Each of the other sources we have reviewed establishes a similar sequence of events for the origins of reserpine and other rauwolfia alkaloids. For example, in *Medicine At Risk*, the author observes: [29]

> . . . the root of the shrub Rauwolfia Serpentina (snake root) was taken up for investigation by CIBA after the war. It was found that out of 24 alkaloids present, only three had sedating and antihypertensive properties of the preparations from the whole root. Separation by chemical means proved virtually impossible so CIBA worked out the structures of the isolated alkaloids and devised synthetic methods for making them. The result was reserpine, CIBA's Serpasil.

The *Merck Index* credits the isolation of reserpine from the root of rauwolfia serpentina to Dorfman and others with U.S. patent 2,833,771 awarded (Schwyzer, Mueller) to CIBA in 1958.[30]

The *Merck Index* provides the following data for the alkaloids (other than reserpine) of rauwolfia serpentina: rescinnamine (MODERIL) attributed to Haack and others with the U.S. pat. 2,876,228 (Ordway, Guerico) in 1959 to Chas. Pfizer and Company and to Riker Laboratories (Klohs and others) in 1961 under U.S. pat. 2,974,144; [31] deserpidine (HARMONYL) isolated by several researchers including Stoll, Hoffman, Schlittler, Klohs, and others with British patents (in 1958) to Penick and Company, Inc. (791,241) and to CIBA (1959) under 809,912 and a Canadian pat. 678,216 to Roussel-UCLAF; [32] syrosingopine (SINGOSERP) attributed to R. A. Lucas and others with a U.S. pat. 2,813,871 in 1957 to CIBA; [33] and alseroxylon (RAUWILOID) which the *Index* simply notes is the generic name for fractionally purified extract of rauwolfia serpentina.[34]

Meprobamate. According to a number of sources, the origins of meprobamate can be traced to work with mephenesin. The *Pharmacological Basis of Therapeutics* notes: [35]

> Developed by Berger (1954) as a longer-acting successor to mephenesin, meprobamate was originally synthesized as a potential muscle relaxant (Ludwig and Piech, 1951). Mephenesin had been introduced in 1946 and tried in a variety of conditions involving not only muscle spasm but also different types of neuroses and psychoses. Its usefulness was felt to be seriously limited because of its short duration of action and unreliable absorption following oral administration. Over 1,200 compounds were investigated before meprobamate was selected and its pharmacological properties were described. The first papers reporting its use in clinical psychiatry appeared in 1955 (Borrus, 1955; Selling, 1955).

The origins of the drug were discussed during the Kefauver hearings: [36]

> Early in the 1940's, Dr. Frank M. Berger as working on muscle relaxants for British Drug Houses in England and there discovered mephenesin. Because of the statutory absence of patent protection on drug products in England at that time, he could not secure a product patent. In 1947 Dr. Berger emigrated to the United States; in 1949 he became director of research for Carter Products; and in the following year a patent application was filed on meprobamate, assigned to Carter Products. In 1953 an arrangement was made for Berger to receive a share in the profits derived from the sale of drugs developed by him. The patent was issued on November 22, 1955, and will run until 1972.

The Canadian report notes: [37]

> Meprobamate was developed as a result of initial work in synthesizing preservatives for use in penicillin preparations. Frank M. Berger had noticed that one of the compounds tested on mice had a muscular relaxant effect. In the search for a more efficient muscle relaxant, Berger and Bradley developed mephenesin. Further work on mephenesin-like compounds resulted in the synthesis of meprobamate.

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[29] See footnote No. 20; page 58.
[30] *1968 Merck Index*; page 912.
[31] *1968 Merck Index*; page 912.
[32] *1968 Merck Index*; page 331.
[33] *1968 Merck Index*; page 1010.
[34] *1968 Merck Index*; page 41.
[35] See footnote No. 5.
[36] "A Study of Administered Prices in the Drug Industry," *Senate Report No. 448; 87th Congress, 1st Session;* July 27, 1961; page 143.
[37] See footnote No. 22; appendix Q.