

February 26, 2009



Cabilly II Recombinant Antibody Patent Survives Reexamination

Prepared by the Biotechnology Practice Group

U.S. Patent No. 6,331,415 ("Cabilly II"), assigned to Genentech, Inc. and City of Hope (collectively "Genentech"), broadly claims a method for co-expression of recombinant heavy and light chains of an antibody from a single host cell, such that the expressed protein subunits can assemble to form a functional antibody. Cabilly II was filed prior to June 5, 1995, and thus is entitled to a 17-year from issue patent term. Accordingly, Cabilly II, which granted on December 18, 2001, is calculated to expire on December 18, 2018. Cabilly II is a continuation application which claims priority benefit to an earlier-filed application which was granted on March 28, 1989, as U.S. Patent No. 4,816,567 ("Cabilly I"). Cabilly I expired on March 28, 2006.

Two requests for *ex parte* reexamination of Cabilly II were filed in 2005. These requests were granted, and the reexaminations were combined. Both reexamination requests contended that the claims in Cabilly II were but obvious variants of the claims in Cabilly I, and thus, Cabilly II, in lieu of a terminal disclaimer, was invalid under the doctrine of Obviousness-type Double Patenting.

During the reexamination, Genentech successfully argued that the claims of Cabilly I were directed to a method for expression of a *single* recombinant antibody subunit protein, *i.e.*, *just* a heavy chain or *just* a light chain, in a host cell, while the claims of Cabilly II were directed to expression of both a heavy chain and a light chain, as separate molecules, in a single host cell.

The reexamination continued through 2008, and included several rounds of written arguments between Genentech and the Examiner, as well as a large number of personal interviews. In support of their position that the claims of Cabilly II were patentably distinct from the claims of Cabilly I, Genentech produced no less than fourteen Declarations from various scientists, including two Declarations by Douglas Rice, a former postdoctoral fellow in the laboratory of David Baltimore at MIT and one Declaration by Richard Axel, of Columbia University. Genentech's arguments, based on the Declarations, generally focused on the contention that the prior art, when combined with Cabilly I did not teach or suggest to a person of ordinary skill in the art that the invention of co-expression of multiple chains in one cell as in Cabilly II was predictable and could have been practiced with a reasonable expectation of success.

On February 23, 2009, the Examiner issued a Notice of Intent to Issue a Reexamination Certificate ("Notice") which was based on the arguments and evidence set forth by Genentech and which provides no further insight into any specific events which may have led Patent Office to reconsider their position, maintained throughout the two-year reexamination, that the Cabilly II claims were obvious variants of the Cabilly I claims.

The reexamination of Cabilly II was an *ex parte* reexamination, so the third party requestors were not a party to the proceedings after the submission of their original requests. Accordingly the third party requestors may not appeal the decision. Cabilly II, however, is not fully “out of the woods.” Centocor, Inc. has filed a request for Declaratory Judgment of invalidity, unenforceability, and noninfringement of Cabilly II in the U.S. District Court for the Central District of California. Discovery is ongoing, and a Markman hearing is tentatively scheduled for May 2009.

Finally, of note in the reexamination proceedings was the disclosure of details relating to yet a third Cabilly application (“Cabilly III”), filed on April 13, 1995. This application was filed prior to the requirement for publication of pending U.S. applications, and thus details of the prosecution have remained “secret.” The Cabilly III application was, up to December 2008, involved in an interference with another patent application, and certain papers from the interference were made public in the reexamination documents. At least some pending claims in Cabilly III are directed to a functional chimeric antibody comprising separate heavy and light chain subunits, produced via co-expression of recombinant heavy and light chains in a single host cell. Genentech prevailed in the interference, and the application has presumably been sent back to the examiner for eventual grant. The available interference documents make it clear that Genentech has filed a Terminal Disclaimer in Cabilly III, disclaiming any patent term which would extend beyond the December 18, 2018 expiration of Cabilly II.

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