



IP FOR IG:

Protection for Antibody-based Assets in the Canadian Market and Beyond



Antibodies (immunoglobulins) and other antibody-derived biologics have become a mainstay of the biotechnology industry, both here in Canada and around the world. Novel antibodies are continuously being designed, modified, expressed and purified for a number of uses, including as therapeutics, diagnostics, or research tools. As is the case with other types of life science technologies, intellectual property (IP) rights must be a key consideration for anyone creating new and innovative antibodies or antibody-based applications. This article provides a brief overview of IP issues and considerations for those engaged in antibody technologies.

Understanding IP Rights Surrounding Antibodies

As is often the case when discussing IP for technologies, the focus here will be on patents and patent protection. However, it is important to note that patents are not and should not be the only type of IP right considered. Trade secrets can be used to protect certain aspects of antibody manufacturing and production particular to an organization. Trademarks, copyright, and industrial designs can all apply to the marketing, branding and selling of products and/or services in the antibody space. For innovative antibody-based therapeutics, a particular type of IP right called data protection can provide an extra layer of protection (beyond the scope of discussion in this article).

Patents are a powerful tool for maximizing value in an innovative technology. An issued patent gives the patent holder a monopoly over the claimed invention for a period of twenty years (plus some extension time in certain jurisdictions) from the patent application filing date. As antibody-based technologies have increased dramatically, so has the number of corresponding patent filings. As of the writing of this article, the total number of published patent documents (i.e., patent applications plus issued patents) with claims to antibodies or antibody-based products is around 300,000 globally, and 20,000 in Canada. The number of patent documents published by the Canadian Intellectual Property Office (CIPO) has increased almost every year, with more than 100 per year since 1990 and more than 1,000 since 2012. Out of the total 20,000 or so total patent documents, the vast majority (>95%) originated, and are owned, by organizations based outside of Canada. With regard to regulatory approvals, monoclonal antibodies now comprise a large proportion of Health Canada-approved innovative drugs each year – specifically: 8/36 in 2015, 7/35 in 2016, and 10/35 in 2017. To our knowledge, most or all of these drugs originated from outside Canada. Many of the up-and-coming Canadian companies profiled in the feature article in this edition of *Biotechnology Focus* follow the types of IP strategies outlined below.

Generally speaking, the strongest patent claims (protection) will focus on the antibody itself, a chemical compound. The claim wording reflects the type of invention, such as an antibody directed against a novel antigen versus against a known antigen. In terms of claiming a novel antibody, functional claims may be available in some patent offices (i.e., claims primarily based on antibody binding properties). Applicants may also claim by reference to the minimally required DNA/protein sequence needed to maintain a desired function. In most cases, this means claiming a specific set of CDR sequences. This provides protection not only for the full-length

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antibody, but also for antibody fragments, which can be as small as a single domain antibody, that contain the specified CDR sequences. Applicants usually try to protect some amount of variability within CDR sequences – as in a consensus sequence. Other types of patent claims may focus on a hybridoma, a therapeutic or diagnostic use, a method of manufacture, or kits containing the antibody. Known antibodies can also form part of a larger claim to a new analytical technique or purification method.

IP considerations for specific antibody applications are now discussed.

Therapeutics

A global race is now well underway to create the next big drug in the form of a monoclonal antibody or other antibody-derived compound. In fact, many of the top selling drugs in the world are antibodies against targets such as TNFalpha (for treating autoimmune disorders), as well as PD-1 and CTLA-4 (for cancer immunotherapy). The most valuable patent for such an antibody is likely to be the original one claiming the composition of matter – i.e., the minimally required antibody sequences. The original patent application will usually also contain claims to a therapeutic use. In certain cases, a patent office may still allow claims to antibodies that bind to a specific epitope.

During development of a therapeutic antibody, follow-on patent filings can and should be considered for additional innovative advances such as: altered sequences or post-translational modifications, therapeutic formulations, new indications, or new therapeutic combinations. For any such follow-on patent, the subject matter being claimed must be considered novel and non-obvious by an examining patent office over the original patent and any other previous public disclosure.

Diagnostics

As in the case of therapeutics, or any antibody application, the most valuable pat-

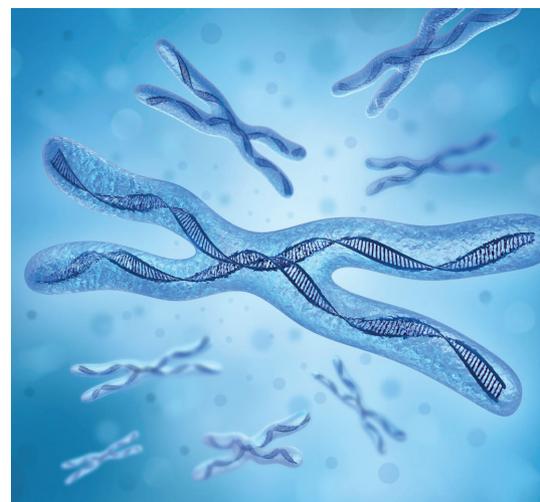
ent claims for a new diagnostic antibody would be those directed to the antibody sequences. In the diagnostic space, novel antibodies may be raised against a newly discovered biomarker for a disease state, and a corresponding diagnostic test would involve detection of the biomarker using a standardized method such as an ELISA. Diagnostic claims can thus include those to detection kits, labeled or tagged versions of the antibody, detection methods using the antibody, or methods of diagnosing a particular disease. In many jurisdictions, including Canada and the US, it is becoming a complex challenge to obtain diagnostic method claims when these are alleged to be simple correlations between the measurement of a biomarker and a disease state. This is not an issue, however, when using inventive antibodies or detection methods.

Research Tools

These tend to be the least glamorous type of antibody technologies, but IP considerations are still important. As with other antibody applications, a proper cost-benefit analysis is important when deciding whether to file a patent on a research tool. In this space, enforceability can be a challenge if the tool is primarily to be used by competitors secretly in house, as compared to a research tool to be widely sold in a kit.

Biosimilars and Patent Litigation

Recent years has seen a global influx of biosimilar antibodies onto the global market as patents for the first set of blockbuster antibody therapeutics begin to expire. Biosimilars, sometimes referred to as subsequent entry biologics (SEBs), are biologic compounds with the same amino acid sequence as a reference biologic, but are not identical, due to complex alterations that can occur during production – for example, post-translation protein modifications or process-specific protein associated impurities. Legal challenges being brought by innovator manufacturers as well as biosimilar



manufacturers are just now making their way through the courts. Recently, in one of the first rulings of its kind, the Federal Court of Canada upheld a patent directed to a use of an innovative antibody (Janssen's infliximab antibody, Remicade™) and granted the counterclaim that an infliximab biosimilar (Hospira's Inflectra™) infringed the patent (Hospira v. Kennedy (2018 FC 259)). The results of a possible appeal, as well as upcoming decisions on other challenges, will provide further guidance regarding the bounds of protection afforded by antibody patents vis-à-vis biosimilar challengers.

Summary

Intellectual property protection is key to protecting and commercializing antibody inventions. The global trend is toward increased antibody patent filing and enforcement. Many Canadian innovators are now active in this space and intend to be part of this IP trend.

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