The *Merck Index* attributes preparations to Ludwig, Piech and to, Berger, with U.S. patents 2,724,720 in 1955 to Carter Products Inc.; for synthesis to Fries, Monkemeyer under a Swiss patent 373,026 in 1963 to Chemische Werkehüls.[39]

Chlordiazepoxide Hydrochloride, and Diazepam. The *Pharmacological Basis of Therapeutics* observes that two benzodiazepine derivatives are presently available, chlordiazepoxide and diazepam. Both are used for the same purpose as meprobamate, mainly for the treatment of anxiety but also for skeletal muscle relaxation and combating alcoholism. According to this source:[39]

> Compounds of this type were initially synthesized by Sternbach in Poland in 1933, and congeneric substances were studied in the United States (see Sternbach and Reeder, 1961). Animal tests indicated that chlordiazepoxide had interesting muscle relaxant, antistrychnine, and spinal reflex-blocking properties. Randall and coworkers (1960) reported that it produced "taming" of a number of species of animals in doses much lower than those producing ataxia or measurable hypnosis. The difficult problem of defining "taming" in animals and of relating this effect to human therapeutic needs has been discussed by Cook and Kelleher (1963); but it was this "taming" effect in monkeys that led to the clinical trial of the drug in human subjects for the determination of antianxiety effects (Randall et al., 1961).

Cooper comments:[40]

> In the 1960's the Swiss have added Librium and Valium to the field . . .

Speaking of Roche, he observes:[41]

> Their discovery, Valium, was actually being marketed in Italy by Ravizza under the name "Noan" one and a half years before Roche had even registered the drug there. In fact clinical trials of the drug were still in progress in the U.S.A. Librium, its slightly older discovery, is being sold by eighteen other companies under eighteen different brand names . . .

The reference in the *Merck Index* to chlordiazepoxide (LIBRIUM) shows the preparation to Strenbach under U.S. patent 2,893,992 in 1959 to Hoffmann-La-Roche:[42] the reference to diazepam (VALIUM) attributes the preparation to Sternbach and Reeder. U.S. patents 3,109,843 in 1963 to Hoffmann-LaRoche and 3,136,815 in 1964 to Hoffmann-LaRoche.[43]

If additional information is needed in connection with any of the above, or a more detailed analysis is required, please let us know.

GLENN MARKUS.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION,
Chevy Chase, Md. January 22, 1969.

MR. BENJAMIN GORDON,
Staff Economist, Senate Committee on Small Business, Room 424, Old Senate Office Building, Washington, D.C.

DEAR MR. GORDON: Although many of the psychotropic and autidepressant agents were synthesized or "discovered" by private pharmaceutical companies, there were some notable exceptions. Dr. H. Laborit, of the French Army, first noted the tranquilizing properties of chlorpromazine when he used this substance as an anesthetic. The first clinical trials of chlorpromazine with psychiatric patients were performed by Drs. Delay and Deniker of St. Anne's Hospital in Paris. These latter investigators have received some financial support from NIMH but I do not believe their early work with chlorpromazine was under NIMH support. The pioneer work with demethylated analogs of imipramine, an antidepressant drug, were performed by Dr. B. B. Brodie of the National Heart Institute. Dr. Brodie synthesized desmethylimipramine which is reported to be a faster acting antidepressant than the parent compound, imipramine. Finally, the early work with lithium salts for the treatment of psychotic excitement was performed by an Australian, Dr. J. F. J. Cade.

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[38] *1968 Merck Index*; page 687.
[39] See footnote No. 5.
[40] See footnote No. 21; page 6.
[41] See footnote No. 21; page 163.
[42] *1968 Merck Index*; page 235.
[43] *1968 Merck Index*; page 341.