# Scorpion Antivenom for North America: Anascorp™ approval by the FDA

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Antivenom development is linked to modern immunology history. Early in the 1890s, Emil von Behring and Shibasaburo Kitatasato demonstrated that immunity against extra-cellular toxins, diphtheria and tetanus, could take place, and that "passive immunization" could save lives. Applying the same principles, Albert Calmette changed the treatment of venom injury forever, by showing that anticobra serotherapy was effective against snakebite. Hideyo Noguchi, at New York's Rockefeller Institute, was unable to confirm Calmette's claims regarding efficacy of cobra antivenom against rattlesnake venom. In 1904, in Mexico, Daniel Vergara Lope Escobar, showed that "Calmette's universal serum" also failed to protect against mortality from Mexico´s scorpions. Vergara Lope made his own antiserum in dogs and it appeared to cure two adults and one baby in Morelos. In 1926, Isauro Venzor and Carlos León de la Peña produced an antivenom for Durango. This development was assigned to the federal Department of Health; then José Monroy Velasco, and a partner named Nájera, left the department to start an antivenom company of their own, Laboratorios MyN. Early in the 40's, Laboratorios Zapata began to compete with MyN for the Mexican antivenom market.

Scorpion sting can be life threatening, especially in children; and the condition is 1,000 times more common in Mexico than in the USA. Starting in the 1940s at Arizona State University (ASU), Dr. Herbert Stahnke made a small amount of scorpion antivenom for US use. During shortages, MyN antivenom was imported, often illegally, to treat Arizona children.

In 1995, Alejandro Alagón was invited by Juan López de Silanes, then the President of Instituto Bioclon, to attend monthly meetings with his technical staff to "talk" about ways to improve the manufacture of antivenoms. In 1996, the Institute of Biotechnology of UNAM signed a research contract with Bioclon to "improve existing antivenoms and to develop new ones." Bioclon, a subsidiary of Laboratorios Silanes, had started its own equine $F(ab')_2$ manufacturing facility in 1990 as a result of a merger between Laboratorios MyN and Laboratorios Zapata. The collaboration between IBt-UNAM and Bioclon rapidly resulted in a significant increase in the purity and neutralization potency of antivenoms; and product safety rocketed concomitantly.

In early 1999, Marilyn Bloom, the last scorpion antivenom producer at ASU, announced her impending retirement to Leslie Boyer, then the Medical Director of the Arizona Poison and Drug Information Center. Coincidentally, two weeks later, Kim Chaix, filming a documentary for National Geographic Television on Mexican scorpions, invited Boyer to travel with his crew. On that trip, Boyer brainstormed with academicians and clinicians and found merit in the Mexican antivenom. Soon, she convinced Juan López de Silanes to provide antivenom for an international study under US FDA surveillance. Mexican antivenom was ready for the big leagues.

Well, not quite. It took a little over 12 years to conduct clinical trials, to carry out toxicity and pharmacokinetic studies, and to fulfill all chemistry, manufacturing and controls requirements of the FDA. Over those years, horse husbandry, immunization schemes and steps for production of the $F(ab')_2$ antivenom were optimized, and dozens of Standard Operating Procedures were developed and validated both for monitoring antivenom manufacturing and for characterizing the final product. Also, immunoassays for measuring venom and antivenom in patient samples were developed and validated. At last, on August 3 of 2011, the antivenom was licensed for the US market, the first 100% Latin American drug to achieve that status.

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