Canadian Patent Appeal Board Upholds Claims to Non-Exemplified Humanized Antibodies

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In a rare and long-awaited piece of good news for antibody patent applications in Canada, the Patent Appeal Board ("the Board") recently allowed claims to non-exemplified humanized antibodies, even in the absence of sequence information for the relevant complementarity determining regions (CDRs) of the counterpart exemplified murine monoclonal antibodies (mAbs).

Commissioner's Decision 1398 (CD 1398)1 appears to overturn longstanding examining practices concerning humanized antibodies. Applicants who have recently deleted claims to humanized antibodies in order to overcome persistent objections may therefore wish to consider adding back these claims in view of the apparent change. Those who have recently decided to drop applications altogether on the basis of unfavourable examination outcomes should consider whether CD 1398 could make the situation for their applications more tenable (in Canada, abandoned applications may be reinstated as of right within one year of the date of abandonment). CD 1398 could also have broader implications in the field of antibody technology, though the scope of its impact will only become clear over time.

The Application

The application considered in CD 1398 described the production of mAbs specific for human glypican-3. These had been produced by immunizing mice with a specific peptide from the target protein, and the sequence of the peptide was disclosed. Two produced mAbs, K6511 and K6534, demonstrated high binding activity to glypican-3. Subsequent testing indicated that these mAbs exerted in vitro activities on a human liver cancer cell line suggesting therapeutic utility in liver cancer. Other experimental results showed that lung cancer cell lines also expressed glypican-3, thereby extending the inferred utility to lung cancer treatment. However, the sequences of these mAbs and their respective CDRs were not provided in the application.

Applying an earlier Commissioner's Decision 1296 ("*Sloan-Kettering*")2, the Examiner handling the application raised familiar objections to dependent claims 5, 10, 15 and 20 for non-compliance with section 84 of the *Patent Rules* (lack of support) and to the specification as it pertained to these claims under subsection 27(3) of the *Patent Act* (lack of enablement). These claims further defined the antibodies as humanized, and

the Examiner stated in the Final Action that sequence information of the binding regions was *required* to adequately support claims by reciting a humanized version of an antibody when the humanized antibody had not been made.

The Board's Decision

The Applicant appealed the Examiner's refusal to grant the patent to the Board. Referring to a more recent Commissioner's Decision 1302 ("*Immunex*")3 – a decision that first opened the door to the patentability of non-exemplified monoclonal antibodies – the Board reiterated its previous finding that:

...there is specific and meaningful functional identity (specific immunoreactivity) between an antibody and its antigen – a fact that is exploited during the apparent routineness of *the preparation of monoclonal antibodies.4*

The Board determined that *Sloan-Kettering* is of "limited general applicability"[5], noting that the decision concerned an application filed in 1990. The assessment of enablement must, according to the Board:

...entail fact-specific determinations that take into account the [common general knowledge (CGK)] and the ordinary skills possessed by the POSITA at the publication date of the patent application.6

The Board stated that:

The evolution of CGK is an important factor for assessing whether the disclosure in this case is sufficient to enable a person skilled in the art to practice the invention as claimed without displaying inventive ingenuity or undertaking undue experimentation as of the relevant date.7

The Board further stated that:

...[Sloan-Kettering] leaves open the possibility that a humanized antibody can be described in ways other than by providing the amino acid sequences of the CDRs... In line with the law and practices of other leading jurisdictions, Canadian examination practice with respect to antibodies has also evolved since [Sloan-Kettering].8

The Board concluded:

[Sloan-Kettering] cannot impose a rigid rule that sequence information of the variable regions of a number of humanized antibodies must be provided in order to adequately describe and enable claims more generally reciting humanized versions of various murine antibodies that may bind to various epitopes of the same antigen.9

The Board was apparently influenced by the fact that the claimed humanized antibodies were ones directed to a fully characterized antigen, that they were presented as alternatives to other types of antibodies, and by the fact that that techniques for their production were well-established and routine by 2002[10.] The Board then effectively extended the rationale of *Immunex*, noting that mAbs and humanized antibodies do not differ in their respective critical binding regions because the humanization process preserves the structural relationship with the target antigen.[11] Ultimately the claims covering non-exemplified humanized antibodies were allowed.

Application to Current Antibody Practice

The decision stands as another example of the Patent Appeal Board reversing current (and longstanding) examining practices. Applicants have been dealing with highly standardized and intransigent objections based on *Sloan Kettering* for many years, and have long been making arguments during examination similar to those submitted by the appellant in CD 1398. Meanwhile, examiners have maintained objections that fail to take into account advances in the art. When pressed about these objections, some examiners have indicated that they are required to adhere to examination policies. This might also explain why the application considered in CD 1398 ended up before the Patent Appeal Board in the first place. The decision therefore seems to highlight an internal disconnect between the Patent Appeal Board and the policy unit of the Canadian Intellectual Property Office.

It is hoped that CD 1398 will not be interpreted as the *Immunex* decision was, i.e. as an indication that only one *narrow* swath of previously objectionable subject matter is now to be accepted. It would be a poor reflection on the Canadian patent system if applicants had to wait for the Patent Appeal Board to opine on each and every technical advancement before decade-old changes in the state of the art can be accepted and considered during examination. It is clearly not ideal to have the Patent Appeal Board in the role of retroactive gatekeeper, routinely tasked with making decisions ten to fifteen years after the fact.

One hopes, rather, that CD 1398 – particularly its acknowledgement of the dynamic state of the art – will serve as a signal from the Patent Appeal Board to the examining divisions that examiners are *not* bound by any static policy, and must have discretion to use their subject matter expertise as well as the relevant law to fully consider the specific facts, circumstances, and merits of the Canadian patent applications in their stewardship.

[1] Re Chugai Seiyaku and Kabushiki Kaisha (CD 1398).
[2] Re Sloan-Kettering Institute for Cancer Research (CD 1296).
[3] Re Immunex Corporation (CD 1302).
[4] supra, note 1 at para 23.
[5] supra, note 1 at para 34.
[6] supra, note 1 at para 35.
[7] supra, note 1 at para 36.
[8] supra, note 1 at para 37.
[9] supra, note 1 at para 38.
[10] supra note 1 at paras 40 and 44.
[11] supra, note 4 at para 48.

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