VACCINE DEVELOPMENT

U.K. CHLAMYDIA VACCINE RESEARCH PROMISING

SOUTHAMPTON, U.K.—A quarter of a century after initially successful vaccine trials against trachoma were followed by bitter disappointment, hopes of immunization against this serious blinding disease are back on the agenda.

Until recently, little progress had been achieved in vaccination against *Chlamydia trachomatis* since the 1960s, when the protection achieved with whole chlamydiae was eclipsed by the later emergence of more severe infections in vaccine recipients than in controls. Now, work by Mike Ward and colleagues at the University of Southampton Medical School indicates that genetically engineered subunit vaccines may afford protection not only against the serovars of *C. trachomatis* responsible for two million cases of blindness worldwide but also against those causing other conditions. In addition to acute urethritis and epididymitis in males, *C. trachomatis* is responsible for an estimated 40 percent of cases of pelvic infertility and is currently undergoing epidemic spread in the U.S. and elsewhere.

Ward and collaborators have concentrated on the major outer membrane protein (MOMP) on the organism. Two years ago, they used recombinant DNA techniques to achieve high-level expression in *Escherichia coli* of recombinant fragments of the MOMP from serovar L1. The *E. coli* recombinants were stable. Working with Wayne Conlan (who moved recently to the Trudeau Institute at Saranac Lake in upstate New York), they have now purified three fragments—approximately three-quarter-, one-half-, and one-quarter-length fragments of serovar L1 MOMP. Because the fragments are expressed as insoluble inclusions in the cytoplasm, this proved comparatively easy: simply preparing and lysing spheroplasts and centrifuging the lysate achieves a substantial degree of purification. (Previous efforts to develop subunit vaccines against *C. trachomatis* have foundered on the difficulty of large-scale production of distinct, purified antigens.

When injected into rabbits together with alhydrogel adjuvant (which would be acceptable for human use), the fragments induced the production of high titers of antibodies that reacted at the surface of viable chlamydiae. The antibodies were of similar epitope specificity to monoclonal antibodies produced by immunization with whole chlamydiae. Immunization with all three fragments generated chlamydia genus-reactive antibodies when sera were tested against various serovars of *C. trachomatis* and *C. psittaci*. Maureen Tuffrey, using a mouse model of human *C. trachomatis* infection at the Clinical Research Centre, Harrow, near London, has been investigating the capacity of the MOMP fragments to confer protective immunity *in vivo*. Preliminary results, to be published later this year in *Fertility and Sterility*, show that oral vaccination reduces colonization of the genital tract following inoculation with viable chlamydiae, whereas injection of the MOMP fragments triggers the production of high levels of Ig antibodies and reduces the severity of disease. These results, which indicate that the mechanisms diminishing disease severity differ from those thwarting colonization, are the first to show that a recombinant chlamydial antigen can afford protection against challenge.

The main source of funding for the Southampton chlamydia research is the Edna McConnell Clark Foundation in the U.S., whose initial $198,000 was followed recently by a $330,000 grant for the next phase of development. The World Health Organization's Human Reproductive Program also supports the work. A third source of finance has been Wellcome Diagnostics (London, U.K.). Its interest is not in MOMP antigens as vaccines but in MOMP antibodies as a basis for developing diagnostic tests for chlamydial antigens. Ironically, Wellcome recently announced both its withdrawal from vaccine production and the closing of its biotech division. **—Bernard Dixon**

PATENT LEGISLATION

EXAMINING THE BOUCHER BILLS

ATLANTA, Ga.—Two bills now before the U.S. Congress seek to correct what many observers believe is a loophole in existing U.S. patent law—one that places an unfair obstacle in the way of commercial development of biotechnology products. The well-documented patent conflict involving Amgen (Thousand Oaks, CA) and Genetics Institute (GI, Cambridge, MA) over erythropoietin (EPO) (*Bio/Technology* **8**:172, Mar. '90; *B/T* **7**:764, Aug. '89) has brought the problem into focus: Despite holding a patent covering certain DNA sequences and host cells related to the production of EPO, Amgen has been unable to prevent GI from importing a version of the hormone manufactured in Japan by GI's corporate partner, Chugai (Tokyo).

Under present U.S. law, an inventor cannot stop a *product* made abroad with the use of a material patented in the U.S. from being imported back into the U.S. unless the inventor also has patent protection for the *process* of using such material. This poses a difficult problem for biotechnology: companies must be able to secure both product and process coverage to effectively deter the competition. But as applied to standard recombinant DNA procedures, an inventor may only be able to obtain patent protection for the recombinant DNA sequence and the host cell; the biotechnological process of using a host cell to produce a protein may be unpatentable because the method is conventional.

Two recent decisions by the Federal Circuit Court of Appeals show how this situation hurts biotechnology companies. In the first case, *In re Durden* (763 F.2d 1406, 226 U.S.P.Q. 359 CAFC 1985), a patent examiner rejected an application for patenting a process for making a chemical compound because that process was obvious (and therefore, as a matter of law, not patentable). The U.S. Patent and Trademark Board of Appeals affirmed the examiner's decision and the Court of Appeals, in turn, agreed. The court ruled that an otherwise obvious chemical process is not made patentable simply because either the specific starting material employed or the product obtained is novel and nonobvious.

The second case involved an appeal of the U.S. International Trade Commission's (ITC) ruling that, under section 337 of the Tariff Act of 1930, it did not have the authority to stop the use of a patented host cell to make a recombinant protein outside the U.S. where the (U.S.) patent did not include process claims. The Court of Appeals stated that the ITC did have jurisdiction to make the determination and that, because the claims did not cover a classic "process," the ITC should not block importation of the product (*Amgen, Inc.* v. *U.S. International Trade Commission*, 902 F.2d 1532, 14 USPQ2d 1734 CAFC 1990). Following these decisions, the Patent and Trademark Office (PTO) will not issue patents on methods where the starting material is novel and nonob-