeding and/or hemorrhagic complications caused by XARELTO;

bb. They deprived patients of a chance for safe, effective and/or successful alternative treatments; and

cc. In all circumstances of this case, they applied callous and reckless disregard for the health and safety of their consumers;

64.1 All of the above ways in which the Respondents were negligent ultimately led to their failure to provide adequate instructions as to how to assess individual risk both at the outset and in the course of treatment, how to reduce that risk in the course of treatment, and how to respond to and manage bleeding in light of the risk;

65. Despite the vast availability of knowledge clearly indicating that XARELTO use is causally-related to severe and irreversible bleeding and/or hemorrhagic complications, Respondents not only failed to provide adequate labelling to warn Class Members of the risks associated with the use of XARELTO, but instead incongruously promoted and marketed XARELTO as a safe and effective drug, effectively appropriating the ability of doctors and patients to make informed decisions regarding their health;

66. The Respondents concealed and failed to completely disclose their knowledge that XARELTO was associated with or could cause life-threatening bleeding as well as its knowledge that they had failed to fully test or study said risk;

67. The Respondents ignored the association between the use of XARELTO and the risk of developing life-threatening bleeding;

68. The Respondents' failure to disclose information that they possessed regarding the failure to adequately test and study XARELTO for life-threatening bleeding risk further rendered warnings for this medication inadequate;

II. FACTS GIVING RISE TO AN INDIVIDUAL ACTION BY THE PETITIONER

69. On or about October 10, 2012, the Petitioner underwent knee replacement surgery on her left knee at the Hôpital Notre-Dame at 1560 Sherbrooke Street East, in Montreal, Quebec;

70. Immediately thereafter, the Petitioner was prescribed XARELTO by her orthopedic surgeon to prevent deep venous thrombosis (DVT) and venous thromboembolism (VTE) and she took the medication as directed;

71. Within days, the Petitioner suffered a massive hemorrhage in her left knee whereby she was given blood and plasma for several hours until the bleeding abated;

72. The Petitioner stopped taking XARELTO immediately upon suffering the bleeding event;

73. After three (3) to four (4) days, the Petitioner was sent directly to a CSSS (*Centre de santé et de services sociaux*) physiotherapy centre located on René Lévesque where she remained to undergo physical therapy for her knee until the end of November 2012;

74. The Petitioner agreed to initiate XARELTO treatment in an effort to prevent DVT and VTE and she relied on claims made by the Respondents that XARELTO has been clinically shown to reduce the risk of DTV and VTE;

75. At no time was the Petitioner made aware of the risks of suffering hemorrhagic complications associated with taking XARELTO;

76. Had the Respondents properly disclosed the risks associated with XARELTO, the Petitioner would have avoided the risk of suffering hemorrhagic complications by not using XARELTO at all or by having her blood closely monitored;

77. The Petitioner has recently discovered, while researching online, that several lawsuits were filed in the United States due to the defects associated with XARELTO and due to the Respondents' conduct related thereto. Complaints have been consistently filed and amended ever since, the whole as appears more fully from a copy of the Complaints and from a copy of Amended Complaints, produced herein *en liasse* as **Exhibit R-24**;

78. As a result of the Respondents' conduct, the Petitioner suffered damages including, but not limited to physical and mental injuries, including pain, suffering, anxiety, fear, loss of quality and enjoyment of life and increased risk of health problems, and the apportioned cost of the XARELTO;

79. Petitioner's damages are a direct and proximate result of her use of the drug XARELTO, Respondent's negligence and/or lack of adequate warnings, wrongful conduct, and the unreasonably dangerous and defective characteristics of the drug XARELTO;

80. In consequence of the foregoing, Petitioner is justified in claiming damages;

III. FACTS GIVING RISE TO AN INDIVIDUAL ACTION BY EACH OF THE MEMBERS OF THE GROUP

81. Every member of the Class has purchased and/or ingested the drug, XARELTO or is the successor, family member, assign, and/or dependant of a person who purchased and/or ingested XARELTO;

82. The Class Members' damages would not have occurred, but for the acts, omissions and/or negligence of the Respondents in failing to ensure that XARELTO was safe to use, for failing to provide adequate warning of the

unreasonable risks associated with using the drug, for false or misleading representations and for omitting to disclose important information to Class Members and to their physicians;

83. In consequence of the foregoing, each member of the Class is justified in claiming at least one or more of the following as damages:

    a. Physical and mental injuries, including pain, suffering, anxiety, fear, loss of quality and enjoyment of life and increased risk of health problems;

    b. Out-of-pocket expenses incurred or to be incurred, including those connected with hospital stays, medical treatment, life care, medications, medical monitoring services, and the diagnosis and treatment of XARELTO side effect services;

    c. Loss of income and loss of future income;

    d. Refund of the purchase price of XARELTO or alternatively, the incremental costs of XARELTO as paid for by the class members and/or by the *Régie de l'assurance maladie du Québec*; and

    e. Punitive damages;

84. As a direct result of the Respondents' conduct, the users' family members and dependants have, had, and/or will suffer damages and loss including:

    a. Out-of-pocket expenses, including paying or providing nursing, housekeeping and other services and/or funeral expenses and other death-related expenses;

    b. Loss of income and loss of future income; and

    c. Loss of support, guidance, care, consortium, and companionship that they might reasonably have expected to receive if the injuries and/or death had not occurred;

85. All of these damages to the Class Members are a direct and proximate result of the use of XARELTO and Respondents' conduct, negligence and reckless failure to adequately disclose necessary information and the risks associated with the drug;

IV. CONDITIONS REQUIRED TO INSTITUTE A CLASS ACTION

A) The composition of the Class makes it difficult or impracticable to apply the rules for mandates to sue on behalf of others or for consolidation of proceedings

86. Petitioner is unaware of the specific number of persons who were prescribed and who ingested (…) XARELTO, which information is confidential; however, it is safe to estimate that it is in the tens of thousands;

87. Class Members are numerous and are scattered across the entire province;

88. In addition, given the costs and risks inherent in an action before the courts, many people will hesitate to institute an individual action against the Respondents. Even if the class members themselves could afford such individual litigation, it would place an unjustifiable burden on the courts. Further, individual litigation of the factual and legal issues raised by the conduct of the Respondents would increase delay and expense to all parties and to the court system;

89. Also, a multitude of actions instituted in different jurisdictions, both territorial (different provinces) and judicial districts (same province), risks having contradictory judgments on issues of fact and law that are similar or related to all members of the class;

90. These facts demonstrate that it would be impractical, if not impossible, to contact each and every member of the Class to obtain mandates and to join them in one action;

91. In these circumstances, a class action is the only appropriate procedure for all of the members of the Class to effectively pursue their respective rights and have access to justice;

B) The claims of the members of the Class raise identical, similar or related issues of law or fact

92. Individual issues, if any, pale by comparison to the numerous common issues that are significant to the outcome of the litigation;

93. The damages sustained by the Class Members flow, in each instance, from a common nucleus of operative facts, namely, Respondents' misconduct;

94. The claims of the members raise identical, similar or related issues of fact or law, namely:

    a) Was Bayer negligent in failing to provide a reasonable warning that XARELTO could cause serious and irreversible bleeding?

b) Does the manner in which Bayer obtained market authorization for XARELTO or the manner in which it marketed XARELTO justify an award of punitive damages?

(…)

95. The interests of justice favour that this application be granted in accordance with its conclusions;

V. NATURE OF THE ACTION AND CONCLUSIONS SOUGHT

96. The action that the Petitioner wishes to institute on behalf of the members of the class is an action in damages, injunctive relief, and declaratory judgment;

97. The conclusions that the Petitioner wishes to introduce by way of an application to institute proceedings are:

GRANT the class action of the Plaintiff (…);

DECLARE that the Defendants failed to provide adequate warnings with regard to the dangerous side effects of XARELTO;

DECLARE the Defendants solidarily liable for the damages suffered by the Plaintiff and (…) the members of the Class;

CONDEMN the Defendants to pay to the Plaintiff damages in an amount to be determined at trial;

RESERVE the right of each of the members of the Class to claim (…) damages related to the use of XARELTO;

ORDER individual recovery of the claims of the members of the Class in accordance with a process to be determined by this Honourable Court;

(…)

(…)

CONDEMN the Defendants to pay interest and additional indemnity (…) according to law from the date of service of the motion to authorize a class action;

(…)

(…)

CONDEMN the Defendants to bear the costs of the present action including expert and notice fees;

RENDER any other order that this Honourable Court shall determine and that is in the interest of the members of the Class;

A) The Petitioner requests that she be attributed the status of representative of the Class

98. Petitioner is a member of the Class;

99. Petitioner is ready and available to manage and direct the present action in the interest of the members of the Class that she wishes to represent and is determined to lead the present dossier until a final resolution of the matter, the whole for the benefit of the class, as well as, to dedicate the time necessary for the present action before the Courts of Quebec and the *Fonds d'aide aux actions collectives*, as the case may be, and to collaborate with her attorneys;

100. Petitioner has the capacity and interest to fairly, properly, and adequately protect and represent the interest of the members of the Class;

101. Petitioner has given the mandate to her attorneys to obtain all relevant information with respect to the present action and intends to keep informed of all developments;

102. Petitioner, with the assistance of her attorneys, is ready and available to dedicate the time necessary for this action and to collaborate with other members of the Class and to keep them informed;

103. Petitioner has given instructions to her attorneys to put information about this class action on its website and to collect the coordinates of those Class Members that wish to be kept informed and participate in any resolution of the present matter, the whole as will be shown at the hearing, the whole as appears more fully from a copy of a redacted chart of potential Class Members who have inputted their information through the CLG webpage, produced herein as **Exhibit R-25**;

104. Petitioner is in good faith and has instituted this action for the sole goal of having her rights, as well as the rights of other Class Members, recognized and protected so that they may be compensated for the damages that they have suffered as a consequence of the Respondents' conduct;

105. Petitioner understands the nature of the action;

106. Petitioner's interests are not antagonistic to those of other members of the Class;

106.2 Petitioner is prepared to be examined out-of-court on her allegations (as may be authorized by the Court) and to be present for Court hearings, as may be required and necessary;

106.3 Petitioner has spent time researching this issue on the internet and meeting with her attorneys to prepare this file. In so doing, she is convinced that the problem is widespread;

B) The Petitioner suggests that this class action be exercised before the Superior Court of Justice in the district of Montreal

107. A great number of the members of the Cass reside in the judicial district of Montreal and in the appeal district of Montreal;

108. The Petitioner's attorneys practice their profession in the judicial district of Montreal;

109. The present application is well founded in fact and in law.

FOR THESE REASONS, MAY IT PLEASE THE COURT:

GRANT the present application;

AUTHORIZE the bringing of a class action in the form of an application to institute proceedings in damages, injunctive relief, and declaratory relief;

APPOINT the Petitioner as representative of the persons included in the class herein described as:

- all persons residing in Quebec who were prescribed and have ingested the drug (…) XARELTO® (rivaroxaban) since 2008, and their successors, assigns, family members, and dependants, or any other group to be determined by the Court;

IDENTIFY the principle issues of fact and law to be treated collectively as the following:

a) Was Bayer negligent in failing to provide a reasonable warning that XARELTO could cause serious and irreversible bleeding?

b) Does the manner in which Bayer obtained market authorization for XARELTO or the manner in which it marketed XARELTO justify an award of punitive damages?

(…)

IDENTIFY the conclusions sought by the class action to be instituted as being the following:

GRANT the class action of the Plaintiff (…);

DECLARE that the Defendants failed to provide adequate warnings with regard to the dangerous side effects of XARELTO;

DECLARE the Defendants solidarily liable for the damages suffered by the Plaintiff and (…) the members of the Class;

CONDEMN the Defendants to pay to the Plaintiff damages in an amount to be determined at trial;

RESERVE the right of each of the members of the Class to claim (…) damages related to the use of XARELTO;

ORDER individual recovery of the claims of the members of the Class in accordance with a process to be determined by this Honourable Court;

(…)

(…)

CONDEMN the Defendants to pay interest and additional indemnity (…) according to law from the date of service of the motion to authorize a class action;

(…)

(…)

CONDEMN the Defendants to bear the costs of the present action including expert and notice fees;

RENDER any other order that this Honourable Court shall determine and that is in the interest of the members of the Class;

DECLARE that all members of the Class that have not requested their exclusion, be bound by any judgment to be rendered on the class action to be instituted in the manner provided for by the law;

FIX the delay of exclusion at thirty (30) days from the date of the publication of the notice to the members, date upon which the members of the Class that have not exercised their means of exclusion will be bound by any judgment to be rendered herein;

ORDER the publication of a notice to the members of the group in accordance with article 579 C.C.P. within sixty (60) days from the judgment to be rendered herein by email to the Quebec Class Members that have joined the Quebec case, by putting the notice up on the Quebec class action registry and the Canadian Bar Association class action database, and by putting the notice up on Class Counsel's website, Facebook and Twitter pages;

(…)

RENDER any other order that this Honourable Court shall determine and that is in the interest of the members of the Class;

THE WHOLE with costs, including all publication and dissemination fees.

Montreal, May 8, 2020

(S) Andrea Grass

_____
CONSUMER LAW GROUP INC.
Per: Me Andrea Grass
Attorneys for the Petitioner

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CANADA

PROVINCE OF QUEBEC
DISTRICT OF MONTREAL

NO: 500-06-000732-152

(Class Action)
SUPERIOR COURT

DIANE GAGNON

Petitioner

-vs.-

BAYER INC.
and
(…)
BAYER CORPORATION
and
(…)
(…)
BAYER AG
and
BAYER HEALTHCARE LLC
(…)

Respondents

NOTICE OF DISCLOSURE OF EXHIBITS

TAKE NOTICE that the Petitioner intends producing the following exhibits at the hearing:

R-1: Retracted;

R-2: Copy of the Press Release entitled “Johnson & Johnson Pharmaceutical Research & Development, L.L.C. submits New Drug Application to FDA for Rivaroxaban” dated July 30, 2008,

Copy of the New Release entitled “FDA Approves XARELTO® (rivaroxaban tablets) to Help Prevent Deep Vein Thrombosis in Patients Undergoing Knee or Hip Replacement Surgery” dated July 1, 2011,

Copy of the Press Release entitled “New Drug Application Submitted to FDA for Rivaroxaban for Prevention of Stroke in Patients with Atrial Fibrillation” dated January 5, 2011, and

Copy of the News Release entitled “FDA Approves XARELTO® (rivaroxaban) to Reduce the Risk of Stroke and Systemic Embolism in Patients with Nonvalvular Atrial Fibrillation” dated November 4, 2011, *en liasse*;

R-3: Copy of the Respondent Bayer Inc.’s report from the *Registraire des enterprises*;

R-4: Copy of Health Canada’s Patent Registers for the Medicinal Ingredient “rivaroxaban” and the Brand Name “XARELTO”, *en liasse*;

R-5: Retracted;

R-6: Copy of the registered “XARELTO” trade-mark from the CIPO database;

R-7: Copy of the registered patent for XARELTO no. 2396561 from the CIPO database;

R-8: Copy of the five (5) Notices of Compliance obtained from Respondent Bayer Canada from Health Canada and copy of the Health Canada Summary Basis of Decision (SBD) for Xarelto dated February 13, 2009, *en liasse*;

R-9: Copy of the New England Journal of Medicine article entitled “Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Total Knee Arthroplasty” dated June 26, 2008,

Copy of the Lancet journal article entitled “Extended duration rivaroxaban versus short-term enoxaparin for the prevention of venous thromboembolism after total hip arthroplasty: a double-blind, randomised controlled trial” dated June 28, 2009, and

Copy of the New England Journal of Medicine article entitled “Rivaroxaban versus Enoxaparin for Thromboprophylaxis after Hip Arthroplasty” dated June 26, 2008, *en liasse*;

R-9A: Copy of the JAMA Internal Medicine article entitled “Research Misconduct Identified by US Food and Drug Administration” dated February 9, 2015;

R-10: Copy of the New England Journal of Medicine article entitled “Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation” dated September 8, 2011,

Copy of the Supplementary Appendix,

Copy of the Disclosure Forms, and

Copy of the Protocol, *en liasse*;

R-11: Copy of the Institute for Safe Medication Practices' Quarter Watch entitled "Monitoring FDA MedWatch Reports - Why Reports of Serious Adverse Drug Events Continue to Grow" dated October 3, 2012;

R-11A: Copy the USFDA Draft Briefing Document for the Cardiovascular and Renal Drugs Advisory Committee (CRDAC) for the meeting dated September 8, 2011,

Copy of the Forbes article entitled "FDA Reviewers Recommend Complete Response Letter for Rivaroxaban (Xarelto)" dated September 6, 2011,

Copy of an extract from Respondent Bayer's website at www.investor.bayer.de entitled "Bayer Confident in Results of ROCKET AF Study to be Reviewed by the FDA Cardiovascular and Renal Drugs Advisory Committee" dated September 6, 2011, and

Copy of thepharmaletter article entitled "Disappointing FDA briefing papers on Bayer/J&Jâs [sic] Xarelto" dated September 7, 2011, *en liasse*;

R-11B: Copy of the letter sent from Public Citizen to the USFDA dated October 20, 2011;

R-11C: Copy of the transcript from the USFDA Center for Drug Evaluation and Research – Cardiovascular & Renal Drugs Advisory Committee conference dated September 8, 2011 and

Copy of the Summary Minutes of USFDA Center for Drug Evaluation and Research – Cardiovascular & Renal Drugs Advisory Committee conference, *en liasse*;

R-11D: Copy of the USFDA Center for Drug Evaluation and Research Summary Review dated November 4, 2011 and

Copy of the Project on Government Oversight article entitled "Drug Problems: Nominee to Head FDA Led Clinical Trial FDA Faulted" dated November 12, 2015, *en liasse*;

R-11E: Copy of the Handelsblatt article entitled “Authorities Target Bayer Blood Thinner” dated December 10, 2015 and

Copy of the PM Group article entitled “Bayer defends Xarelto as pivotal trial scrutinised” dated December 10, 2015, *en liasse*;

R-11F: Copy of the USFDA Approval Letter dated November 4, 2011,

Copy of the USFDA Summary Review dated November 4, 2011, and

Copy of he USFDA Medical Reviews dated November 4, 2011, *en liasse*;

R-11G: Copy of the New York Times article entitled “F.D.A. Asks If Faulty Blood Monitor Tainted Xarelto Approval” dated February 22, 2016,

Copy of the USFDA recall alert entitled “Alere Recalls INRatio® and INRatio2® PT/INR Monitoring System Due to Incorrect Test Results” dated 2016,

Copy of an extract from nonparty Alere’s website at www.inr-care.com containing a list of all recalled devices, and

Copy of non-party Alere’s recall notification entitled “URGENT: MEDICAL DEVICE RECALL – Alere INRatio®/INRatio®2 PT/INR Monitoring System” dated July 26, 2016,

Copy of the New England Journal of Medicine article entitled “Point-of-Care Warfarin Monitoring in the ROCKET AF Trial” dated February 25, 2016, and

Copy of the Medscape article entitled “BMJ: Rivaroxaban Maker Withheld INR Device Concerns From FDA in ROCKET AF” dated September 30, 2016, *en liasse*;

R-12: Copy of the New England Journal of Medicine article entitled “Oral Rivaroxaban for Symptomatic Venous Thromboembolism” dated December 23, 2010,

Copy of the Expert Review of Cardiovascular Therapy Clinical Trial Report entitled “Oral rivaroxaban after symptomatic venous thromboembolism: the continued treatment study (EINSTEIN-Extension study)” dated July 2011, and

Copy of New England Journal of Medicine article entitled “Oral Rivaroxaban for the Treatment of Symptomatic Pulmonary Embolism” dated April 5, 2012, *en liasse*;

R-13: Copy of the Journal of Neurosurgery article entitled “Race against the clock: Overcoming challenges in the management of anticoagulant-associated intracerebral hemorrhage” dated August 2014;

R-13A: Copy of Health Canada’s list of adverse reaction reports;

R-13B: Copy of Health Canada’s list of adverse reaction reports and

Copy of the actual reports, *en liasse*;

R-13C: Copy of the Quarter Watch report dated September 23, 2015;

R-14: Copy of an extract from the website www.xarelto.com and copy of the Respondent-sponsored WebMD webpage for XARELTO available at www.webmd.com, *en liasse*;

R-14A: Copy of the Quarter Watch report dated January 9, 2013;

R-14B: Copy of the Quarter Watch report dated October 17, 2013;

R-14C: Copy of the Quarter Watch report dated May 7, 2014;

R-14D: Copy of the Respiratory Medicine Case Reports case report entitled “Fatal pulmonary hemorrhage after taking anticoagulation medication” dated 2015;

R-15: Copies of the Product Monographs for XARELTO last revised on:

- September 10, 2008,
- September 14, 2011,
- January 11, 2012,
- February 13, 2012,
- July 18, 2012,
- April 12, 2013,
- June 5, 2013,
- August 28, 2013,
- July 10, 2014,
- February 20, 2015,
- May 22, 2015,
- July 20, 2015,
- September 1, 2016, *en liasse*;

R-15B: Copy of the XARELTO product monograph dated September 20, 2019;

R-16: Copy of the Globe Newswire News Release entitled “Portola Announces Phase 3 ANNEXA-R Study of Andexanet Alfa and Factor Xa Inhibitor XARELTO(R) (rivaroxaban) Met Primary Endpoint With High Statistical Significance” dated January 9, 2015 and copy of the non-yet-registered trade-mark “ANNEXA” (Application Number: 1707663) which was filed on December 17, 2014 *en liasse*;

R-16A: Copy of the Press Release entitled “Portola Pharmaceuticals Receives Complete Response Letter from FDA for Biologics License Application for AndexXa™ (andexanet alfa)” dated August 17, 2016 and

Copy of the Globe Newswire article entitled “Portola Pharmaceuticals Enters into $50 Million Loan Agreement with Bristol-Myers Squibb and Pfizer for Continued Development of AndexXa™ (andexanet alfa)” dated December 19, 2016, *en liasse*;

R-16B: Copy of the USFDA “Summary Basis for Regulatory Action” dated May 3, 2018;

R-16C: Copy of the USFDA Accelerated Approval letter dated May 3, 2018,

Copy of the USFDA Supplement Approval letter dated December 31, 2018,

Copy of the Portola Pharmaceuticals press release entitled “U.S. Food and Drug Administration Approves Portola Pharmaceuticals’ Prior Approval Supplement for Andexxa® Generation 2 Manufacturing Process” dated December 31, 2018,

Copy of the MPR article entitled “FDA Approval Expands Access to Factor Xa Inhibitor Antidote Andexxa” dated January 3, 2019, and

Copy of the Patented Prices Review Board Canada report entitled “Meds Entry Watch New Medicines Approved in 2018”, *en liasse*;

R-16D: Copy of an extract from the Portola website at http://andexxa.com,

Copy of the ANDEXXA package insert, *en liasse*;

R-17: Copy of the Drugs.com article entitled “Janssen, Forest Labs dominate top five in spent advertising” dated September 2013;

R-18: Copies of four (4) Bayer Annual Reports for the years 2008, 2012, 2013, and 2014, *en liasse*;

R-18A: Copy of the PM Group's Top Pharma List for the years 2013 and 2014, *en liasse*;

R-19: Copy of an extract from the Respondents' website at www.xarelto.com;

R-20: Copy of the Drugwatch article entitled "Xarelto Report: Prescriptions Rise despite Hike in Bleeding Events" dated November 13, 2014 and copy of the Associated Press article entitled "FDA Rejects Wider Use of J&J's Xarelto for 3rd Time" dated February 14, 2014, *en liasse*;

R-21: Copy of the letter sent from the USFDA's Office of Prescription Drug Promotion to Johnson & Johnson dated June 6, 2013;

R-22: Copy of an extract from the Respondents' website at www.xarelto.com;

R-23: Copy on an extract from the Respondents' website at www.xarelto.ca;

R-24: Copy of the U.S. Complaints, and

Copy of Amended U.S. Complaints, *en liasse*;

R-25: Copy of a redacted chart of potential Class Members who have inputted their information through the CLG webpage.

Montreal, May 8, 2020

(S) Andrea Grass

_____
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Nº: 500-06-000732-152

(Class Action)
SUPERIOR COURT
DISTRICT OF MONTREAL

DIANE GAGNON
Petitioner

-vs.-

BAYER INC. *et al.*
Respondents

THIRD AMENDED APPLICATION TO AUTHORIZE THE BRINGING OF A CLASS ACTION & TO APPOINT THE PETITIONER AS CLASS REPRESENTATIVE
(Art. 574 C.C.P and following)

COPY

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