Legal Backgrounder

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CANADIAN COURT DECISION PLACES BROAD CLASS OF PATENTS IN JEOPARDY

by

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A disturbing recent decision from the Federal Court of Canada, *Eli Lilly Canada Inc. v. Novopharm Ltd.*, calls into question the validity of many patents in the pharmaceutical and chemical fields.[1] The decision, which threatens to escape timely appellate review, dramatically alters the patent disclosure requirements in a way that conflicts with global patent practice and Canada's international treaty obligations.

The Court Decision. The case involves Lilly's patent on "olanzapine" — a safe, atypical antipsychotic drug discovered after a 15-year search in a previously described class containing millions of individual chemical compounds. The wholly nonobvious constellation of advantageous properties possessed by this "selection invention" had long been sought in the prior art.

The Canadian olanzapine patent was nonetheless found to be deficient. The defect was not lack of novelty, utility, or inventive step, or failure to teach how to make and use the invention, or even failure to identify in the patent text the newly discovered properties that made olanzapine patentable. Instead, the fatal deficiency was said to lie in the failure to include in the text of the patent application the underlying data and protocols, embodied in thousands of pages of experimental records, *proving* the existence of these properties.[2] In essence, the court created a "super-sufficiency" disclosure requirement for selection inventions in Canada and then found it not satisfied, thus allowing immediate regulatory approval of Novopharm's competing generic product. The court's rejection of the textual description of the advantages of olanzapine as "simply rhetoric"[3] conflicts with well-settled legal principles not only in Canada but throughout the rest of the developed world and represents a repudiation of Canada's obligations under the Patent Cooperation Treaty (PCT) and other international agreements.

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[1] *Eli Lilly Canada Inc. v. Novopharm Ltd.* (June 5, 2007, Citation 2007 FC 596, Docket T-1532-05). The full text is available at http://decisions.fct-cf.gc.ca/en/2007/2007fc596/2007fc596.html.

[2] *Id*. at paragraphs 152-162.

[3] *Id*.

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Patents and Drugs. Patent systems are designed to reward the successful search for that which is new and useful where reasonable predictability is lacking. There is no field of human endeavor more fraught with unpredictability and opportunities for failure, nor more important to the well-being of society, than the development of medicines for human use. Successful drugs must combine therapeutic efficacy and safety in one of nature's most complicated and least understood systems — the living human being. Ultimate success in this area often comes as a result of painstaking sifting through mountains of chaff represented by generally known classes of compounds in the search for the few grains of wheat — individual molecules in which these twin qualities are combined. Thus, a moment of intellectually honest reflection compels the recognition that a viable research-based pharmaceutical industry is essential to meet the health challenges of the future and that a fair and reliable patent system is crucial to the viability of the pharmaceutical industry. Abandonment of well-settled legal principles and international treaty obligations resulting in premature generic competition is antithetical to these objectives.

Selection Inventions in the Pharmaceutical Industry. When Isaac Newton developed the laws of motion in the 17th century, he acknowledged that he did so "by standing upon the shoulders of [the scientific] Giants" that preceded him.[4] It is thus with all important inventions, and particularly so in pharmaceutical research and development.

In the search for new medicines, the first step is the development of new chemistries that permit the manufacture of new classes of compounds. Due to the complexity of the organic molecules used in medicine, the discovery of a new class of molecules not uncommonly comprehends within its scope millions and millions of possible variations on the new theme. But the discovery of a new class of compounds, like Columbus' discovery of the New World, only opens the door for further exploration of the territory. Just as long and tedious searching within the confines of the new continent led years later to the discovery of gold in California, so too can long and tedious searching among the members of the newly discovered class of compounds be required to find the one molecule within that new territory that is particularly useful as a human medicine.

This is a so-called selection invention. When the search for it is undertaken by many, punctuated by repeated failure over many years, and yields a unique and desirable constellation of properties that could not have been predicted based on chemical structure, such a selection invention has, until now, uniformly been recognized as patentable.

Olanzapine — A Prototypical Selection Invention. The development of olanzapine, briefly summarized here, has been extensively documented in previous judicial decisions.[5] Since the early 1970s, the entire industry had been searching for a safe, atypical antipsychotic drug — one that could treat the symptoms of schizophrenia without causing the horrible movement disorders that resulted from administration of typical antipsychotic drugs and without causing a variety of intolerable side effects. The first atypical antipsychotic drug — clozapine — was found to destroy white blood cells in some patients, leading to a number of deaths in early clinical trials. In the ensuing search for a replacement, a host of new classes of compounds were naively described in the literature as putative antipsychotic drugs. One-by-one, however, all the development candidates drawn from these classes of compounds failed in the clinic, either for lack of efficacy or lack of safety.

The prior art in this case was such a 1970s-vintage patent filed by Lilly based on the identification of a new class of compounds then thought on the basis of animal tests to have antipsychotic activity. Consistent with the experience of the rest of the industry, however, the two most promising candidates selected from this class both failed. One led to white blood cell problems in animal tests and the other led to elevated liver and muscle enzymes that forced its withdrawal from clinical trials.

By 1990, it was clear that the chemical properties that yielded atypical antipsychotic efficacy were unknown, as were the chemical properties that led to the host of unwanted side effects in failed drug candidates.

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[4]Letter to Robert Hooke, Feb. 5, 1676.

[5]*See* notes 6 and 7, *infra*.

Small structural changes in these chemicals were known to yield dramatic and unpredictable changes in properties, whereby the only way to confirm that a safe, atypical antipsychotic drug had been developed was to test it in actual human schizophrenia patients.

In a last ditch effort to find such a molecule, Lilly selected olanzapine — one of the millions of compounds encompassed by the class originally described in the 1970s — for such a test. The initial clinical trials of olanzapine revealed that it was an effective antipsychotic drug, less likely to cause movement disorders in the clinic, with no negative effect on white blood cells, and with an apparently reduced effect on liver and muscle enzymes. A patent application describing the structure of olanzapine, the method of making and using it, and this unique set of properties was promptly filed. Olanzapine went on to become one of the most widely prescribed antipsychotic drugs in the world. Based on thousands of pages of additional evidence constituting the underlying data establishing the properties of olanzapine, the validity of both the U.S.[6] and Canadian[7] olanzapine patents has previously been sustained.

The Decision Conflicts with Existing Law and Treaty Obligations. Patent applications were never intended to be encyclopedias of all the evidence establishing patentability. They are instead the vehicle by which the inventor teaches persons who are already skilled in the technology to which the invention relates how to make and use the invention. The most that has ever been required regarding the usefulness of the drug or beneficial properties of the drug upon which patentability is predicated is a statement in the application of what those utilities and properties are. If the utility of the invention, or the adequacy of the disclosure, or the existence of an inventive step were called into question either during the patent procurement process or in subsequent enforcement proceedings, it has always been the tradition in the developed world that additional evidence bearing on these issues would be received.

These requirements for a sufficient disclosure are so well settled that they have been embodied in the PCT, which has been in force for more than 25 years and to which 137 countries, including Canada, Great Britain, the United States, Japan, and virtually the entire European community are signatories. The requirements for the description of the invention in an application under the PCT are explicitly and succinctly set forth in Article 5: "The description shall disclose the invention in a manner sufficiently clear and complete for the invention to be carried out by a person skilled in the art."

As a signatory to the PCT, Canada is obliged not to impose additional requirements for an adequate patent disclosure beyond those required by the PCT. Article 27(1) explicitly states: "No national law shall require compliance with requirements relating to the form or contents of the international application different from or additional to those which are provided for in this Treaty and the Regulations."

If further evidence supporting the asserted beneficial properties of the claimed invention is to be required, it is clear that signatories to the PCT cannot require that information to be contained in the patent application itself but may instead require that any needed additional evidence be submitted separately. This is abundantly clear from Article 27(6), which states: "The national law may require that the applicant furnish evidence in respect of any substantive condition of patentability prescribed by such law."

Indeed, this has been the custom and practice in Canada, the United States, and the European community for decades prior to this decision. In the European Patent Office, "[t]he relevant arguments and evidence to be considered by the examiner for assessing inventive step may either be taken from the originally-filed patent application or submitted by the applicant during the subsequent proceedings . . . ."[8] Like other jurisdictions, the U.K. court has held that the advantages must be identified, but such identification does not require proof by

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[6]*Eli Lilly & Co. v. Zenith Goldline Pharms. Inc.*, 364 F. Supp. 2d 820 (N.D. Ind. 2005), *aff'd*, 471 F.3d 1369 (Fed. Cir. 2006).

[7]*Eli Lilly Canada Inc. v. Apotex Inc.*, 2007 FC 455 (2007).

[8]Guidelines for Examination in the EPO, Part C, Chapter IV, 9.11.

comparative data.[9] In the United States, advantages of the invention are to be described in the patent application,[10] but rules and detailed examination procedures provide for submission of evidence supporting the asserted advantages by declaration.[11]

Beyond the foregoing, the Canadian court's adoption of a "super-sufficiency" disclosure requirement in the area of pharmaceutical chemistry appears also to violate Canada's obligations under Article 27.1 of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS). That agreement requires that "patents shall be available and patent rights enjoyable without discrimination as to . . . the field of technology."

Left uncorrected, it will soon become clear that the Canadian court has painted with too broad a brush. The rule it has announced will actually invalidate hundreds if not thousands of extant patents in a whole spectrum of unpredictable technologies. In the chemical, biological, agricultural, and paper industries, for example, selection inventions are also ubiquitous. The inability reasonably to predict the impact on important industrial products and processes of changes in the nature of materials used in them spawns trial and error experimentation and resulting selection inventions. If members of these industries are not distressed by this decision, they are simply not paying attention.

The Need for Appellate Review. The negative impact of this ruling is multiplied by the procedural posture of the case. If an immediate appeal is denied, the decision is tantamount to the wrongful grant of a compulsory license to a valid and hugely valuable patent. This case arises under Canada's Patented Medicines Act, Section 55.2, which provides summary proceedings to determine whether a generic manufacturer's allegation of invalidity is justified. If the court rules in favor of the innovator, an appeal by the generic manufacturer can be heard. However, if the court rules in favor of the generic interest, the Minister of Health is free to issue immediate marketing authorization for the generic product. In the past, the Canadian courts have held that once the Minister has approved the generic product the appeal of the ruling in a Section 55.2 action becomes moot, the only recourse being to commence patent infringement proceedings. Because such proceedings commonly last many years and often consume the entire remaining patent term, the exclusive marketing right the patent was to have conveyed is irretrievably lost. This procedure stands in stark contrast to the procedural protections available under the Hatch-Waxman Act in the United States. There, a decision in favor of the generic manufacturer is immediately appealable. Surely, this is a case where the Canadian appellate court can and should exercise its discretion to address promptly whether this new patentability requirement imposed by this court decision has placed Canada in non-compliance with its treaty obligations.

Conclusion. The consequences of the court's decision in *Eli Lilly Canada Inc. v. Novopharm Ltd.* are far-reaching. Many industries rely on selection invention patents, now of doubtful validity in Canada, to protect their innovations. Further, as this case sets out a new and separate disclosure standard for such patents, it violates both the non-discrimination requirements of TRIPS and the disclosure requirements of the PCT. Hopefully, the appeals court will use its discretion to resolve this matter. Otherwise, it will be up to the Canadian Parliament to get Canada back on the right track.

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[9] *See* TERRELL ON THE LAW ON PATENTS (16th ed. Sweet and Maxwell, London, 2006), at 294.
[10] *In re Davies*, 475 F.2d 667 (C.C.P.A. 1973).
[11] 37 C.F.R. § 1.132; Manual of Patent Examining Procedure §§ 716.01-716.06.