U. S. PATENT ISSUED TO LOCAL SCIENTIST
FOR WARTIME IMPROVEMENT OF PENICILLIN

Plentiful Supply, Lower Cost of
Drug Due to Genetical Research

As an outcome of experiments done in his Cold Spring Harbor laboratories during the war, a United States patent for "Production of Penicillin" was issued on July 27 to Dr. M. Demerec, director of the Carnegie Institution Department of Genetics. Application for the patent, made in September, 1946, was arranged by the Government, for the purpose of protecting the public rights in the use of a superior strain of Penicillium and the method by which it was produced. Dr. Demerec has assigned his patent to the United States Government.

The method covered by the patent resulted in a large increase of the output of penicillin several years ago at a time when the need, for use in treating war casualties, was critical. Penicillin is produced from the mold Penicillium, which belongs to the same group as the common green mold present in Roquefort cheese. In the commercial large-scale production of penicillin, success depends largely on the use of superior strains of Penicillium--that is, strains giving a high yield of the antibiotic substance. In the first work on penicillin production, starting in 1942, yields of only 2 to 5 units per cubic centimeter of culture medium were the highest that could be obtained; but at the present time yields of around 700 units per cc. are routine. This enormous increase has been due mainly to the introduction of superior strains of the organism, one of which was the strain X-1612, produced and tested in Dr. Demerec's laboratory, and later put into commercial use with strikingly successful results. Thus it can be said that the present wide availability of this drug, at much lower cost than formerly, is directly owing to the application of genetical research.

In the early years of the war, when the need for larger supplies of penicillin was very urgent, Dr. Demerec was confident that superior strains of the penicillin-producing mold could be obtained by genetical experiments, using X-rays or other radiations. Plans for such experiments were submitted to government agencies, and preliminary work was begun in the Carnegie laboratories, pending funds for the

support of a full-scale research project. Such funds were eventually provided by a War Production Board contract in 1944, under which the Cold Spring Harbor laboratory cooperated with several others--including Stanford University and the Universities of Minnesota and Wisconsin--in a rush project aimed at production of high-yielding strains of Penicillium for use in penicillin manufacture.

Mrs. Eva R. Sansome and Dr. H. E. Warmke supervised the experiments, aided by several research assistants who included Mrs. Paul Buchanan and Miss Constance Mitchell, of Huntington, and Miss Jean Hamblett, of Huntington Station. In six months' intensive work, the Carnegie laboratory selected and tested many thousands of X-ray-treated strains, sending about 500 of the highest yielders to the University of Minnesota for further testing with their large-scale equipment. One of these 500 strains, called X-1612, proved to be the highest yielder known up until that time, both in laboratory tests and in commercial production. It enabled penicillin manufacturers to triple their output of the precious drug immediately, without increase of labor, equipment, or materials.

The method used by Dr. Demerec and his co-workers to produce strain X-1612 is described in detail by the United States Patent 2,445,748. It was based on the knowledge that genetical mutations, or hereditary changes, can be brought about in most organisms by treatment with X-rays or other radiations. The preliminary experiments showed that in the case of Penicillium some of these mutations would lead to higher yields of the penicillin substance. X-ray treatment with about 75,000 roentgen units was found to be most effective for this purpose. After X-raying, the spores of the mold were germinated, isolated and grown under special conditions, and then assayed for penicillin content.