Workshop N
Snake Antivenom Immunoglobulins (Antisera)

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Global Shortage of Snake Antivenoms

- Animal blood derived snake anti-venom immunoglobulins (antivenoms) are listed by WHO as Essential Medicines, however:
- A global shortage exists of appropriate, safe and effective antivenoms to address a critical health need:
  - Snake venoms can cause paralysis and respiratory arrest, coagulopathy including fatal hemorrhage, irreversible kidney failure and severe tissue damage
  - An estimated 5 million people are bitten per year resulting in 2.5 million envenomings, 100,000 deaths and three times as many amputations and other disabilities
  - Most victims are women, children and farmers living in poor rural communities with sparse medical resources
  - Children suffer more severe effects due to smaller body mass than adults
  - Supply failure is imminent in Africa and parts of Asia
Shortage of Antivenoms is Complex

- Poor availability of antivenoms in part reflects poor quality and quantity of data on snake bites
  - Underestimation of needs leads to low demand for production and to failures of procurement and distribution
- In the face of low demand, several manufacturers have ceased production and prices have risen dramatically making treatment unaffordable for the majority in need
- Preparation of quality antivenoms from the correct immunogens (venoms) is technically challenging
- Poor regulation and the marketing of inappropriate antivenoms has eroded confidence in product use
WHO Actions to Address the Global Shortage of Snake Antivenoms

- WHO has raised awareness of the issue among stakeholders
- WHO has established:
  - Guidelines for the Production, Control and Regulation of Snake Antivenom Immunoglobulins (www.who.int/bloodproducts/snakeantivenoms)
  - A worldwide database on clinically important venomous snake species, their geographical distribution and the available relevant antivenoms (maps, pictures, products, manufacturers) (http://apps.who.int/bloodproducts/snakeantivenoms/database)
  - A website hosting both the Guidelines and the WHO Database (http://www.who.int/bloodproducts/snakeantivenoms)
WHO Database: Medically Important Snakes
Distribution maps, pictures & antivenoms

Red or orange question marks (?)
Indicates expected presence not yet confirmed due to lack of exploration

Allocation to CATEGORY 1 shown in red
(Indicates common, widespread species that causes numerous snake bites with high morbidity, disability or mortality)

Allocation to CATEGORY 2 shown in orange
(Indicates highly venomous and capable of causing morbidity, disability or mortality, but exact country data lacking, or less frequently implicated in these countries)
Applications for Website Data

- The data contained in the website has a number of applications, including:
  - Identifies the most widely distributed, and medically important species, enabling rational identification of key reference venoms needed in specific regions;
  - Assist procurement offices to determine appropriate antivenom selections for a given location;
  - Cross-matching of species distributions to health facility locations for the purpose of distributing appropriate antivenom supplies;
  - Provides manufacturers with data on the priority species for antivenom development in a given geographical area.
Product Recommendations

- There are relatively few products for which WHO has evidence of registration with relevant NRA’s and good quality, published evidence of acceptable safety and efficacy.
- Several manufacturers would not provide data on the species used to provide immunizing venoms (i.e.: location of origin or supplier data)
- Products without evidence of registration by an appropriate NRA were excluded.
- Products for which no positive preclinical or clinical data available were also excluded.
WHO Website: Target Audiences

- Central information source for data on the current availability of antivenoms for specific species.
- Aimed at a wide audience, that includes:
  - National Regulatory Agencies
  - Ministries of Health
  - Antivenom Manufacturers
  - Medical Professionals, Health Workers
  - Procurement Personnel in Industry and NGO’s
- Objective is to use the web site to disseminate accurate data to improve supply and distribution.
Website Demonstration
WHO - Health Systems and Services: Quality and Safety of Medicines - Blood Products and related Biologicals

Venomous snakes and antivenoms search interface

This search interface can be used to explore the global distributions of venomous snake species, and access information on antivenom products and their manufacturers. Users can search by region, subregion, country, territory or other geographical areas using the drop-down choices in the first panel below, or if the name of a particular snake is known it can be selected, or entered into the second panel so that users can go directly to that entry. Information on antivenom products and their manufacturers is accessible from the drop-down lists in the last panel.

Please select or enter your search term in one or more of the relevant fields below:

Search by Region or Location
Region: [Select a region] Sub region: [Select a subregion] Country, territory, or geographical area: [United States of America]

Search by Snake species
Common name: [Select a name] Species name: [Select a name]
Snake name: [Search] (Please enter at least 3 letters of the name)

Search by Antivenom products
Product name: [Select a product] Manufacturer: [Select a manufacturer]

For information supporting this database: WHO Guidelines on production, control and regulation of snake antivenom immunoglobulins.
### SEARCH RESULTS

Your search for "United States of America" generated the following results:

For information supporting this database, please see: WHO Guidelines on production, control and regulation of snake antivenom immunoglobulins.

<table>
<thead>
<tr>
<th>Link*</th>
<th>Cat**</th>
<th>Common name</th>
<th>Species name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please click here</td>
<td>1</td>
<td>Western rattlesnake</td>
<td>Crotalus viridis</td>
</tr>
<tr>
<td>2</td>
<td>Harlequin coral snake</td>
<td>Micrurus fulvius</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Texas coral snake</td>
<td>Micrurus tener</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Massasauga</td>
<td>Sistrurus catenatus</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Pygmy rattlesnake</td>
<td>Sistrurus miliarius</td>
<td></td>
</tr>
</tbody>
</table>

*Click on the thumbnail image to view more detailed information
**Highest risk category within the geographical range of the species
Species information

Common name: Harlequin coralsnake
Species name: Micrurus fulvius
Taxonomic family: Elapidae

Other common names:
Florida coralsnake, Eastern coralsnake

Previous species names:
None

Regions / Sub-regions where this species is present:
Americas: North America

Antivenoms:
Product: Antivenin (Micrurus fulvius)
Manufacturer: Wyeth (owned by Pfizer)
Country of origin: United States of America
Comments: The US FDA has extended the expiry date of remaining stock (Lot No. 4030020) until 31 October 2010.
Species information

Common name: Puff adder

Species name: Bitis arietans

Taxonomic family: Viperidae

Other common names:
None

Previous species names:
None

Regions / Sub-regions where this species is present:
- Africa: Central Sub-Saharan Africa
- Africa: East Sub-Saharan Africa
- Africa: North Africa
- Africa: South Sub-Saharan Africa
- Africa: West Sub-Saharan Africa
- Middle East: Middle East

Antivenoms:
- Product: FAV-Afrique
  Manufacturer: Sanofi-Pasteur
  Country of origin: France

- Product: Faviarept
  Manufacturer: Sanofi-Pasteur
  Country of origin: France

- Product: Polyvalent Snake Antivenom
  Manufacturer: National Antivenom & Vaccine Production Center (NAVPC)
  Country of origin: Saudi Arabia

- Product: SAIMR Polyvalent Snake antivenom
  Manufacturer: South African Vaccine Producers (SAVP)
  Country of origin: South Africa
WHO GUIDELINES ON PRODUCTION, CONTROL AND REGULATION OF ANTIVENOM IMMUNOGLOBULINS

A - Collection of venoms

B – Horse Immunization Protocols

C – Starting material of animal derived sera

D – Fractionation & Purification process
Guiding Selection of Reference Venoms

- Combined with distribution data assembled for the website project, the annex to the Guidelines provides information needed for experts to further prioritize essential venoms for use in antivenom production.

- Regional reference venoms are essential as:
  - Sources of standardized immunogens for raising antivenoms;
  - Reference materials for standardized preclinical assessment by both manufacturers and NRA’s.
  - Creates a framework for uniform comparison.
Questions for the Panel Discussion

• How can the "WHO Guidelines on production, control and regulation for snake antivenoms" be used to advance regulation in your country or region?
• How can regulators best impact the development of appropriate products in their countries or regions?
• How can experienced regulatory authorities on regulation of snake antivenoms can help development of regional reference venoms?
• What mechanisms could advance information and knowledge within the countries?
• How can WHO help to strengthen implementation of snake antivenoms regulation and cooperation among regulators?