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# Potency evaluation of antivenoms in Brazil: The national control laboratory experience between 2000 and 2006 ☆

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**Abstract**

Envenoming from snakebites is an important public health issue in Brazil. In 2005, 28,597 cases were notified (15 cases/100,000 inhabitants), 87.5% due to *Bothrops* and 9.2% to *Crotalus* genus. Antivenoms available in Brazil are liquid preparations containing purified equine Fab′2. Since 1987, the National Institute for Quality Control in Health (INCQS/FIOCRUZ) has been testing all lots prior to batch release. Between 2000 and 2006, 619 lots of antivenoms were tested, comprising 2,513,690 ampoules. The potency assay was performed only for bothropic and crotalic antivenoms (485 lots corresponding to 1,866,726 ampoules) due to the unavailability of the other reference venoms. This paper aims to report the last 7-year activities of INCQS on the quality control, batch release and potency evaluation of antivenoms.


*Keywords:* Antivenoms; Potency evaluation; *Bothrops*; *Crotalus*

## 1. Introduction

Envenoming by poisonous animals is an important public health issue in Brazil. In 2004, it was the second cause of human intoxications representing 24.75% of the notified cases, following the intoxications caused by medicines with 28.95% (SINITOX, 2007). In 2005, 28,597 cases of snakebites were notified, representing an incidence of 15 cases/100,000 inhabitants/year. The genus *Bothrops* is responsible for 87.5% of all snakebites recorded yearly (13 cases/100,000 inhabitants), followed by *Crotalus* with 9.2% (1.4 cases/100,000 inhabitants),

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*Lachesis* 2.7% (0.4 cases/100,000 inhabitants) and *Micrurus* 0.6% (0.09 cases/100,000 inhabitants) (Ministério da Saúde do Brasil, 2007). In Brazil, envenomation by *Bothrops* has a low lethality rate (0.31%) in patients treated with antivenom (Ministério da Saúde do Brasil, 2001), but in severe cases local effects may lead to permanent tissue loss, disability or member amputation (Gutiérrez and Lomonte, 1989) and local necrosis may result in life-threatening complications such as tetanus and septicemia (Cardoso et al., 1998). Accidents due to *Crotalus*, *Lachesis* and *Micrurus* have a lethality rate of 1.87%, 0.95% and 0.36%, respectively. Scorpions (*Tityus* spp.) are responsible for an incidence of 8000 accidents/year (3 cases/100,000 inhabitants) with a lethality of 0.58%. There are three genus of spiders with medical importance in Brazil: *Phoneutria*, *Loxosceles* and *Latrodectus*, with an incidence of 1.5 cases/100,000 inhabitants and a lethality of 0.33%. The caterpillar *Lonomia obliqua* is also important, causing a severe heamorrhagic syndrome, but no reliable epidemiological data are available (Ministério da Saúde do Brasil, 2001).

Until now, the antivenom therapy remains the only specific treatment for envenomation by poisonous animals (Chippaux and Goyffon, 1998). Currently, antivenoms available in Brazil are liquid preparations containing purified equine Fab′2, manufactured by four public laboratories: Centro de Produção e Pesquisa de Imunobiológicos, Fundação Ezequiel Dias, Instituto Butantan and Instituto Vital Brazil (Ministério da Saúde do Brasil, 2001). These laboratories produce several antivenoms formulations: antibothropic-pentavalent (*Bothrops jararaca* 50%, *Bothrops jararacussu*, *Bothrops alternatus*, *Bothrops moojeni* and *Bothrops neuwedii*, 12.5% each), anticrotalic (*Crotalus durissus terrificus*), antibothropic-crotalic, antibothropic-lachetic (*Lachesis muta*), antibothropic-lachetic-crotalic, anti-elapidic (*Micrurus frontalis*), antiscorpionic (*Tityus serrulatus*), anti-arachnidic-polyvalent (*Tityus* spp., *Phoneutria* spp. and *Loxosceles* spp.), antiloxoscelic (*Loxosceles gaucho*, *Loxosceles intermedia* and *Loxosceles laeta*) antilatrodectic (*Latrodectus curacaviensis*) and antilonomic (*Lonomia obliqua*), comprising 619 lots and 2,513,690 ampoules from 2000 to 2006 (Table 1). Antivenoms are distributed free of charge to hospitals all over Brazil by the National Immunization Program.

The production of mono- and polyspecific antisnake venoms in Brazil begun in 1901 at Instituto Butantan, São Paulo (Brazil, 1907). Since 1987, prior to batch release INCQS, the National Control Laboratory of the Ministry of Health of Brazil has been testing all lots of antivenoms for phenol, sodium chloride, protein, protein nitrogen, ammonium sulphate, pH, volume, sterility and pyrogen (the test for abnormal toxicity was done until 2001). The potency test is performed only for bothropic and crotalic antivenoms due to the unavailability of other reference venoms.

Table 1
Antivenoms analysed by INCQS between 2000 and 2006

| | Total | Lab A | Lab B | Lab C | Lab D |
|---|---|---|---|---|---|
| Bothropic | 295* (1,188,980) | 186 (596,418) | 40 (409,909) | 66 (178,637) | 3 (4016) |
| Crotalic | 109 (435,545) | 72 (213,580) | 20 (165,493) | 17 (56,472) | – |
| Bot-Crot | 43 (138,525) | 28 (77,089) | 11 (48,248) | 4 (13,188) | – |
| Bot-Laq | 35 (102,284) | 20 (53,093) | 7 (32,971) | 8 (16,220) | – |
| Bot-Laq-Crot | 3 (1392) | 3 (1392) | – | – | – |
| Elapidic | 32 (107,034) | 20 (57,347) | 12 (49,687) | – | – |
| Scorpionic | 48 (345,630) | 29 (182,420) | 16 (140,675) | 3 (22,535) | – |
| Arachnidic (polyvalent) | 30 (134,650) | 30 (134,650) | – | – | – |
| Loxoscelic | 7 (12,618) | – | – | – | 7 (12,618) |
| Latrodectic | 1 (407) | – | – | 1 (407) | – |
| Lonomic | 16 (46,625) | 16 (46,625) | – | – | – |
| Total | 619 (2,513,690) | 404 (1,362,614) | 106 (846,983) | 99 (287,459) | 10 (16,634) |

( ) = Number of ampoules.
Bot-Crot = Polivalent antibothropic/crotalic.
Bot-Laq = Polivalent antibothropic/lachetic.
Bot-Laq-Crot = Polivalent antibothropic/lachetic/crotalic.
*Number of lots.