JOINT TRAUMA SYSTEM CLINICAL PRACTICE GUIDELINE

Snakebite Envenomation

Guide providers in the evaluation and treatment of patients after snakebites

CONTRIBUTORS

COL Joseph Maddry, MD
Jordan Max Benjamin, NRP FAWM
Benjamin German, MD
Collin Dye, ATP
Evan Baines, MD
Alexandra Fields, MD
Jihoon Lee, ATP
Andi Champion, NRP, CCP, WP-C
Douglas Rinderknecht, WP-C FAWM
Christopher Pecori, PA-C (MDFR Venom One)
Marcos Collazo, NRP, RN
Karen Muschler, DO
Nicklaus Brandehoff, MD
Dan Mosely, MD
Spencer Greene, MD
Bryan Wilson, MD
Dan Brillhart, MD
Matthew Kilroe, MD
Nicholas Studer, MD
Tyler Webb, MD
COL Jennifer Gurney, MC, USA

Previous contributors: Lt Col Andrew Hall, MD; CAPT Edward Otten, MD; CPT Justin Grisham, DO; Dennis Jarema, 18D; Ben Abo, DO; Sean Keenan, MD; SFC Paul Loos, 18D; MSG Michael Remley, ATP; MAJ Kevin Maskell; Jennifer Hinners, MD, MPH; LTC Carl Skinner; Robert French, MD; Frank Butler, MD; Elizabeth Mann-Salinas, PhD; COL Stacey Shackelford, MD

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Urgent Reference

If you are currently OCONUS with a snakebite patient, contact the DoD ADVISOR Hotline (+1-833-238-7756), and refer to the **NEURO Algorithm**, **HEMO/CYTO Algorithm**, or **ASYMPTOMATIC Algorithm** to start treatment. For adverse reactions, see REACTION Algorithm and CPG sections on pretreatment and treatment of reactions.

Pre-Mission Planning: Always familiarize yourself with the specific antivenoms needed for your area of operation prior to deployment. For specific regional antivenom and dose recommendations, start with the **Regional Antivenom Selection Flowcharts**, then the **Antivenom Dosing by Product table in Appendix H**.

TABLE OF CONTENTS

Summary of Changes

Major revision for enhanced usability including:

1. New ACLS-style STAT treatment algorithms with streamlined bedside decision-making.
2. Expanded and updated antivenom profiles, dosing guidance, and BB-IND usage instructions in addition to FDA considerations.
3. New printable rapid-reference tools to enhance usability in austere environments including Antivenom Dosing by Product and Pre-Mission AV selection flowcharts.
4. Reorganized guidelines by CCMD for faster pre-mission planning and point-of-care use, including a suggested packing checklist.
5. INDOPACOM expanded + enhanced coverage with new dedicated regional pathways for Taiwan, Japan, Korean Peninsula, China / East Asia, and elsewhere.

QUICK GUIDE TO USING THE NEW SNAKEBITE CPG

This CPG provides comprehensive guidance on how to manage snakebites in all geographic Combatant Commands (CCMD), with clear steps for providers of all levels to follow in the field, and the clinic.

"How do I examine and treat snake envenomation patients?"

Perform a **rapid snakebite exam** to determine if the patient is currently **symptomatic** (NEURO vs HEMO/CYTO syndromes) **or asymptomatic** for snake envenomation, then follow the appropriate STAT treatment algorithms below:

Symptomatic treatment algorithms:

1. NEURO dominant syndrome = refer to Symptomatic NEURO Algorithm
2. HEMO and/or CYTO dominant syndrome = refer to Symptomatic HEMO/CYTO Algorithm

***NOTE**: For specific Antivenom doses, refer to Appendix H, Table 1: Antivenom Dosing by Product*

Asymptomatic (suspected dry bite or non-venomous snake):

1. Refer to Asymptomatic Algorithm
2. Once a symptomatic patient begins to improve and control is achieved after the correct dose of antivenom, follow the Control Algorithm for assessment pathway and disposition guidance.

Within the CPG text, review Universal Approach, Initial Priorities, and Focused Assessment for a more detailed guide to identifying the syndrome, determining severity, managing ABCs, and trending.

"How do I know when I have given the right dose of antivenom?"

Keep giving antivenom until key S/Sx stop getting worse (initial control) - pain will begin to improve; edema will stop progressing; all active bleeding will stop; vision, speaking, swallowing, and breathing will begin to improve; and systemic instability will stabilize. For a detailed list of clinical endpoints indicating that **initial control** has been achieved, see Figure 4 - Identifying Initial Control by Syndrome. Once initial control has been achieved, follow the Control Algorithm.

"How do I find which antivenom(s) and doses I need for deployment?"

1. To select the appropriate regional antivenoms, refer to the regional antivenom selection flowcharts.
2. To find the **High** and **Low** Doses recommended for each product, refer to Appendix H: Antivenom Dosing by Product or find the short form regional entries in the regional section for each CCMD.

Detailed product pages containing additional information (coverage, formulation, preparation, administration, etc) can be found in the regional sections (Appendix B – G). Both the NEURO Algorithm and HEMO/CYTO Algorithm contain blank boxes and are designed to print and fill in the details for the products you need.

"What do I do to prevent or treat reactions to antivenom?"

See Pretreatment to Prevent Reactions, Treatment of Adverse Reactions, Antivenom Reactions Algorithm.

"If my patient arrives with a tourniquet or constricting band, how should I remove it?"

Tourniquets and constricting bands may worsen snakebite outcomes and must be removed according to the Tourniquet Algorithm.

"What if I do not have antivenom (yet), or used it all?"

Reference Special Circumstances for full explanation. They have a very high morbidity and high mortality rate, and may require Supportive Care for weeks to months, if they survive.

Pre-Mission Planning: Review & Print Prior to Deployment

"What parts of the CPG should I reference and print to prepare for use while deployed?"

If you are deploying, everyone should print at a minimum **Appendix A – STAT treatment algorithms** (NEURO, HEMO/CYTO, Asymptomatic, Control, and Tourniquet algorithm) + your specific CCMD Appendix.

- **Print for AFRICOM** - Appendix A + Appendix B
- **Print for CENTCOM** - Appendix A + Appendix C
- **Print for EUCOM** - Appendix A + Appendix D
- **Print for INDOPACOM** - Appendix A + Appendix E
- **Print for NORTHCOM** - Appendix A + Appendix F
- **Print for SOUTHCOM** - Appendix A + Appendix G
- **Print for ALL CCMDS**: Appendix I - Class VIII Medical Material

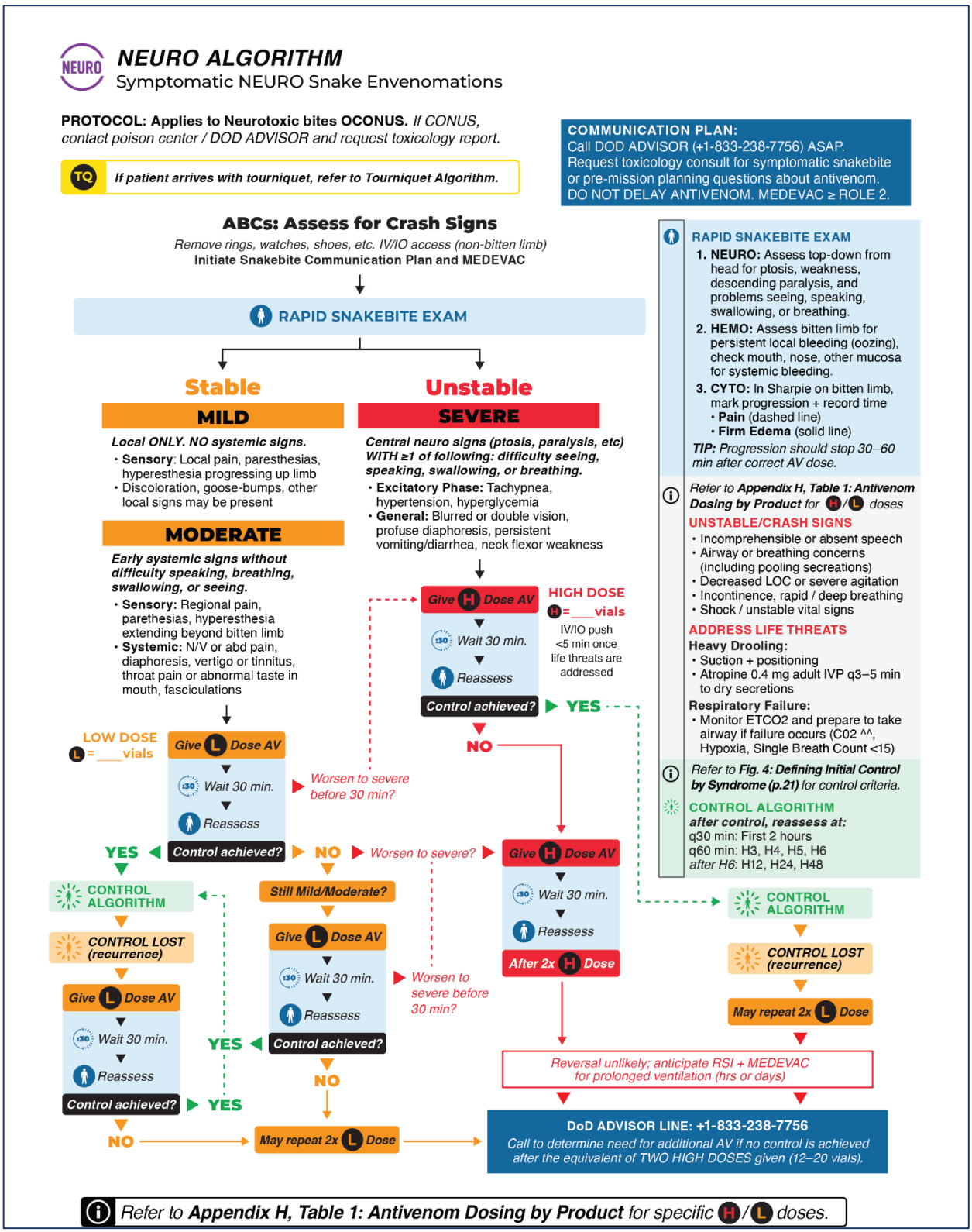
If need for antivenom dosing by product for all CCMDs simultaneously - Print Appendix H, Table 1: Antivenom Dosing by Product + Appendix H, Pre-Mission Flowcharts: Regional Antivenom Selection

Print & Fill Your Own Doses – When you print the NEURO Algorithm and HEMO/CYTO Algorithm, fill in the blanks for High and Low dosing from the products listed in Appendix H: Antivenom Dosing by Product. If you need more than 1 antivenom for either syndrome to obtain coverage in your region, print & copy the blank symptomatic algorithm pages you need and fill them in for all antivenoms you are carrying.

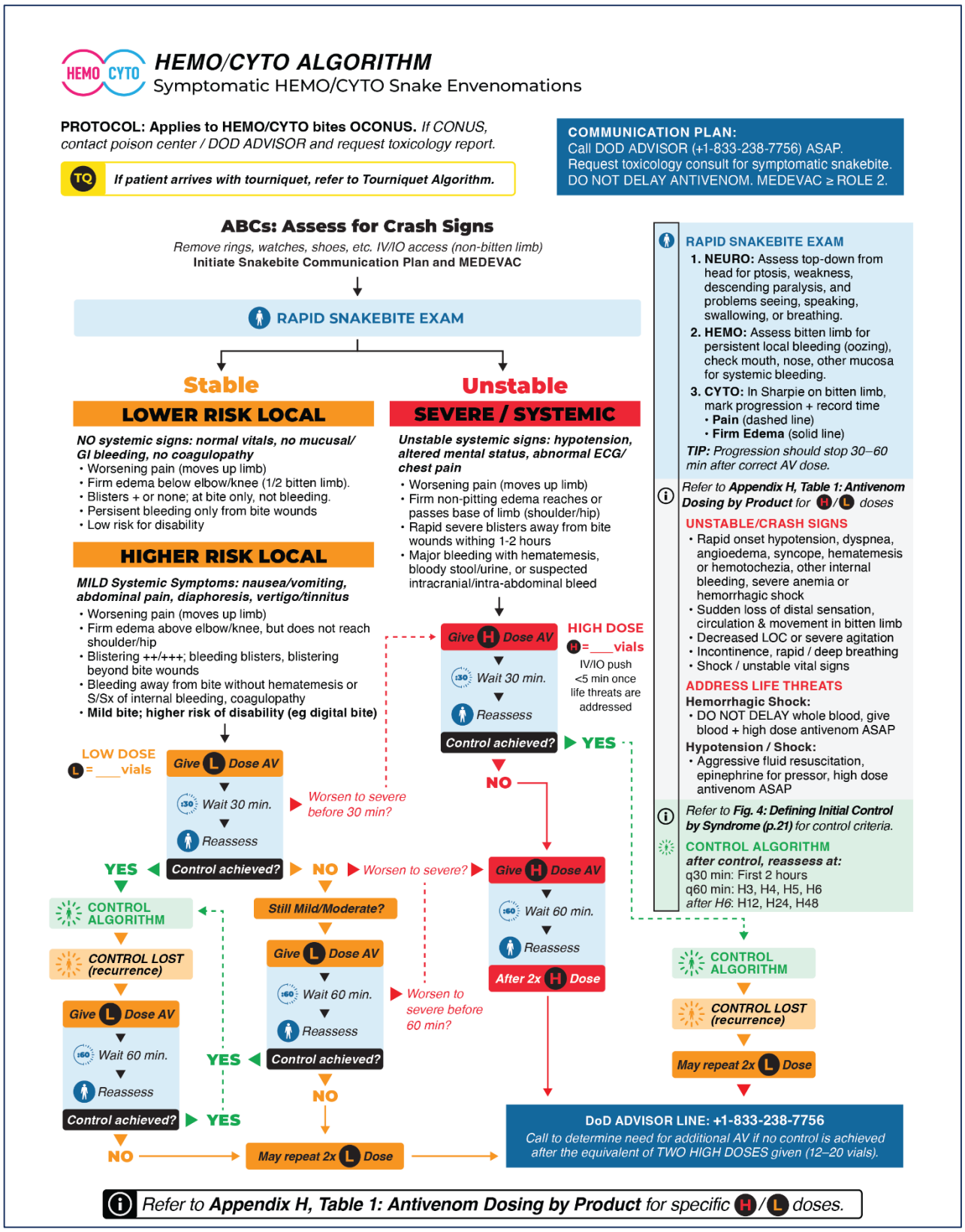
STAT TREATMENT ALGORITHMS

- Symptomatic NEURO Algorithm
- Symptomatic HEMO/CYTO Algorithm
- ASYMPTOMATIC Algorithm
- Control Algorithm
- Tourniquet Algorithm
- Antivenom Reactions Algorithm

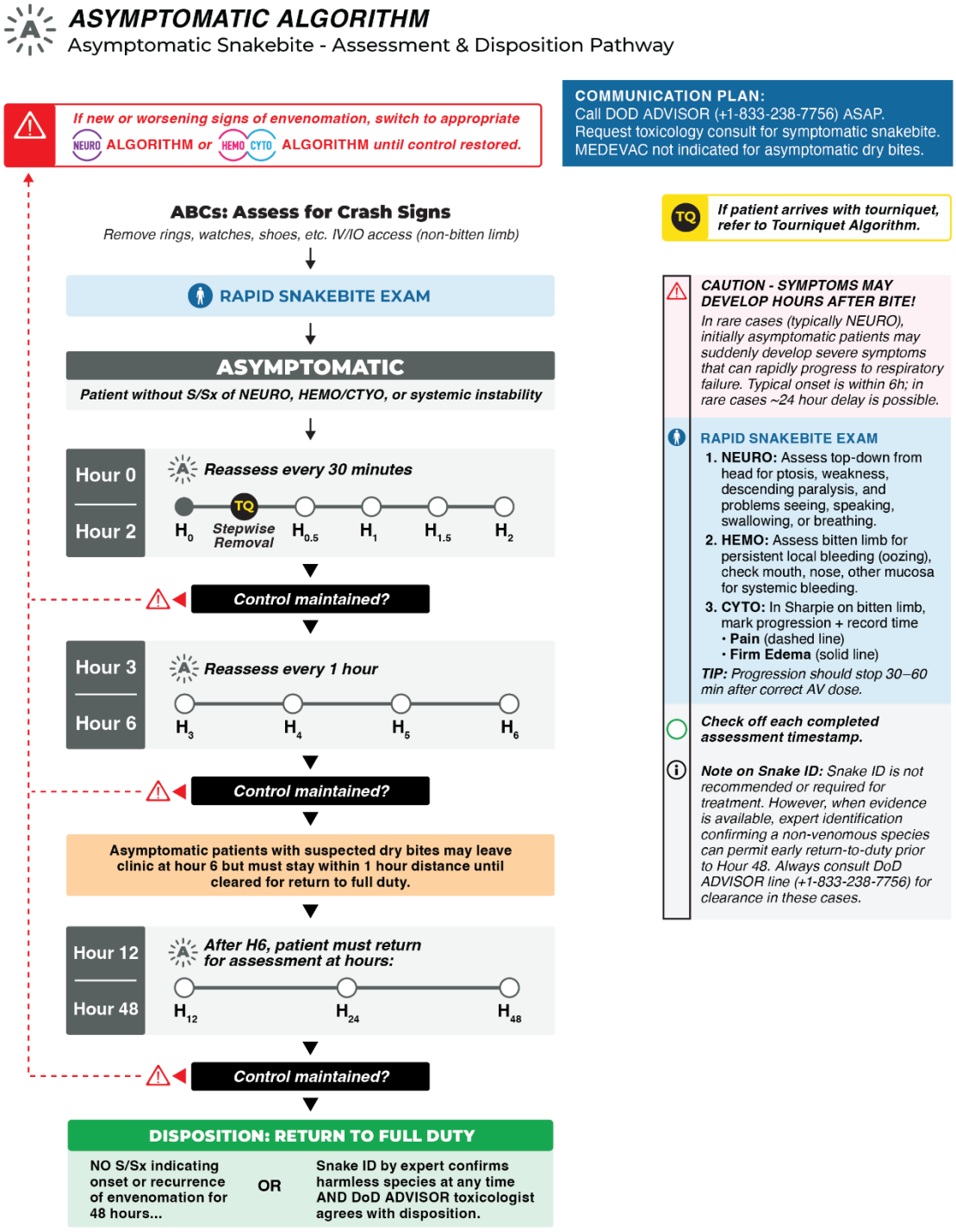
NEURO ALGORITHM



HEMO/CYTO ALGORITHM



ASYMPTOMATIC ALGORITHM



CONTROL ALGORITHM

CONTROL ALGORITHM
Control Achieved - Assessment & Disposition Pathway

This algorithm outlines assessment intervals and disposition decisions for **symptomatic snakebite patients** with NEURO, HEMO/CYTO, or systemic instability **once control has been achieved** after the correct dose of antivenom has been given. ***TIP:*** *Snakebites are dynamic, frequent reassessment is used early to catch evolving clinical signs, intervals gradually lengthen as risk reduces.*

COMMUNICATION PLAN:
Call DOD ADVISOR (+1-833-238-7756) ASAP.
Request toxicology consult for symptomatic snakebite.
DO NOT DELAY ANTIVENOM. MEDEVAC ≥ ROLE 2.

If control lost at any time *(S/Sx of envenomation develop) during this algorithm,* ***you have recurrence*** *and must treat using the appopriate* NEURO **ALGORITHM** *or* HEMO CYTO **ALGORITHM** *until control is restored.*

TQ ***If patient arrives with tourniquet, refer to Tourniquet Algorithm.***

REPEAT

RAPID SNAKEBITE EXAM

at the following times:

Hour 0 — Hour 2
Reassess every 30 minutes
H_0 (TQ *Stepwise Removal*) $H_{0.5}$ H_1 $H_{1.5}$ H_2

Control maintained?

Hour 3 — Hour 6
Reassess every 1 hour
H_3 H_4 H_5 H_6

Control maintained?

Symptomatic patients should remain in clinic until asymptomatic (control maintained) for 48 hours without recurrence.

Hour 12 — Hour 48
After H6, Patient must return for assessment at hours:
H_{12} H_{24} H_{48}

Control maintained?

DISPOSITION: RETURN TO FULL DUTY

NO S/Sx indicating onset or recurrence of envenomation for 48 hours... **OR** **Snake ID by expert confirms harmless species at any time AND DoD ADVISOR toxicologist agrees with disposition.**

RAPID SNAKEBITE EXAM

1. **NEURO:** Assess top-down from head for ptosis, weakness, descending paralysis, and problems seeing, speaking, swallowing, or breathing.
2. **HEMO:** Assess bitten limb for persistent local bleeding (oozing), check mouth, nose, other mucosa for systemic bleeding.
3. **CYTO:** In Sharpie on bitten limb, mark progression + record time
   - **Pain** (dashed line)
   - **Firm Edema** (solid line)

TIP: *Progression should stop 30–60 min after correct AV dose.*

Check off each completed assessment timestamp.

Control must be maintained for a full 48 hours (or non-venomous ID confirmed) prior to return to full duty. If control is lost, restart the 48h timer to disposition.

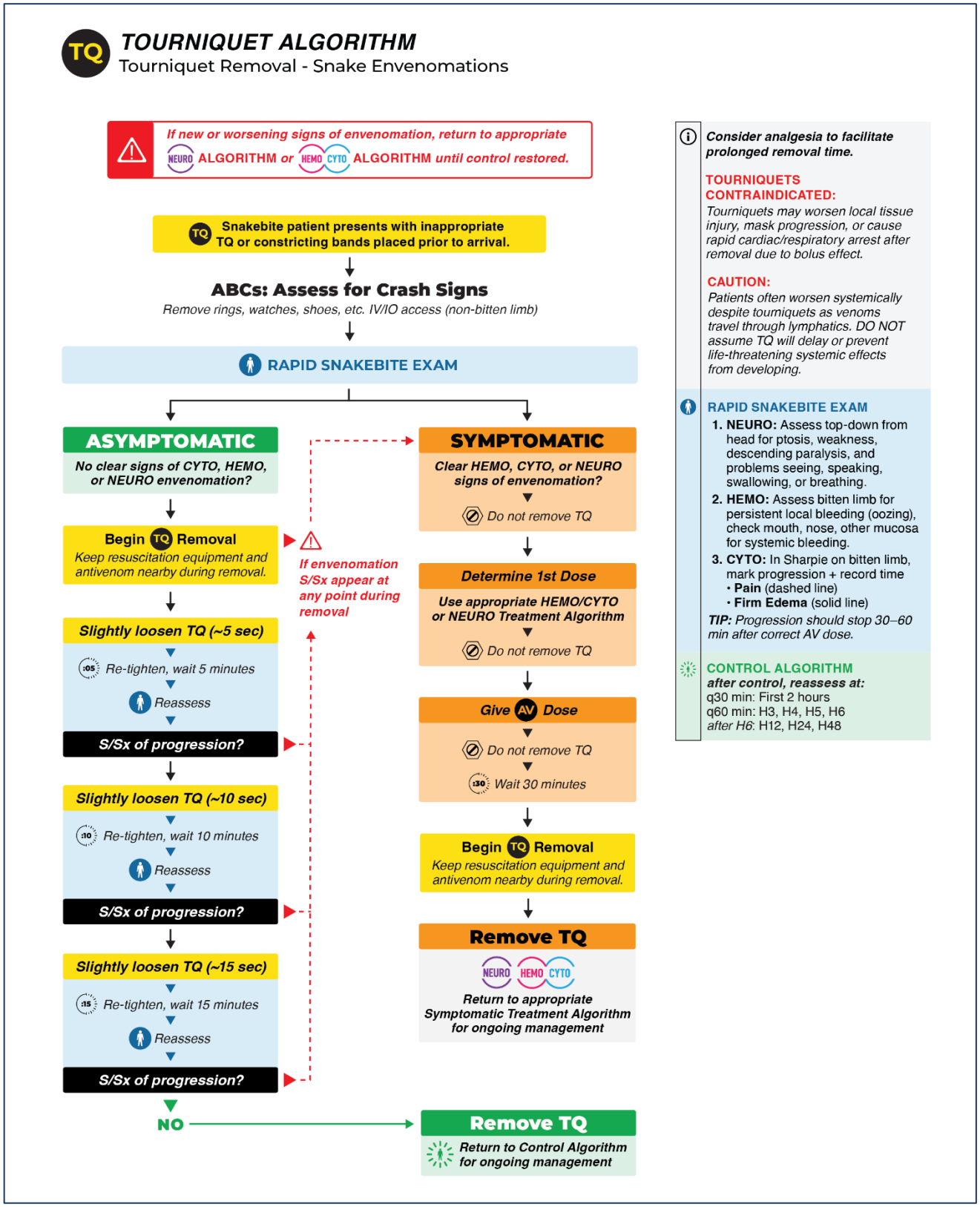
Note on Snake ID: *Snake ID is not recommended or required for treatment. However, when evidence is available, expert identification confirming a non-venomous species can permit early return-to-duty prior to Hour 48. Always consult DoD ADVISOR line (+1-833-238-7756) for clearance in these cases.*

HEMO DISPOSITION:
Patients with coagulopathy and/or systemic bleeding will require 2 weeks of bleeding precautions & serial labs prior to clearance for full return to duty as per unified treatment algorithm (US standards).

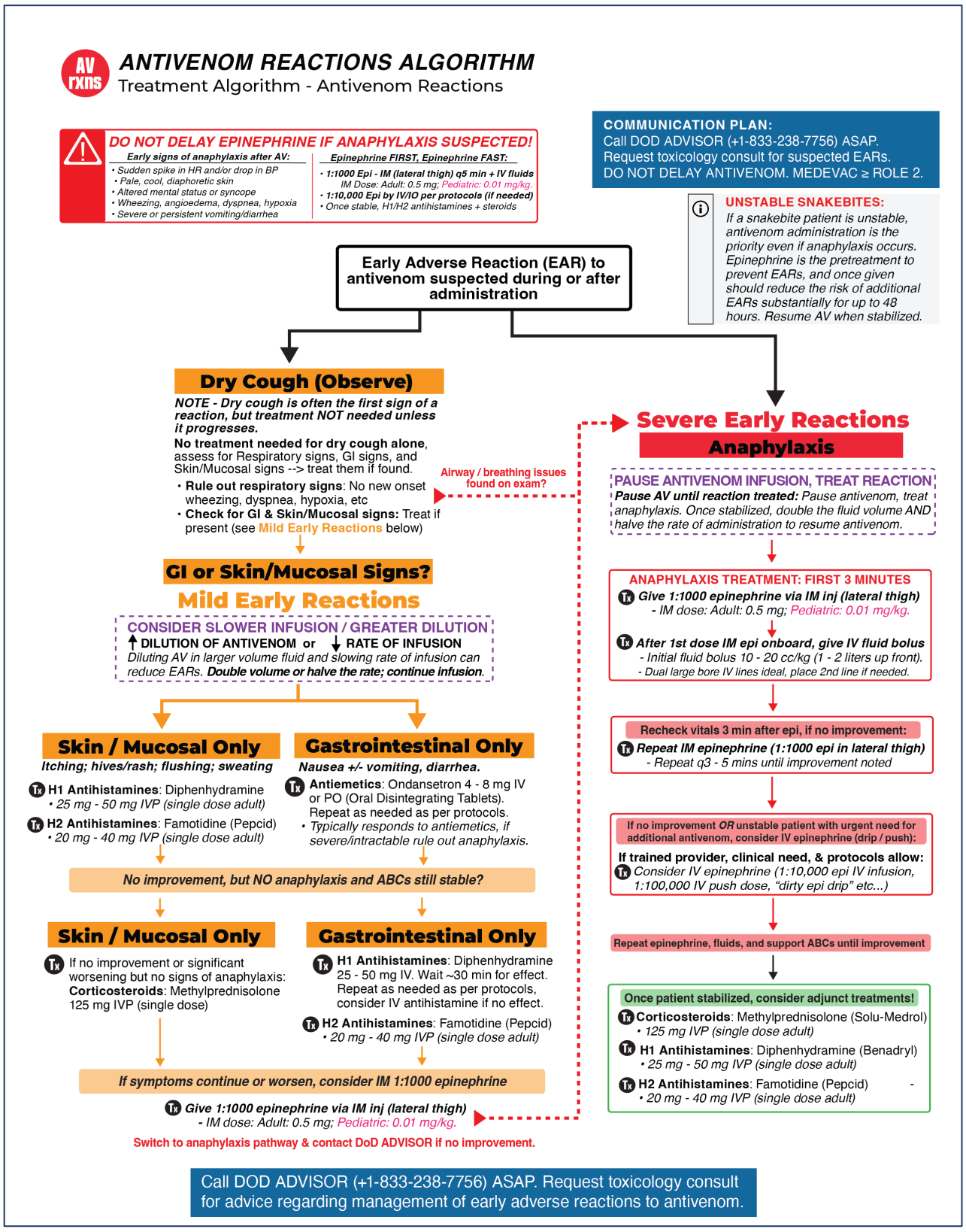
CAUTION - Polyphasic Recurrence and Venom Depot Effect
In some cases, initial control may be lost as additional venom is released from depots in tissue compartments. The risk is highest in the first 6 hours after control but may occur more than 24 hours later. If recurrence occurs, return to the appropriate treatment algorithm and give additional AV doses until control is regained. ***Patient must remain in control for 48h without recurrence prior to disposition.***

Refer to ***Fig. 4 - Defining Initial Control by Syndrome (p. 21)*** *for control criteria by syndrome.*

TOURNIQUET ALGORITHM



ANTIVENOM REACTIONS ALGORITHM

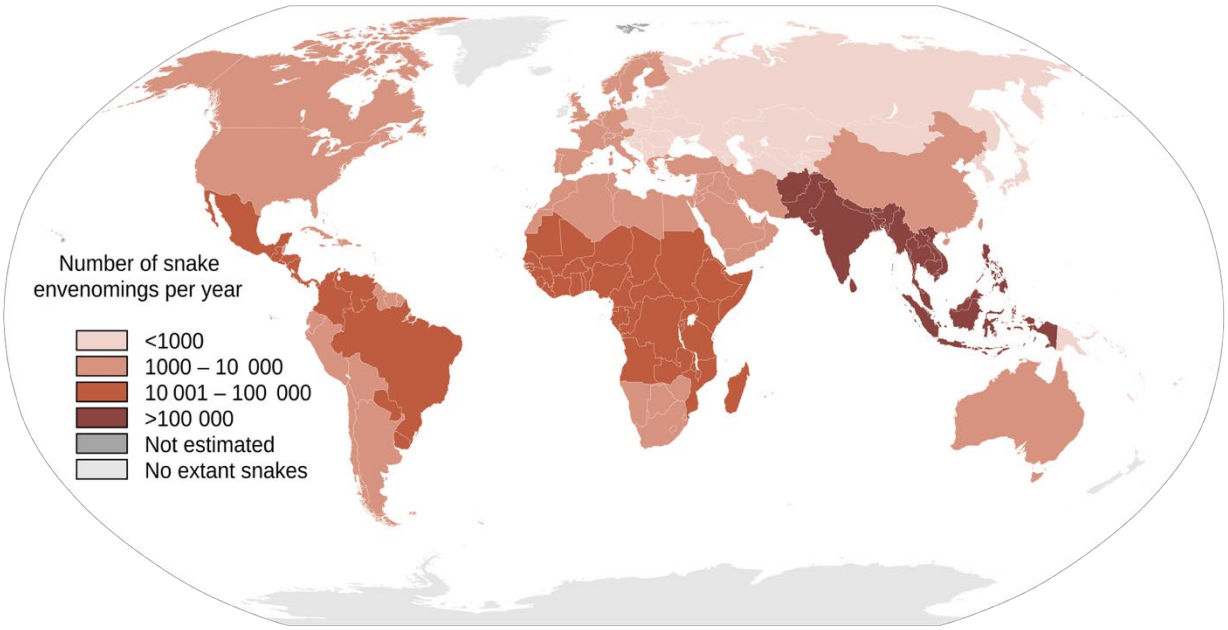


BACKGROUND

Snakebite, recently declared a neglected tropical disease and global health priority by the World Health Organization (WHO), results in an estimated 2.5 million envenomations, 138,000 deaths and over 500,000 cases of permanent disability worldwide every year.[1–10] Snake, spider, and scorpion envenomations are a common environmental and occupational hazard for military forces worldwide.[11–46] The consequences of an envenomation range from mild local effects to permanent disability or death, and the outcome is largely determined by the time to antivenom treatment and the level of training of the medical providers involved. Clinical outcomes and survival of the snakebite patient require administering antivenom quickly and immediate care by trained medics or medical professionals. Antivenom and appropriate early care are critical to saving lives and preventing long-term complications like amputations, blindness, or loss of limb function.

Venomous snakebites can induce a range of clinical syndromes, largely categorized by the primary type of toxin in the venom. Cytotoxic venoms, found in snakes like spitting cobras, copperheads, and puff adders cause severe localized tissue damage. This manifests as painful progressive swelling that starts at the bite site and can spread rapidly, leading to complications such as blistering, tissue death (necrosis), and compartment syndrome, a condition where swelling cuts off blood circulation. Hemotoxic venoms, on the other hand, disrupt the body's ability to clot blood, leading to bleeding from various sites, including the gums, nose, and the bite wound itself. Snakes such as Russell's vipers, saw-scaled vipers, and boomslangs possess hemotoxic venom, which can cause coagulopathy, a condition of abnormal blood clotting, and in severe instances, disseminated intravascular coagulation (DIC).

Neurotoxic venoms primarily affect the nervous system, causing progressive weakness and paralysis. Symptoms of neurotoxic envenomation include drooping eyelids (ptosis), blurred vision, difficulty breathing, and can advance to paralysis of the respiratory muscles, which can be fatal. Cobras, kraits, and mambas are well-known for their neurotoxic venom. Systemic instability is a broader category of effects that can result from various types of snake venoms and their systemic impacts. This can include a mix of syndromes (eg HEMO + CYTO), such as painful progressive swelling combined with bleeding, as seen in bites from many vipers including rattlesnakes, gaboon vipers, the Fer-de-lance, and others. It can also manifest as life-threatening systemic complications like dangerously low blood pressure (hypotension), shock, acute kidney injury, and acute respiratory distress syndrome (ARDS), which can be triggered by fluid loss from cytotoxic effects, widespread bleeding from hemotoxic effects, or direct shock-inducing venom components.



Once a snakebite occurs, it is a race against time to prevent severe local tissue damage and deadly systemic symptoms. Some types of necrosis caused by cytotoxic venoms cannot be reversed but can be prevented by early antivenom administration (or arrested before further damage can occur in cases of late antivenom treatment).[1,7,47-49] Hemotoxic venoms can induce bleeding and clotting abnormalities within minutes, which progresses over hours or days into widespread external and internal bleeding. Neurotoxic venoms can act rapidly and be fatal. When a neurotoxic snake bite occurs, rapid antivenom administration prior to the onset of respiratory failure can arrest the progression of descending paralysis before serious systemic manifestations develop.[1,50,51] In many cases paralysis will reverse rapidly. When paralysis cannot be reversed before mechanical ventilation is needed (e.g. late-presenting krait envenomations), antivenom still plays a key role: clearance of unbound circulating venom, which permits recovery of damaged nerve terminals and reduces time to extubation to an average of 2 – 5 days versus weeks of ventilation in untreated patients. Every hour wasted between bite and antivenom administration is strongly associated with sharp increases in mortality and the development of chronic or permanent sequelae including amputation, disfigurement, PTSD, blindness, kidney injury, infections, and partial or complete loss of function of the bitten limb.[4,7,8,52–58]

This CPG provides comprehensive guidance on how to manage snakebites in all geographic CCMDs, with clear steps for providers of all levels to follow in the field and the clinic.

GENERAL PRINCIPLES OF SNAKEBITE MANAGEMENT

Don't try to ID the snake. **You don't need to know the snake's species to treat the patient. Trying to catch or kill the snake is dangerous and wastes time. Focus on the patient's symptoms**.

Venomous snakebites fall into three main types (syndromes) plus an additional can't miss HALO diagnosis: neurotoxic (paralyzes the nervous system), hemotoxic (affects blood), cytotoxic (destroys tissue), and systemic instability/sudden collapse. Every dangerous snakebite will show at least one sign from these syndromes, and those signs will continue to worsen until antivenom is given to neutralize the threat. Treatment depends on the presence and progression of clinical signs, not the snake's identity.

Figure 1. Snakebite Clinical Triads

For patients who present with rapid instability / sudden collapse syndrome, refer to Sudden Collapse Syndrome section for more information.

CLINICAL PEARLS ON SNAKEBITES & ANTIVENOM TREATMENT

1. **Treat based on symptoms, not the snake.**

   Even if a patient says they were bitten by a dangerous snake (like a mamba), don't give antivenom unless they show signs of envenomation (e.g., swelling, bleeding, or weakness). If a patient has symptoms but thinks the snake was harmless, treat them based on what you see.

2. **Antivenom is the main treatment.**
    - Antivenoms are safe and effective and carry a low risk of allergic reactions compared to the high risk of venom damage. Many can be carried in the field at ambient tropical temperatures with no special storage required – these products are labeled as FREEZE-DRIED/UNREFRIGERATED in the antivenom product pages later in this document.
3. **Use IV or IO routes only** (not IM or SQ, even if the package says so). IV is best, but IO works in emergencies.[54,59]
4. **Antivenom dosage is not weight-based** and there is no difference in dosing between adults and children.
5. **Follow the dosing recommended in this CPG unless instructed otherwise by a DoD ADVISOR Toxicologist or other approved snakebite expert**. DO NOT follow the package insert, as they rarely reflect clinical or evidence-based best practices.
6. **Keep giving antivenom until symptoms stop getting worse (INITIAL CONTROL) –** see Identifying Initial Control by Syndrome): pain will begin to improve; edema will stop progressing; all active bleeding will stop; vision, speaking, swallowing, and breathing will improve; and systemic instability will stabilize. Overdosing isn't a concern, but watch for late allergic reactions (e.g., rash or fever) 1–3 weeks later, which can be treated with antihistamines or steroids.
7. Some snakebite patients will experience secondary recurrences (similar to polyphasic anaphylaxis) where **control is lost** and symptoms suddenly begin to worsen and progress again. This is usually within the first 0 - 6 hours after initial control but rarely can occur 24 – 48 hours later.
    - This is why the control algorithm stacks more frequent assessments in the first hours after control is achieved: reassess q30 minutes for the first two hours after initial control is achieved
8. When **control is lost and recurrence occurs**, give additional doses of antivenom according to the appropriate treatment algorithm (NEURO or HEMO/CYTO).
    - When control is achieved again, restart the 48-hour clock on the Control Algorithm for assessment intervals and disposition decisions. Symptoms must be controlled for 48 hours without signs of worsening progression before disposition can be achieved. When in doubt, consult a DoD toxicologist via the ADVISOR line.
9. **DO NOT give test doses** to check for allergies; they don't work and waste time.[60–63] Pretreatment with IM epinephrine is the only effective means of reducing reaction risk, see Pretreatment to Prevent Reactions.
10. **Track progression / evolution of symptoms over time. Write down the following:**
    - When the bite occurred (time/date) + time elapsed prior to arrival
    - Speed and degree of progression between bite → presentation
    - Time when the first dose of antivenom is given (defined as Hour 0, written as H0)
    - Assessment and disposition instructions (including timing of repeated assessments) is detailed in the Control Algorithm.
11. **Snakebites can change fast.**
    - A patient might start with only local pain or swelling (cytotoxic) but later develop systemic bleeding (hemotoxic) or progressive weakness (neurotoxic). Check for all three syndrome types at every assessment and adjust treatment as needed (see rapid assessment box in treatment/assessment algorithms). Consult a Medical Toxicologist as soon as possible.
    - Within the United States, a Medical Toxicologist can be reached via a Poison Control Center by calling 800-222-1222. Within the Department of Defense, a Medical Toxicologist can be reached via the Advanced Virtual Support for Operational Forces (ADVISOR) teleconsultation service by calling 833-ADVSRLN (833-238-7756)/ DSN: 312-429-9089 and requesting a toxicology consult.
12. If a reaction occurs, see Antivenom Reactions Algorithm and Treatment of Adverse Reactions.

WHO SHOULD CARRY ANTIVENOM & UNDER WHAT CIRCUMSTANCES?

QUALIFICATIONS

Antivenom administration should be performed by medical providers capable of providing advanced life support and trained to a minimum level of paramedic (or DoD equivalent) and higher (i.e., 68W3P, SOCM, 18D, PJ, IDC, IDMT, RN, PA, MD or DO, etc).

CIRCUMSTANCES

All qualified medical providers who may be responsible for treatment of a snakebite casualty OCONUS, with ground CASEVAC times exceeding 60 minutes to facilities equipped with appropriate regional antivenoms in sufficient quantities, should carry the equivalent of 2 high doses or 4 low doses of the appropriate regional antivenoms to enable timely definitive treatment with antivenoms at the point of injury.

NON-FDA APPROVED ANTIVENOMS RECOMMENDED IN THIS CPG

Following repeated questions to JTS about using non-FDA-approved antivenoms after publication of the Global Snake Envenomation Management CPG (2020), the JTS Working Group consulted with FDA's Center for Biologics Evaluation and Research (CBER) to provide clarification and guidance regarding the regulatory framework for DoD medical providers, procurement officers, and commanders who need to obtain the foreign antivenoms listed in this CPG.

Snakebite treatment OCONUS requires the use of non-FDA-approved foreign antivenoms through the Biological-Based Investigational New Drug (BB-IND) pathway.

Non-FDA-approved antivenoms are the only options for treating snakebites outside the United States. None of the 26 foreign antivenoms recommended for OCONUS use in this CPG are FDA-approved, and the FDA does not expect or require them to obtain approval because they are indicated for exotic snakes that are not native to the United States. Instead, the FDA provides a specific legal pathway to facilitate lawful importation, storage, and use of these products: the Biological IND (BB-IND) with Expanded Access under 21 CFR 312 Subpart I. The antivenom BB-IND pathway has been utilized for decades by zoos and private snake keepers, allowing U.S. citizens to procure and administer these lifesaving products with required annual reporting.

DoD is already utilizing the BB-IND pathway to support use of foreign antivenoms.

In AFRICOM, INDOPACOM, SOUTHCOM, EUCOM, and part of NORTHCOM (Mexico), first-line therapy for snakebite utilizes non-FDA-approved antivenoms obtained through the BB-IND/Expanded Access program. The Surgeon General-Department of the Army (TSG-DA) holds the BB-INDs for all antivenoms listed in this CPG, and the Defense Health Agency's Office of Regulated Activities and Force Health Protection (FHP) Division oversees importation, compliance tracking, and regulatory oversight. Logistics and procurement should follow this established pathway to meet the standard of care and JTS Performance Improvement (PI) objectives.

What type of reporting and documentation is required by the FDA for BB-IND?

Antivenoms accessed through BB-IND require annual and case-specific reporting to FDA CBER. Annual reports are filed each year (FDA Form 1571) and detail whether any antivenom was used in the previous 12 months. When a patient is treated, FDA Form 1572 (found on the FDA website: https://www.fda.gov/about-fda-reports-manuals-forms/forms) is submitted in the annual report and a case report is filed as well. As the BB-IND holder for the US military, the ORA, acting on behalf of TSG-DA is responsible for submitting these reports to the FDA. If any antivenom is administered, please contact a Medical Toxicologist via the Advanced Virtual Support for Operational Forces (ADVISOR) teleconsultation service by calling 833-ADVSRLN (833-238-7756)/ DSN: 312-429-9089 and the Toxicologist will assist in ensuring compliance with FDA guidelines for the use of antivenoms with an IND or in submitting an emergency IND number if one does not already exist.

Who should I contact with questions about obtaining antivenom for my local formulary?

Contact Force Health Protection (FHP) with questions regarding antivenom procurement via the **FHP 24/7 Emergency Phone: 301-401-2768 or e-mail:** usarmy.detrick.medcom-usammda.mbx.force-health-protection@health.mil.

The U.S. Food and Drug Administration (FDA) does not adjudicate nor approve antivenoms required outside the United States. Code of Federal Regulations (CFR) Title 21 Part 312 classifies these pharmaceuticals as Investigational New Drugs (IND). Therefore, sourcing of these antivenoms occurs through alternate pharmaceutical supply chains. Oversight for IND falls under the Department of Health Operational Medical Systems (DHA OPMED) Force Health Protection (FHP) Division (https://dha.mil/Offices-and-Programs/OPMED/FHP) with regulatory support provided by U.S. Army Medical Research and Development Command's (MRDC) Office or Regulated Activities (ORA). However, the antivenoms will need to be purchased and acquired by the Combatant Command or on the local market by medical personnel. We recommend contacting the appropriate Geographical Combatant Command Surgeon General's Office to assist in acquiring and stocking antivenom if there is the credible risk of snake envenomation for which the risks and costs of maintaining and storing said antivenom are appropriate. If medical personnel must acquire the appropriate antivenom on the local economy, it is advised that great caution is taken to ensure the antivenom is legitimate, unexpired, and appropriately stored given that selling and marketing of fraudulent antivenom does occur in developing countries.

UNIVERSAL APPROACH TO THE SNAKEBITE PATIENT

INITIAL PRIORITIES

1. Focus on ABCs (Airway, Breathing, Circulation) and antivenom.
    a. Check ABCs first and fix any immediate life threats (e.g., trouble breathing or shock).
    b. If the patient has sudden collapse (shock, swelling, confusion, or bleeding within 30 minutes), follow the Sudden Collapse Syndrome Treatment Protocol.
    c. Establish IV or IO access in a non-bitten limb for antivenom or fluids.
    d. Treat emergent secondary issues that may be present (such as anaphylaxis or hypovolemic shock) according to standard clinical protocols.
    e. Establish IV or IO access in a non-bitten limb before proceeding.
2. ***DO NOT apply constricting bandages or tourniquets*** as these may worsen local tissue injury and increase the risk of permanent disability.[64–66]

If patient arrives with tourniquet, refer to Tourniquet Algorithm.

If a tourniquet is already in place, see Tourniquet Algorithm. Do not remove it until you are ready to treat and resuscitate the patient as a rapid decompensation can occur.[67,68]

3. If and when conditions allow, minimize patient activity, and loosely immobilize the bitten limb to reduce movement without constricting tissues.
    a. If antivenom isn't available, get the patient to a facility with antivenom as fast as safely possible, even if they have to walk.
    b. If conditions allow during transport, maintain the bitten limb in a position of comfort that is elevated below the level of the heart.
    c. Once the patient has arrived at a medical facility with antivenom, aggressively elevate the bitten limb (aim for a minimum 60º angle in a supine patient if possible and tolerated by patient) to reduce oncotic pressure on swollen tissues.
4. Evaluate for specific signs and symptoms of snake envenomation. Refer to the STAT treatment algorithms in Appendix A for specific criteria for initial antivenom treatment and repeat doses for additional information.

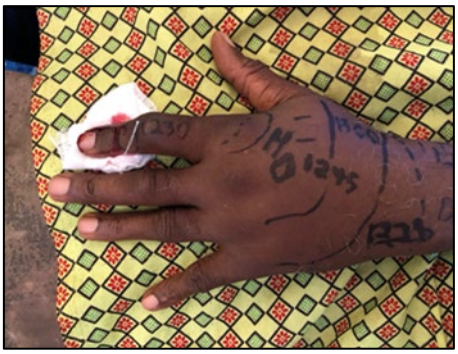
5. Consult a Medical Toxicologist as soon as possible. Within the United States, a Medical Toxicologist can be reached via a Poison Control Center by calling 800-222-1222. Within the Department of Defense, a Medical Toxicologist can be reached via the Advanced Virtual Support for Operational Forces (ADVISOR) teleconsultation service by calling 833-ADVSRLN (833-238-7756)/ DSN: 312-429-9089.

FOCUSED ASSESSMENT & EXAMINATION

Perform a physical examination and history focused on identifying signs and symptoms of neurotoxic, hemotoxic, cytotoxic, and systemic instability envenomation syndromes. ***General approach is to identify syndrome → determine severity → administer initial LOW, MEDIUM, or HIGH DOSE antivenom based on syndrome AND current severity → reassess and retreat as needed based on response of key STOP/GO criteria for additional doses.***

1. Mark the bite site. Circle the site of the bite wound and write the specific time that it occurred with a permanent marker on the patient. Don't rely on fang marks—bites may look like punctures, scratches, or nothing at all.
2. Check for cytotoxic signs (tissue damage). Look for pain, swelling, or tissue destruction. Mark the edge of pain (dashed line) and swelling (solid line) with a marker and note the time.

Figure 2. Marking Progressive Pain and Edema

On bitten limb in Sharpie: Circle bite wound, record time when bite occurred	*On bitten limb, chart progression with Sharpie: Mark leading edges of both **pain (dashed line)** and **firm edema (solid line)** + record time*	*Edema can be firm (non-pitting) or soft (pitting). We care about firm edema; start above the swelling and palpate down until you feel the change from soft to firm. That is the leading edge you want to mark*
		
Note: Oozing blood from bite wound diagnostic for HEMO	***Note**: Worsening pain progresses up the limb faster than edema until control is achieved. **Note**: Pain improves faster than edema when control is achieved (~30-60 min after AV).*	***Note**: Edema will stop getting worse (progressing up limb) when control is achieved, but it will take several days to go down. **DO NOT** chase persistent edema. Treat for edema when the firm edge is progressing. Stop treating when it halts.*

3. Check for hemotoxic signs (bleeding). Look for bleeding at the bite that lasts over 30 minutes or bleeding from gums or other areas (mouth, gums or other mucosa).[1,69–72]
4. Check for neurotoxic signs (nerve issues).
5. Rapid examination for signs of **neuromuscular weakness (neurotoxic syndrome**)
    a. Evaluate respiratory muscle weakness by single breath count (SBC) testing [72] and repeat periodically to trend improvement or deterioration in respiratory function over time.
        - Ask the patient to take a deep breath and count out loud as high as they can without breathing again and repeat periodically to trend improvement or deterioration in respiratory function over time.
        - Normal SBC is approximately 50 and SBC < 20 is associated with the need for mechanical ventilation.

- If spirometry is available, this can be used in place of the single breath count test by evaluating the negative inspiratory force (NIF) and/or forced vital capacity (FVC).

- **Conduct gross assessment** and pay particular attention to the following:
  - Signs and symptoms of descending flaccid paralysis: Ptosis (upper eyelid drooping), diplopia (double vision), neck flexor muscle weakness, bulbar weakness, difficulty speaking, difficulty swallowing, etc.[1,54,73]
    - Signs and symptoms of parasympathetic / cholinergic crisis: SLUDGE mnemonic - Salivation, Lacrimation, Urination, Defecation, GI distress, Emesis.

6. Perform and/or check the clinical laboratory tests listed below (if available).
   - Complete Blood Count (CBC), Hemoglobin, or Hematocrit.
   - Clotting tests (PT, PTT, INR, Fibrinogen).
     - Simple coagulation test for austere environments: Use the Whole Blood Clotting Test (WBCT) as described in Appendix J to diagnose and monitor coagulopathy if advanced labs not available.
   - Comprehensive Metabolic Panel (CMP) and Creatine Kinase (CK).

LAB TESTS

Advanced laboratory tests include:

- Complete Blood Count (CBC)
- Hemoglobin (Hb) or Hematocrit (HCT) if no CBC but separate testing for either Hb or HCT is available
- Prothrombin Time (PT), Partial Thromboplastin Time (PTT), and International Normalized Ratio (INR)
- Fibrinogen
- Comprehensive Metabolic Panel (CMP)
- Creatine Kinase (CK)

Simple coagulation test for austere environments: Use the Whole Blood Clotting Test (WBCT) as described in Appendix J to diagnose and monitor coagulopathy if advanced labs are not available.

TRANSPORT FACTORS

1. If the patient is being medically evacuated from the field or between roles of care, confirm that the receiving facility has an adequate supply of the appropriate regionally specific antivenoms listed in this CPG to ensure treatment coverage against local species of concern. Alternatively, have the antivenom transported to the patient.

***NOTE**: Evacuation is not an alternative to antivenom administration. A patient whose snakebite warrants evacuation will require antivenom. The earlier it is given the greater the chance of full recovery without permanent disability. DO NOT delay administration of antivenom in the field to a patient with an envenomation.*

2. If clinical evidence of envenomation is present and treatment is occurring in a hospital setting, always admit to a bed with continuous vital sign monitoring if available. If treating in the field, continuously monitor patient trends for signs of progression, improvement, or deterioration.
3. If no initial clinical evidence of envenomation, follow the Asymptomatic Algorithm for assessment intervals and disposition guidance.

SYSTEMIC INSTABILITY & SUDDEN COLLAPSE SYNDROME

In rare cases, a patient may rapidly deteriorate in the first 5 - 30 minutes after the bite and present with profound hypotension, tachycardia, angioedema, altered level of consciousness, etc.[1,122–130] These patients should be aggressively treated for severe anaphylaxis and severe envenomation simultaneously. Treat anaphylaxis aggressively according to anaphylaxis protocols. Treat the envenomation with an initial high dose (at least 6 vials) of antivenom by rapid IV push, and support the patient with airway management, fluids, and other interventions as appropriate.[122,123,125,131,132] Most patients presenting with hypotension or angioedema are responsive to epinephrine, but may require IV epinephrine infusions to achieve this effect if they are unresponsive to IM epinephrine.[122]

SUDDEN COLLAPSE SYNDROME TREATMENT PROTOCOL

Patient presents within 30 minutes of the bite with rapid onset shock (hypotension with inadequate tissue perfusion) ± angioedema, altered mental status, systemic bleeding, and/or diarrhea.[1] Stabilize with IM or IV epinephrine and fluids as per anaphylaxis protocols.

4. Intubate for airway edema if not rapidly responsive to epinephrine.
5. Follow epinephrine immediately with a high dose of the appropriate regional antivenom given by rapid IV or IO push during the resuscitation.
6. Maintain blood pressure with IV or IO fluids and epinephrine until antivenom has taken effect to reverse the hypotension.

DEFINING CLINICAL SNAKEBITE SYNDROMES, SEVERITY, & INITIAL CONTROL

Signs and symptoms differentiating mild, moderate, and severe presentations of neurotoxic, hemotoxic, and cytotoxic syndromes are detailed below. Rapid reference criteria for determining severity by syndrome is included in the STAT treatment algorithms for symptomatic patients with NEURO and HEMO/CYTO envenomations.

Clinical Pearl: Worsening progressive pain may be present with any syndrome. Increasing pain severity and/or ascending pain up the bitten limb may be present for all snake envenomations and is an early diagnostic indicator of envenomation. Edema and/or blistering with progressive pain is the definition of the cytotoxic syndrome. If there is worsening pain with hemotoxic or neurotoxic symptoms, chart it and expect improvement after the appropriate antivenom dose.

Clinical Pearl: Treatment Endpoint = Control. Snakebite treatment is dynamic and the total dose of antivenom needed is determined by the amount of venom injected into the patient. Continue administering antivenom according to the STAT treatment algorithms until **Initial Control** has been achieved – refer to **Defining Initial Control by Syndrome** for specific clinical endpoints indicating that initial control has been achieved. When initial control is maintained through all the assessment points detailed in the **control algorithm**, then **permanent control** has been achieved.

Figure 3. Defining Syndromes & Severity

Severity	Neurotoxic Syndrome	Hemotoxic Syndrome	Cytotoxic Syndrome
Mild **(LOW DOSE)**	**Local S/Sx (bitten limb only)**: Paresthesia, hyperesthesia, neuropathic pain, piloerection, muscle spasms/fasciculations progressing proximally up the bitten limb **but not beyond the shoulder or hip** **Systemic S/Sx:** Nausea, Abdominal pain without persistent vomiting or diarrhea, mild diaphoresis. Throat pain without hypersalivation. **Normal speech, breathing, and swallowing.**	**Local bleeding > 30 mins post bite OR Coagulopathy without bleeding; NO systemic bleeding.** Blood continues oozing or leaking from bite wound >30 mins after bite. Abnormal coagulation without bleeding = mild hemotoxic bite. Worsening pain often present but may be absent	**Worsening Pain (↑ severity / leading edge moves ↑ limb):** *Worsening progressive pain increasing both numerically (e.g. 5/10 → 8/10) and positionally (leading edge moving proximally up the limb).* • **Firm Edema: *below elbow or knee*** • **Blistering:** Absent/minimal; small blisters at bite (not bleeding)
Moderate **(LOW DOSE)**	**Local S/Sx → Regional S/Sx (beyond bitten limb):** Paresthesia, hyperesthesia, neuropathic pain, piloerection, muscle spasms / fasciculations **extending past the shoulder or hip**; often regional or hemiplegic. **Systemic S/Sx**: Persistent vomiting and/or diarrhea; blurred or double vision, auditory, or other sensory disturbances; diaphoresis. **Nasal voice or diminished voice possible but no slurred or incomprehensible speech or difficulty breathing.**	**Systemic bleeding WITHOUT hematemesis or other internal bleeding**. • *Distant bleeding from bite likely at gums, nose, other mucosa;* • *petechiae/purpura and other local skin signs of bleeding likely on bitten limb.* **NO GI bleeding**; **NO suspicion** for intrabdominal or intracranial/meningeal bleeding. • Local bleeding likely continuing from bite wound • Coagulopathy likely (WBCT+ or other blood work)	• **Worsening pain (moves ↑ limb)** • **Firm edema *passes elbow/knee*;** *does not reach shoulder/hip* • **↑↑ blistering / tissue damage:** *increased number of blisters forming, larger size of blisters/bullae, greater distance of blistering from the bite site (several inches or more from bite), blisters may have blood or serosanguinous fluid inside. Usually confined to less than ½ of bitten limb*
Severe **(HIGH DOSE)**	**Bilateral ptosis with progressive neuromuscular paralysis causing difficulty speaking, swallowing, or breathing**; hypersalivation; profuse diaphoresis; incontinence; ***Shock or otherwise unstable patient*** **Excitatory Phase:** Severe agitation and restlessness; Kussmaul respirations (rapid/deep tachypnea); hypoxia from airway obstruction; hyperglycemia; hypertension; severe DKA-like appearance **Decompensatory Phase:** Respiratory failure with hypercapnia +/- hypoxia; Hypotension; Bradycardia; Bradypnea	• **Severe or rapid systemic bleeding**: **WITH HEMATEMESIS, BLOODY STOOLS or** intra-abdominal / intracranial bleeding suspected. *Severe anemia; hemorrhagic shock possible!* • Local bleeding likely continuing from bite wound, *but sometimes local bleeding stops when GI bleeding starts* • Coagulopathy likely (WBCT+ or other blood work) • **Significant systemic signs (abnormal ECG, chest pain, AKI, etc)** • ***Altered mental status, shock, or otherwise unstable patient***	• **Worsening pain (moves ↑ limb)** • **Firm edema: *reaches or passes shoulder/hip*** *(base of limb)* ***OR*** *symptomatic bite to head, neck, or torso* • **Rapid, severe, widespread blistering:** *multiple large bleeding blisters forming along bitten limb / distant from bite site within first hours. May extend beyond ½ of bitten limb, or very severe if not > ½ bitten limb.* • **Significant systemic signs** *(abnormal ECG, chest pain, AKI, etc)* • ***Altered mental status, shock, or otherwise unstable patient***

S/Sx = Signs & Symptoms; SBC = Single Breath Count Test; LOC = Level of Consciousness; WBCT = Whole Blood Clotting Test

DEFINING INITIAL CONTROL BY SYNDROME: CLINICAL ENDPOINTS INDICATING ADEQUATE ANTIVENOM DOSING HAS BEEN ACHIEVED

Figure 4. Defining Initial Control by Syndrome.

Initial Control - NEURO	Initial Control - HEMO	Initial Control - CYTO	Initial Control – SYSTEMIC INSTABILITY
Progressive neurologic deficits **stop worsening and begin to improve**: Vision, speech, swallowing, and respiratory function stabilize or improve **Associated symptoms improve:** Agitation, vomiting, diarrhea, hypersalivation **Vital signs normalize** if previously abnormal **Sensory symptoms improve**: Pain and paresthesias decrease **Bulbar function improves**: Improved ability to cough and swallow (reversal of bulbar weakness)	**Active bleeding resolves within 30–60 minutes of an adequate antivenom dose:** - No ongoing external bleeding or local oozing - No hematemesis or hematochezia - Vital signs stabilize/normalize **Coagulopathy may persist despite control of bleeding:** Laboratory abnormalities may take 6–24+ hours to normalize - *Do NOT redose antivenom solely for abnormal labs in the absence of active bleeding* - ***Redose only if active bleeding recurs or persists*** **Consult a toxicology expert (e.g., DoD advisor) for:** - *Persistent coagulopathy without bleeding* - *Unclear clinical progression*	**Pain starts improving:** - Decrease in pain severity - Distal regression of the leading edge of pain (moves back toward bite site) **Edema progression halts:** - Leading edge of swelling stops advancing proximally - Reduction in edema is not expected acutely (often delayed by days) ***Note - Primary goal for edema is halting progression, not immediate reversal***	**Unstable vitals stabilize** - Signs like profound hypotension, tachycardia, tachypnea, etc should rapidly improve within 30 minutes of correct antivenom dose **Systemic signs and symptoms should improve:** - Chest pain, altered mentation, seizures, hemodynamic instability, etc should rapidly improve within 30 minutes of correct antivenom dose

QUICK GUIDE TO ANTIVENOM ADMINISTRATION

Antivenom dosing, preparation, and administration recommendations vary by product. Coverage, initial dosing, preparation, and administration of antivenoms are included in this CPG. Each antivenom recommended in the CPG has a rapid reference on dosing and key notes needed in the Regional Sections as well as in Appendix H: Antivenom Dosing by Product. Each antivenom also has a detailed product page with dosing, mixing / administration instructions, and additional information within its respective regional section (Appendices B – E).

Note on Antivenom Infusions versus Direct IV/IO Push:

For most first line antivenoms in this CPG, administration using either a) 100, 250, or 500 mL IV bag of isotonic fluids (0.9% NS ideal; Lactated Ringers is acceptable) with 10-minute IV/IO infusion or b) direct IV push is recommended in order to get a full dose of antivenom onboard as quickly as possible and neutralize venom before further damage has occurred.

However, if this is not possible, it is acceptable to dilute antivenom in any size bag of isotonic solution you have available and give over 10 – 30 minutes.

While the amount of antivenom given should not change based upon the patient's size, smaller volumes of isotonic fluids may be indicated (especially in pediatric patients) to avoid volume overload or worsening dependent edema of bitten limb.

ADJUNCT TREATMENTS, SUPPORTIVE CARE, ONGOING MONITORING, AND ADDITIONAL ANTIVENOM DOSES

SUPPORTIVE CARE & ONGOING MANAGEMENT

Provide supportive care and address secondary issues related to the envenomation as follows:

1. Anticipate the need for aggressive airway management with intubation and prolonged ventilation in all patients presenting with neurotoxic envenomation, particularly those who present late with impending respiratory failure or fail to respond to antivenom. Ptosis is an early sign of central neurotoxicity indicating need for antivenom and likely progression to respiratory failure without timely antivenom administration.
    - For any neurotoxic snakebite producing a cholinergic crisis, consider atropine 0.5 mg IV/IO titrated by auscultation to dry up bronchial and oral hypersecretions posing a risk to airway or breathing.

      Repeat original dose every 5 minutes until resolution of crackles, rales, and bronchospasm has been achieved. Pediatric atropine doses should be weight based at a dose of 0.01 mg/kg, up to 0.5 mg.
    - For neurotoxic snakebites in the Middle East, North Africa, and Central Asia without cholinergic crisis, but causing ptosis and respiratory muscle weakness, consider administering, in addition to antivenom, a trial dose of 0.5 mg atropine followed by 1.0 mg neostigmine IV/IO to temporarily reverse neuromuscular weakness and delay the need for intubation. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to a maximum of 0.25 mg atropine with 0.5 mg neostigmine.[54,74–77]

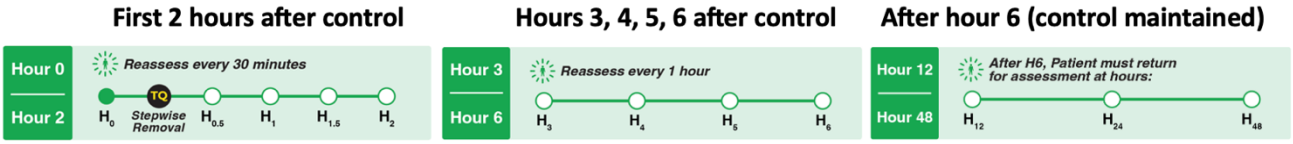
      Not all patients will respond, but those who do will show temporary improvement (reversal of ptosis, increased respiratory muscle strength, etc.). If no response to neostigmine, do not readminister. If positive response is achieved, repeat every 1 - 4 hours as needed (maximum dose in 24 hours = 10 mg adults / 5 mg pediatric) until antivenom has definitively reversed the paralysis.
2. For hemotoxic envenomations, all internal and external active bleeding should cease within 30 – 60 minutes of antivenom administration once the appropriate dose has been given. Packed red blood cell or whole blood transfusion can be considered if the patient is in hemorrhagic shock.[17,69,70, 78-82] Platelets, fresh frozen plasma, cryoprecipitate, TXA, and ***other agents are not effective in these cases*** due to the mechanism of the venoms.
3. Ketamine and fentanyl are preferable for analgesia. ***Histamine release from morphine may mimic signs of an allergic reaction or worsen hypotension.*** Acetaminophen may be used but ***NSAIDs are contraindicated*.**
4. It is important to keep the limb significantly elevated (> 60º is ideal) whenever possible to limit dependent edema and swelling.
5. **DO NOT** routinely de-roof or aspirate blisters, bullae, or blebs unless they are causing significant discomfort or uncontrolled rupture appears imminent. If abscess is suspected, treat according to existing protocols for abscess management.
6. Avoid fasciotomy for snakebites unless absolutely necessary. Compartment syndrome is rare in snakebites, and evidence suggests that patients treated with antivenom alone – without fasciotomy – generally experience better outcomes, including shorter recovery times and reduced long-term morbidity.[83–86] Appropriate use of antivenom should typically resolve elevated intracompartmental pressures caused by envenomation. However, in deployed settings, constraints such as limited antivenom supplies due to delayed procurement or depletion during evacuation may complicate management. **In such cases (prior to performing a fasciotomy), consult a DoD ADVISOR toxicologist to guide decision-making and ensure the best possible outcomes.**
7. **DO NOT routinely administer PROPHYLACTIC ANTIBIOTICS unless signs and symptoms of an infection are present.** Direct infections are rare from most snakebites when prompt, appropriate treatment is given (washing with soap and water).[54] Bites from certain snakes (Asian cobras) have higher rates of infection.

8. **ADMINISTER ANTIBIOTICS FOR SUSPECTED INFECTIONS**, which may be common in local nationals with late-presenting bites who arrive with significant secondary infections due to unsanitary traditional treatments, poor hygiene conditions + widespread tissue compromise.

ONGOING MONITORING & NEED FOR ADDITIONAL ANTIVENOM

1. Monitor the patient closely for signs of progression every 30 minutes in the initial hours of treatment until initial control of symptoms has been achieved (see Defining Initial Control by Syndrome). Detailed intervals for assessment and treatment are included in the new ACLS-style NEURO, HEMO/CYTO, and Asymptomatic algorithms.
2. After initial control, reassess for signs and symptoms of NEURO and HEMO/CYTO syndromes according to the appropriate Control Algorithm in Appendix A.

Figure 5. Timeline of Assessments After Control



3. In the new treatment protocols, providers are instructed to contact DoD ADVISOR to discuss need for additional antivenom after the equivalent of TWO high doses or FOUR low doses have been given to patient (a high dose for most recommended products is defined as ~10 vials and a low dose is ~5 vials**, meaning that providers are strongly advised to seek toxicology consult if considering more than 20 vials)**.

   This recommendation exists for several reasons:

   a. Most products recommended in the CPGs are high potency and rarely require more than 20 vials equivalent.

   b. In some cases, providers may not realize that control has been achieved (e.g. inappropriately re-dosing for persistent laboratory coagulopathy without clinical bleeding). In others, there may be a need to switch to an alternative 2nd line antivenom or the patient is an exceptional case with very large amounts of venom injected requiring higher than usual antivenom dosing (e.g. multiple bites, very large snake that bit and held on, etc.).

4. **Persistent coagulopathy without bleeding:** If coagulopathy persists (without bleeding) 24 hours after antivenom was given, contact DoD ADVISOR toxicologist to discuss need for additional antivenom.
5. Continuous monitoring for recurrence of symptoms must be performed. Occasionally, pockets of venom can be trapped in swollen tissue compartments and escape into the bloodstream once circulation has improved. This is called recurrence and is most common within the first 6 - 24 hours after a severe bite with extensive swelling and blistering.[78,87–93] Recurrence is addressed in the symptomatic NEURO & HEMO/CYTO and Control algorithms.

   a. Continuous clinical monitoring includes hourly checks of vital signs, urine output, and detailed assessment for new or worsening signs of neurotoxic, hemotoxic, or cytotoxic envenomation.

   b. Serial laboratory studies including CBC, CMP, PT/PTT/INR, CK, fibrinogen levels (or WBCT if no advanced testing available) may be repeated every 2 hours while signs of envenomation persist.

   c. If indications of recurrence are detected, **treat according to the recurrence pathways** in the symptomatic NEURO and HEMO/CYTO algorithms.

   d. When control has been achieved again, return to the Control Algorithm and restart the 48-hour timer to disposition decision. Control must be maintained for a full 48h without recurrence to discharge a previously symptomatic snakebite. Contact DoD ADVISOR toxicologist for advice in these cases.

DISCHARGE RECOMMENDATIONS: CONTROL & ASYMPTOMATIC ALGORITHMS

1. If patients were ever symptomatic, they should be held for at least 48 hours after resolution of all signs and symptoms, and the following steps should be completed prior to discharge (Control Algorithm):
    a. Repeat blood tests before releasing the patient to ensure resolution of coagulopathy.
    b. Administer a booster dose of tetanus toxoid if needed.
    c. Patients should be instructed to return if any new or worrying signs or symptoms develop.
    d. **Patients with significant hemotoxic envenomations require 2 weeks of bleeding precautions and serial labs showing normalization before return to duty!**
    e. If patient has polyphasic recurrence, restart treatment algorithm and timeline to discharge.
2. Serum sickness is characterized by flu-like symptoms ± rash that typically develops between 1 - 3 weeks after antivenom administration. It is rare with highly purified modern antivenoms but may occur more frequently with some of the second and third line antivenoms listed in this CPG.[94–97] Serum sickness may be uncomfortable but is not dangerous. Management is either symptomatic, or, in the case of significant discomfort, can be treated with oral antihistamines and/or oral steroids if needed.[94,95,97–99]
3. If patients were asymptomatic for 6 hours, they can leave the clinic but should remain within 1 hour distance and must return every 6 hours for reassessment until hour 48 or snake ID confirmed as non-venomous by expert as detailed in the asymptomatic algorithm. Symptoms usually begin 6 hours after bite but may have delayed onset on the order of days.

    Refer to the Asymptomatic Algorithm for detailed assessment intervals and disposition guidance.

ADVERSE REACTIONS TO ANTIVENOM

PRETREATMENT WITH EPINEPHRINE TO PREVENT EARLY REACTIONS

Epinephrine is the only prophylactic treatment (pretreatment) that has been shown to effectively reduce the incidence of early adverse reactions (EARs) such as anaphylaxis.[60,98,133–136] See Antivenom Reactions Algorithm.

1. ***DO NOT pretreat with steroids or antihistamines, as they not only have no benefit prior to a reaction but may reduce the efficacy of epinephrine as a pretreatment for EARs.[134,273]***
2. ***DO NOT administer test doses of antivenom to check for hypersensitivity.[60–63]***

Relative contraindications to epinephrine pretreatment include age > 70, hypertension, ischemic heart disease, history of stroke, suspected or confirmed intracranial hemorrhage. No absolute contraindications.

1. Pretreatment with epinephrine prior to antivenom administration is not indicated by default for all antivenoms, and is recommended only under the following circumstances:
    a. Unstable snakebite patients with signs of shock.
    b. Known history of atopy (asthma, eczema, etc.), equine hypersensitivity, or severe reactions to antivenom in the past.
    c. Use of certain second or third line antivenom due to the high rate of serious EARs associated with these products.
2. Standard epinephrine pretreatment protocol:
    a. Adult dose is 0.25 mg of 1:1000 epinephrine given by IM injection several minutes prior to antivenom administration.
    b. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.[60,134,135,137,138]

c. Alternatively, consider establishing two intravenous catheters (one for the antivenom and one for epinephrine) and preparing an epinephrine infusion that can be immediately initiated in the event an allergic reaction to the antivenom occurs.

ALPHA-GAL SYNDROME AND INCREASED RISK OF EARLY ADVERSE REACTIONS

Practice implication: Alpha-gal Syndrome is not a contraindication to antivenom when envenomation is life or limb threatening but warrants pre-treatment with epinephrine and up-tiering of risk management (infusion strategy, ICU capable monitoring, product selection). There are NO absolute contraindications to antivenom for a patient with a significant symptomatic envenomation).

Early but compelling clinical evidence suggests that patients with Alpha-Gal syndrome (a mammalian meat allergy) may experience higher rates of reaction in response to antivenoms due to conservation of the alpha-gal epitope in mammalian antibody proteins. Some early studies from the United States indicated higher rates of reactions with with the $F(ab')^2$ Anavip versus CroFab which is a F(ab), but other studies have shown that patients who reacted to CroFab tolerated Anavip.[274–276] Regardless, pretreatment should be considered for patients with elevated risk factors (patient from high prevalence area, medical Hx suspicious for alpha-gal, etc) and in patients with known or suspected alpha-gal syndrome. If both CroFab and Anavip are available for a CONUS bite with a known history or high risk of alpha-gal, it may be worth discussing CroFab as first line if available due to possible lower risk of reaction with a medical toxicologist. If a patient had a reaction to CroFab or Anavip CONUS, it may be worth discussing switching to the alternative product with a medical toxicologist.

While additional research is needed, the key points are as follows:

1. In US servicemembers and other patients with a known or suspected history of alpha-gal syndrome, pretreatment with 1:1000 epinephrine prior to antivenom may be advisable due to early evidence indicating higher incidence of EARs including anaphylaxis. Pretreatment with epinephrine has not been proven to reduce the incidence of these reactions, but has strong evidence base to support its use in typical EARs and the MAST cell stabilization resulting from epinephrine may also benefit these patients.
2. If a patient with known or suspected alpha-gal syndrome has a reaction to one antivenom and a second line alternative exists, it may be appropriate to try a different product if additional doses are needed.
3. In all cases, it is advisable to contact DoD advisor line and consult a toxicologist (or contact poison control if CONUS) in cases where an alpha-gal sensitivity is known or suspected.
4. ***In all cases, antivenom should not be delayed for patients suffering from instability or other possible threats to life or limb due to envenomation. Be prepared to treat the reaction if it occurs but do not delay antivenom for sick patients.***

ADVERSE REACTIONS TO ANTIVENOM: TREATMENT

TREATMENT OF ADVERSE REACTIONS
PRINCIPLES OF EARLY ADVERSE REACTION (EAR) MANAGEMENT

Most EARs to antivenom are mild and limited to either skin and mucosal signs, gastrointestinal signs, or both. In some cases, patients may experience a severe reaction (anaphylaxis), this can be life-threatening and should be treated aggressively. Refer to the Antivenom Reactions Algorithm for a stepwise approach to management of mild, moderate, and severe reactions.

When a reaction has occurred but is mild, simply increasing the antivenom's dilution (for example, moving the remaining dose from a 50 mL bag of NS into 100 mL of NS), increase the duration of infusion (for example, from 15 mins to 30 mins) and treating the skin/mucosal or GI signs with antihistamines or antiemetics may resolve the problem. With mild reactions, start by either increasing the dilution of the antivenom (add more fluid to the antivenom infusion), decreasing the rate of infusion, or both. When a severe reaction such as anaphylaxis occurs, pause the antivenom infusion, treat the reaction, then resume it using twice the volume of dilution and half the rate of administration. In most cases, epinephrine given to treat a

severe reaction will also reduce the risk of subsequent reactions for up to 48 hours. Always contact DoD ADVISOR if you have questions about reaction management.

***NOTE**: Refer to the detailed Antivenom Reactions Algorithm for guidance on the approach to reactions.*

MILD OR MODERATE REACTION DURING INFUSION

1. Manage mild or moderate reactions (e.g. nausea, vomiting, urticaria, pruritus, chills, fever, etc.) symptomatically as needed with antiemetics, antihistamines, steroids, etc. as shown in the Antivenom Reactions Algorithm.
2. **Consider increasing the volume of dilution of the antivenom and/or slowing the rate of infusion.** You may be able to treat symptomatically with antiemetics, antihistamines, etc. without the need to stop the infusion. If the patient fails to improve to first line medications or appears to be worsening, consider giving a dose of IM epinephrine and then resuming at a slower rate once the symptoms are improving.
3. If the infusion was paused, reassess the patient once the reaction has been controlled; if the antivenom treatment criteria for cytotoxic, hemotoxic, or neurotoxic syndromes have not resolved completely then resume the infusion at a slower rate over 30 minutes.
4. If giving via push, dilute the remaining dose of antivenom in a 100 - 500 mL bag of normal saline and give as 30-minute infusion.

SEVERE REACTION (ANAPHYLAXIS) DURING INFUSION

1. Pause the infusion and treat according to the anaphylaxis treatment protocol and the Antivenom Reactions Algorithm.
2. Reassess the patient once the reaction has been controlled; if the antivenom treatment criteria for cytotoxic, hemotoxic, or neurotoxic syndromes have not resolved completely then resume the infusion at a slower rate or larger volume of fluid (e.g., if 250 bag, dilute in 500 cc) over 30 minutes.
3. If giving via push, dilute the remaining dose of antivenom in a 100-250 mL bag of normal saline and give as 30-minute infusion.
4. If the reaction occurs, stop the infusion, and consult a physician expert via telemedicine to discuss next steps for management.

ANAPHYLAXIS TREATMENT PROTOCOL

NOTE**: **Intubate for airway edema not rapidly responsive to epinephrine.

If anaphylaxis occurs after antivenom administration, treat according to the following protocol (also refer to the Antivenom Reactions Algorithm):

1. **First line treatment of anaphylaxis is rapid administration of 1:1000 epinephrine** (initial adult dose = 0.5 mg IM (0.01 mg/kg IM in pediatric patients) in the lateral thigh for rapid absorption). Epinephrine can be repeated as needed until the patient has stabilized and/or an intravenous or intraosseous infusion administered as per standard protocols if the patient fails to respond to IM doses.

   Epinephrine should always be given prior to antihistamines or steroids to counter the immediate life-threats of bronchospasm and vasodilation.

2. After epinephrine has been given:
   a. Give methylprednisolone 125 mg IV (2 mg/kg IV in pediatric patients).
   b. Give diphenhydramine 50 mg IV (1-2 mg/kg IV in pediatric patients).
   c. Consider adding an H2 antihistamine such as famotidine.

If anaphylaxis occurs during administration of antivenom, stop the antivenom administration to treat the reaction, then resume the antivenom administration as described below. [15,61,95,99,128,129,140–146]

LATE REACTIONS TO ANTIVENOM (SERUM SICKNESS)

1. Serum sickness is characterized by flu-like symptoms ± rash that typically develops between 1-3 weeks after antivenom administration. Serum sickness may be uncomfortable, but it is not dangerous.
2. Management is either symptomatic with antihistamines, acetaminophen, or with a course of oral steroids for patients who are in significant discomfort.[94,95,97–99]

SPECIAL SITUATIONS

IF ANTIVENOM IS UNAVAILABLE

1. Antivenom is the gold standard of care for symptomatic snake envenomations. Early treatment is the best strategy to prevent death, amputation, or other serious disability. Management of snake envenomations when antivenom is not available should be directed at getting the patient to the antivenom (or vice versa) as quickly as possible to prevent irreversible damage to organs and tissues.
2. Mission planning before deployment should include research and procurement of the appropriate regionally specific antivenom(s) recommended in this CPG for your area of operation. If currently deployed without antivenom, efforts to acquire the appropriate antivenom(s) recommended in this CPG for your area of operations should be initiated through proper channels as fake or low-quality antivenoms are frequently found in local pharmacies throughout Africa and elsewhere in the developing world.
3. For specific management until antivenom can be obtained, follow the checklist and skip the steps related to antivenom administration until it has been obtained.

Refer to Supportive Care measures for specific recommendations. Without antivenom, prognosis is poor. Expect high mortality, permanent disability, and supportive care for weeks or longer.

MILITARY WORKING DOGS / MULTIPURPOSE CANINES

All antivenoms can be administered to military working dogs (MWD) and multipurpose canines according to the treatment criteria and initial doses listed in this CPG; other management should be based on the Arachnid and Snake Envenomation, MWD CPG.

LATE PRESENTATIONS & TREATMENT DELAYS

There is no defined time limit to antivenom therapy for a symptomatic snakebite. Early antivenom within the first minutes or hours after a bite is the best means of preventing morbidity or mortality, but antivenom remains effective at resolving reversible issues like coagulopathy and preventing further irreversible tissue damage even in patients who present many hours or days after the snakebite.[56,69,78,146,147]

OUTDATED INTERVENTIONS THAT SHOULD NOT BE PERFORMED

1. DO NOT cut, suck, electrocute, burn, or use chemicals on the envenomation site.
2. **DO NOT apply constricting bandages, tourniquets, or other circulation-reducing intervention!**
   TQ *If patient arrives with tourniquet, refer to Tourniquet Algorithm.*
3. DO NOT use venom extractors or other commercial snakebite first aid kits.[148–152]

4. DO NOT administer test doses of antivenom to check for hypersensitivity as these are ineffective and waste both time and antivenom.[60–63]
5. DO NOT administer antihistamines or steroids as prophylactic pretreatment for prevention of anaphylaxis or other early adverse reactions (EARs) to antivenom as neither is effective as a premedication.[133,134]

OCULAR ENVENOMATION BY SPITTING COBRAS (VENOM OPTHALMIA)

Spitting cobras have modified fangs that allow them to spray venom into the eyes of a predator or perceived threat.[153–155] The snakes aim at the glint of sunlight reflecting off of the target's eyes and the venom spray widens like buckshot. The venom is harmless unless it enters the eyes (causing instantaneous burning, lacrimation, blurred vision, etc.) or the bloodstream by injection (such as a bite), through open wounds on the skin or inside of the mouth, or by ingestion (such as drinking a glass of venom with an ulcer). If a significant amount of venom enters the bloodstream through an open wound and produces typical symptoms of a snakebite, it is treated with antivenom like any other envenomation. For ocular exposure alone without signs of systemic envenomation, antivenom is not indicated and the management is like any ocular chemical exposure with copious irrigation. Spitting cobras can also deliver a venomous bite, so it is important to rule out an actual snakebite in patients who have encountered one of these snakes.

SIGNS AND SYMPTOMS

Immediate signs and symptoms of venom ophthalmia include intense local pain, swelling and/or spasms of the eyelid, lacrimation, and leukorrhea.[156] The primary concern is corneal epithelial injury which can lead to blindness by secondary infection or scarring if not treated correctly.[7,25,54,156–158] Treatment of venom ophthalmia is relatively simple and similar to managing a patient who has been splashed in the eyes with a harmful chemical solution.

FIRST AID

Confirm that the patient did not experience a snakebite in addition to the ophthalmia. Immediately irrigate the eye with copious quantities of water, normal saline, or a bland fluid such as milk if nothing else is available. Remove clothing and decontaminate the patient from head to toe with soap and water to prevent second re-exposure to dried venom.[54]

CLINICAL MANAGEMENT

Apply topical anesthetic eye drops (tetracaine) to facilitate thorough irrigation and examination of the affected eyes. Irrigate the eyes thoroughly using water or normal saline for ≥ 15 minutes.[156]

Fluorescein stain and examination using a slit lamp or ophthalmoscope for corneal injury. If present, treat with antimicrobial eye drops (such as ofloxacin or moxifloxacin) or ointments and mydriatics. Reassess daily with slit lamp or ophthalmoscope examination. If absent, consider benefits vs risks of antimicrobial eye drops.

ADDITIONAL TREATMENTS TO CONSIDER

Topical eye drops containing either epinephrine (1:1000) or phenylephrine (10%) are reported to immediately relieve the burning sensation produced by the venom.[54,156]

CONTRAINDICATED TREATMENTS

Antivenom (topical or systemic) **IS NOT** indicated for patients with ocular exposure to snake venom.[54,156,159] Topical steroids are contraindicated for these patients.

RISKS OF NON-RECOMMENDED ANTIVENOMS & LOCAL PROCUREMENT

Providers should adhere to the 29 antivenoms and dosing recommended in this CPG for use by military personnel, which have been evaluated by a multidisciplinary, mixed panel of leading civilian and military subject matter experts for safety, efficacy, and suitability for use in the unique environment of operational and austere medicine.

Note: If unable to source the recommended antivenoms and considering use of a non-recommended antivenom in an emergency context (or in the case of any general questions regarding antivenom use), ***contact the DoD ADVISOR line (+1 (833) 238-7756 (1-833-ADVSRLN) DSN: (312) 429-9089) and request toxicology consult ASAP.*** *Many non-recommended products carry significant risks and toxicology consult is critical to avoiding preventable death or disability.*

The global landscape of antivenoms is complex, fragmented, and characterized by a wide range of safety, efficacy, tolerability, and clinical evidence across the more than 110 distinct antivenoms currently manufactured worldwide.[264] This is further complicated by the logistical and ethical barriers which make it extraordinarily difficult to conduct randomized clinical trials and nearly impossible to do so with placebo control, the lack of universal definitions of severity (making it difficult to interpret the context of efficacy when studies are performed), and many other challenges.[265] The end result is chaotic, poorly controlled, and difficult to interpret: some products are widely relied upon by local clinicians and experts despite the lack of any formal trials; others are marketed as safe and effective based solely off of preclinical "test tube" studies conducted despite well-documented translational gaps between preclinical findings and real world effectiveness; some local formulations may enter the market without any studies whatsoever.[266,267] Unfortunately, this has led to widespread confusion, frequent misinformation, and sensationalistic media reports which inaccurately characterize effective products as ineffective (despite published clinical evidence demonstrating otherwise) or ineffective and potentially dangerous products as effective (despite either a lack of any clinical data or the existence of initial data indicating inefficacy and potentially dangerous dose-dependent toxicity).[268–271]

RISKS OF USING NON-RECOMMENDED ANTIVENOMS & PROCUREMENT OUTSIDE OF RECOMMENDED CHANNELS

Figure 6. Risks of Using Non-Recommended Antivenoms

Category	Issues & Recommendations	Specific Risks
Grey market or local procurement *Antivenom (**AV**) acquired outside DoD procurement catalogue or manufacturer-recommended distributors.*	**Issue:** Increased mortality/morbidity due to 1) counterfeit products or 2) authentic products that have been improperly stored or handled, which may reduce efficacy or increase adverse reactions. **Recommendation:** Only procure recommended AV through DoD procurement catalogue or manufacturer-recommended distributors. *Manufacturers often provide a list of official distributors when asked.*	**Counterfeit products** are well documented in Asian and African markets, many of them contain NO ANTIBODIES and unknown fillers. These products have no efficacy and may provoke dangerous reactions. **Improper storage & handling** of authentic products purchased on grey markets can reduce efficacy or increase reactions, leading to potential for increased mortality. Manufacturers generally maintain oversight of storage and handling through their distributors to prevent quality issues when products enter the market; purchasing outside these channels introduces significant unknowns.
Safety and efficacy *Only recommended AVs in the CPG have been validated by SMEs as sufficiently safe & effective for inclusion.*	Many non-recommended AVs lack sufficient peer-reviewed evidence, unpublished but high quality data, validated field experience, or SME consensus for inclusion. **Recommendation:** Recommended AVs have been identified as suitable or necessary for inclusion based on validated efficacy and safety across each of these domains.	**Safety and efficacy** of all recommended antivenoms included the CPG was validated by an expert panel through a combination of published clinical and preclinical evidence, unpublished data, and SME experience using the products. Many non-recommended AVs were excluded due to 1) lack of adequate evidence or experience demonstrating efficacy, 2) alleged efficacy based solely on preclinical studies, often contradicted by anecdotal reports from field providers indicating possible low efficacy or high risk, 3) availability of an equivalent product demonstrating superior safety and efficacy. A small number of products were included with high efficacy but high rates of reaction because they are the only effective option available for a given coverage gap; **in these cases, premedication is recommended in the product pages**
Suitability in austere & operational settings *Purity, stability without refrigeration at high or low temperatures, broad or narrow coverage enabling treatment without snake ID.*	**Recommendation:** All products have been assessed for suitability in austere and operational medicine settings. Refer to the **Appendix H** for dosing, indications, coverage, special considerations (such as need for pretreatment) for all recommended antivenoms listed in the CPG.	Whenever possible, freeze-dried, field-stable, broad-spectrum polyvalents were recommended that enable providers to carry in the field for extended duration without temperature concerns and to treat without snake ID. These qualities are provided in detail on the product pages, found in the regional sections for each CCMD. The **Rapid AV Table** summarizes key info for each AV recommended in the CPGs.

PERFORMANCE IMPROVEMENT (PI) MONITORING

POPULATION OF INTEREST

All patients bitten by snakes.

INTENT (EXPECTED OUTCOMES)

1. All patients bitten by a snake will be managed according to the steps outlined in the Universal Approach to Snakebite Assessment, Diagnosis, and Treatment section, with an emphasis on the clinical syndrome of envenomation, and not on the identity of the snake species.
2. When a broad-spectrum antivenom does not exist for a given syndrome in a given area, the regional algorithms will be used to determine the most appropriate antivenom therapy.

3. Appropriate antivenom will be given at the earliest possible role of care, including in the pre-hospital setting if available, with appropriate documentation of dosage, preparation, administration procedures, and qualified performing provider.
4. Rapid patient assessment and frequent reassessment will be documented.
5. Tetanus prophylaxis will be given to all patients.
6. When antivenom is unavailable, patient will be evacuated urgently to capable role of care, and lack of capability and mitigation strategy is documented.
7. Fasciotomy for suspected compartment syndrome will be avoided unless absolutely necessary (delayed evacuation or depletion of antivenom supply), and DoW ADVISOR Toxicology consultation will be performed and documented prior to fasciotomy.
8. Documented DoW ADVISOR Toxicology telemedicine consult will be performed for any questions, concerns, or unusual manifestations that arise.

PERFORMANCE/ADHERENCE METRICS

1. Patients with clinical syndromes of envenomation who received administration of antivenom at the earliest available role of care.
2. Documentation of antivenom dosage, preparation, administration procedures, and qualified performing provider.
3. Rapid assessment and frequent reassessment is performed, with attention to clinical signs and symptoms of envenomation.
4. Patients urgently evacuated to capable role of care when antivenom unavailable.
5. Tetanus prophylaxis administered.
6. Elevated compartment pressures are managed with repeated administration of antivenom, and fasciotomy is avoided if possible
7. DoD ADVISOR Toxicology telemedicine consultation performed for all questions, concerns, or unusual manifestations that arise.

DATA SOURCES

- Patient Record
- Department of Defense Trauma Registry (DoDTR)

SYSTEM REPORTING & FREQUENCY

The above constitutes the minimum criteria for PI monitoring of this CPG. System reporting will be performed annually; additional PI monitoring and system reporting may be performed as needed. The system review and data analysis will be performed by the Joint Trauma System (JTS) Chief and the JTS PI Branch.

RESPONSIBILITIES

It is the trauma team leader's responsibility to ensure familiarity, appropriate compliance and PI monitoring at the local level with this CPG.

REGIONALLY SPECIFIC SNAKEBITE TREATMENT SECTIONS

There are several different antivenoms included in this CPG for snakebite treatment in African Command (AFRICOM), Central Command (CENTCOM), Indonesia-Pacific Command (INDOPACOM), European Command (EUCOM), Northern Command (NORTHCOM), and Southern Command (SOUTHCOM). The coverage, initial dosing, preparation, and administration vary between products and details for each of them are included. Simplified algorithms for selecting and dosing each antivenom are also included in each regional section below.

Whenever possible, broad-spectrum, field-stable antivenoms are recommended to enable syndromic diagnosis and treatment at the point of injury without the need to identify the species responsible for the bite. Citations of the relevant literature on safety, efficacy, and dosing for each product are provided in the references section.

Determine the appropriate first line antivenom for your area of operations prior to deployment using this section, then refer back to the Universal Approach to Snakebite Assessment, Diagnosis, and Treatment earlier in the document for detailed instructions and a stepwise approach to snakebite management throughout the course of care. Abbreviated antivenom guidelines for each regional combatant command are included below.

CATEGORIZATION OF MEDICALLY SIGNIFICANT SNAKE SPECIES

The World Health Organization (WHO) classifies the risk posed by various venomous snakes by designating each species as either Category 1 or Category 2 as described below. WHO guidelines state that the "species listed in Category 1 within a country, territory or area should be considered as being of highest priority for antivenom production on the basis that available knowledge implicates them as being responsible for the greater burden in that particular setting." [160]

WHO Category 1: Venomous Snakes of Highest Medical Importance

Defined as "highly venomous snakes which are common or widespread and cause numerous snakebites, resulting in high levels of morbidity, disability or mortality."

WHO Category 2: Venomous Snakes of Secondary Medical Importance

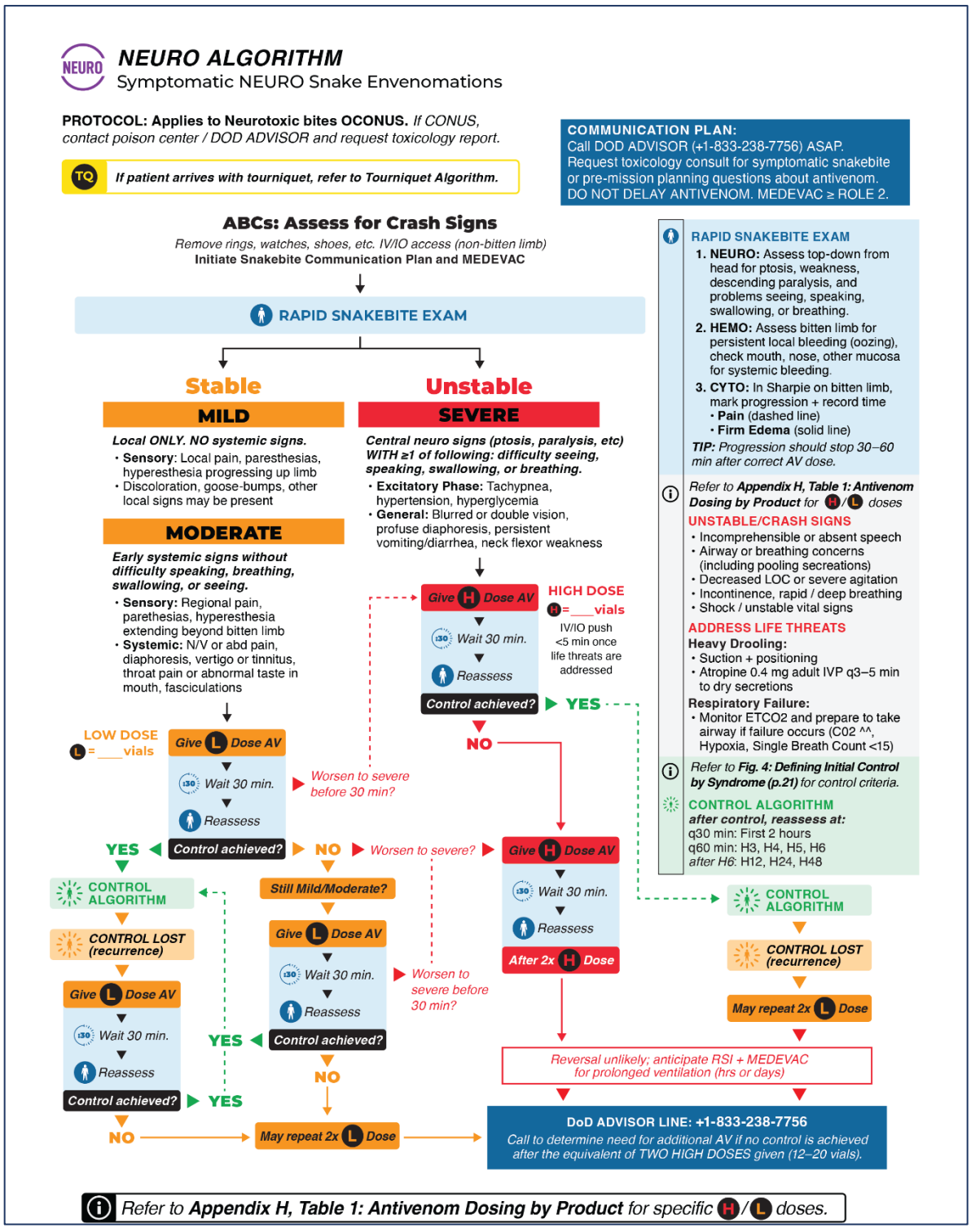
Defined as "highly venomous snakes capable of causing morbidity, disability or death, for which exact epidemiological or clinical data may be lacking; and/or which are less frequently implicated (due to their activity cycles, behavior, habitat preferences or occurrence in areas remote to large human populations)."

NOTE: Antivenom Infusion versus Direct Push: *For most first line antivenoms in this CPG, administration using either a) 100, 250, or 500 mL IV bag of isotonic fluids (0.9% NS ideal; Lactated Ringers is acceptable) with 10-minute IV/IO infusion or b) direct IV push is recommended in order to get a full dose of antivenom onboard as quickly as possible and neutralize venom before further damage has occurred. However, if this is not possible you may dilute antivenom in any size bag of isotonic solution and give over 10 – 30 minutes. While the amount of antivenom given should not change based upon the patient's size, smaller volumes of fluids may be indicated in pediatric patient's to avoid volume overload.*

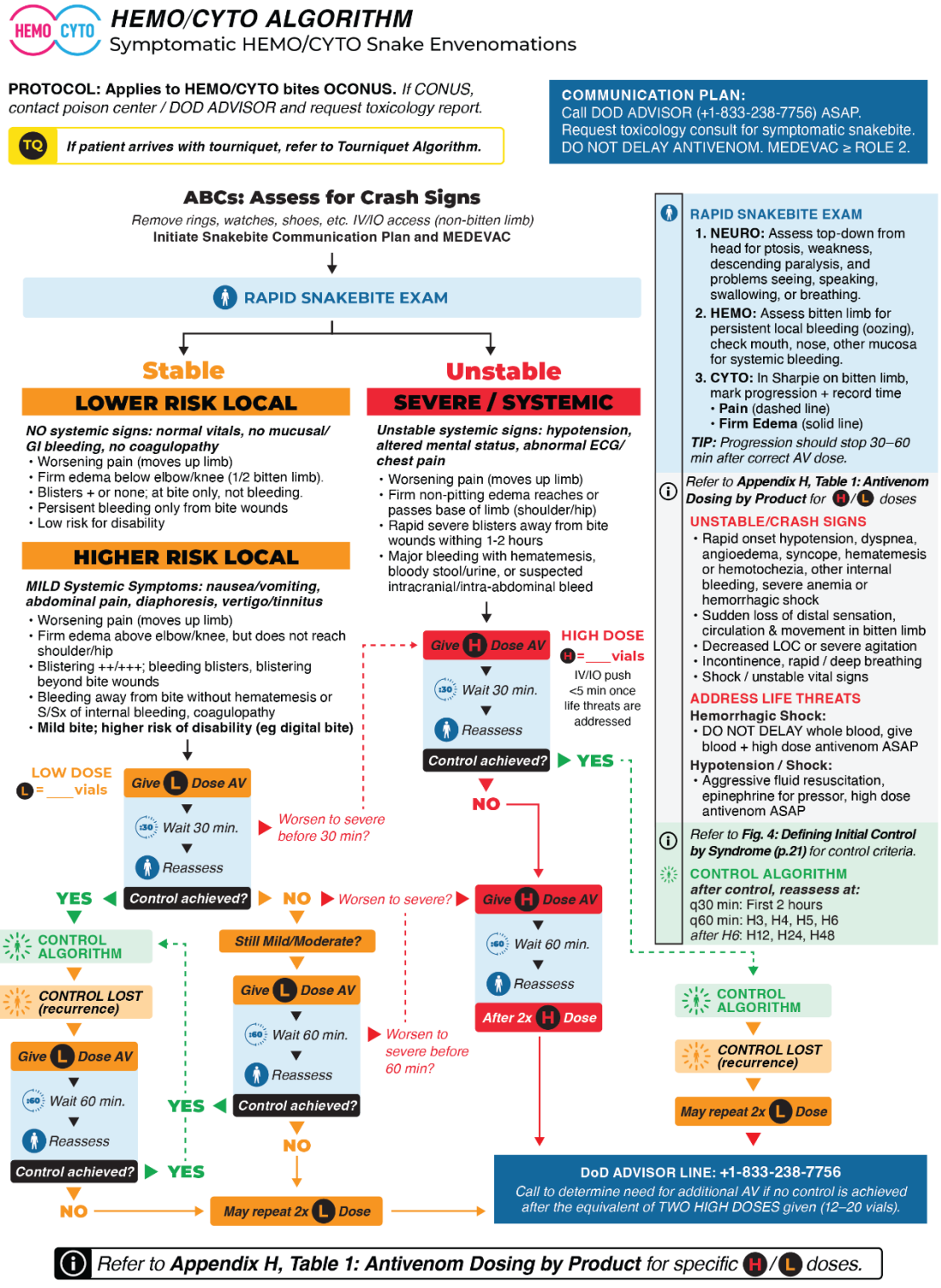
CONTACT: ***For emergency consultations, or additional information about snake bite management or this CPG, call the ADVISOR telemedicine hotline 833-ADVSRLN (833-238-7756) / DSN: 312-429-9089 and select toxicology from the phone menu.***

APPENDIX A: STAT TREATMENT ALGORITHMS

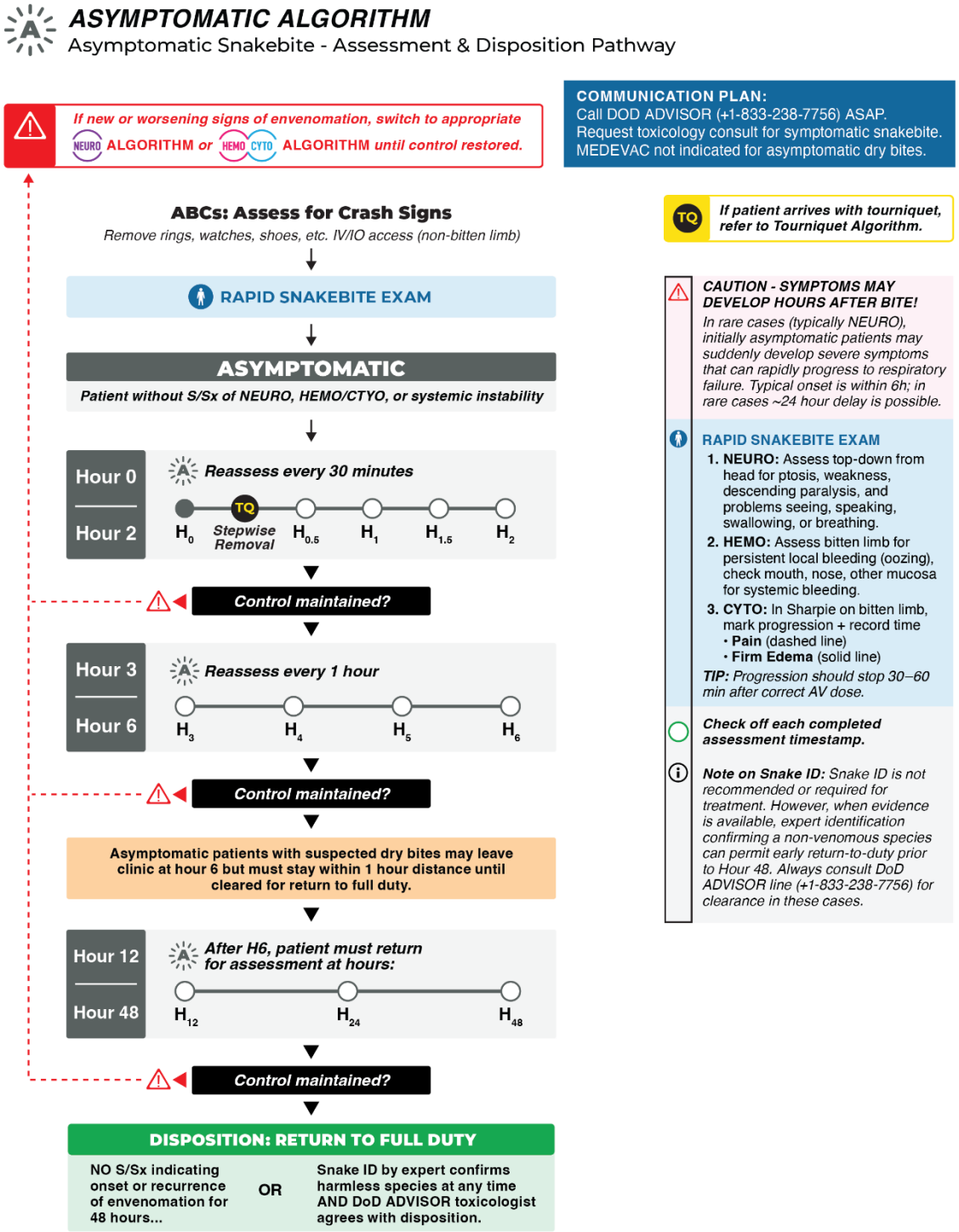
SYMPTOMATIC NEURO ALGORITHM



SYMPTOMATIC HEMO/CYTO ALGORITHM



ASYMPTOMATIC ALGORITHM



CONTROL ALGORITHM

CONTROL ALGORITHM
Control Achieved - Assessment & Disposition Pathway

This algorithm outlines assessment intervals and disposition decisions for **symptomatic snakebite patients** with NEURO, HEMO/CYTO, or systemic instability **once control has been achieved** after the correct dose of antivenom has been given. ***TIP:*** *Snakebites are dynamic, frequent reassessment is used early to catch evolving clinical signs, intervals gradually lengthen as risk reduces.*

COMMUNICATION PLAN:
Call DOD ADVISOR (+1-833-238-7756) ASAP.
Request toxicology consult for symptomatic snakebite.
DO NOT DELAY ANTIVENOM. MEDEVAC ≥ ROLE 2.

If control lost at any time *(S/Sx of envenomation develop) during this algorithm,* ***you have recurrence*** *and must treat using the appopriate* NEURO **ALGORITHM** *or* HEMO CYTO **ALGORITHM** *until control is restored.*

If patient arrives with tourniquet, refer to Tourniquet Algorithm.

REPEAT

RAPID SNAKEBITE EXAM

at the following times:

Hour 0 – Hour 2 — *Reassess every 30 minutes*
H_0 — *Stepwise Removal* — $H_{0.5}$ — H_1 — $H_{1.5}$ — H_2

Control maintained?

Hour 3 – Hour 6 — *Reassess every 1 hour*
H_3 — H_4 — H_5 — H_6

Control maintained?

Symptomatic patients should remain in clinic until asymptomatic (control maintained) for 48 hours without recurrence.

Hour 12 – Hour 48 — *After H6, Patient must return for assessment at hours:*
H_{12} — H_{24} — H_{48}

Control maintained?

DISPOSITION: RETURN TO FULL DUTY

NO S/Sx indicating onset or recurrence of envenomation for 48 hours... **OR** **Snake ID by expert confirms harmless species at any time AND DoD ADVISOR toxicologist agrees with disposition.**

RAPID SNAKEBITE EXAM

1. **NEURO:** Assess top-down from head for ptosis, weakness, descending paralysis, and problems seeing, speaking, swallowing, or breathing.
2. **HEMO:** Assess bitten limb for persistent local bleeding (oozing), check mouth, nose, other mucosa for systemic bleeding.
3. **CYTO:** In Sharpie on bitten limb, mark progression + record time
   - **Pain** (dashed line)
   - **Firm Edema** (solid line)

TIP: *Progression should stop 30–60 min after correct AV dose.*

Check off each completed assessment timestamp.

Control must be maintained for a full 48 hours (or non-venomous ID confirmed) prior to return to full duty. If control is lost, restart the 48h timer to disposition.

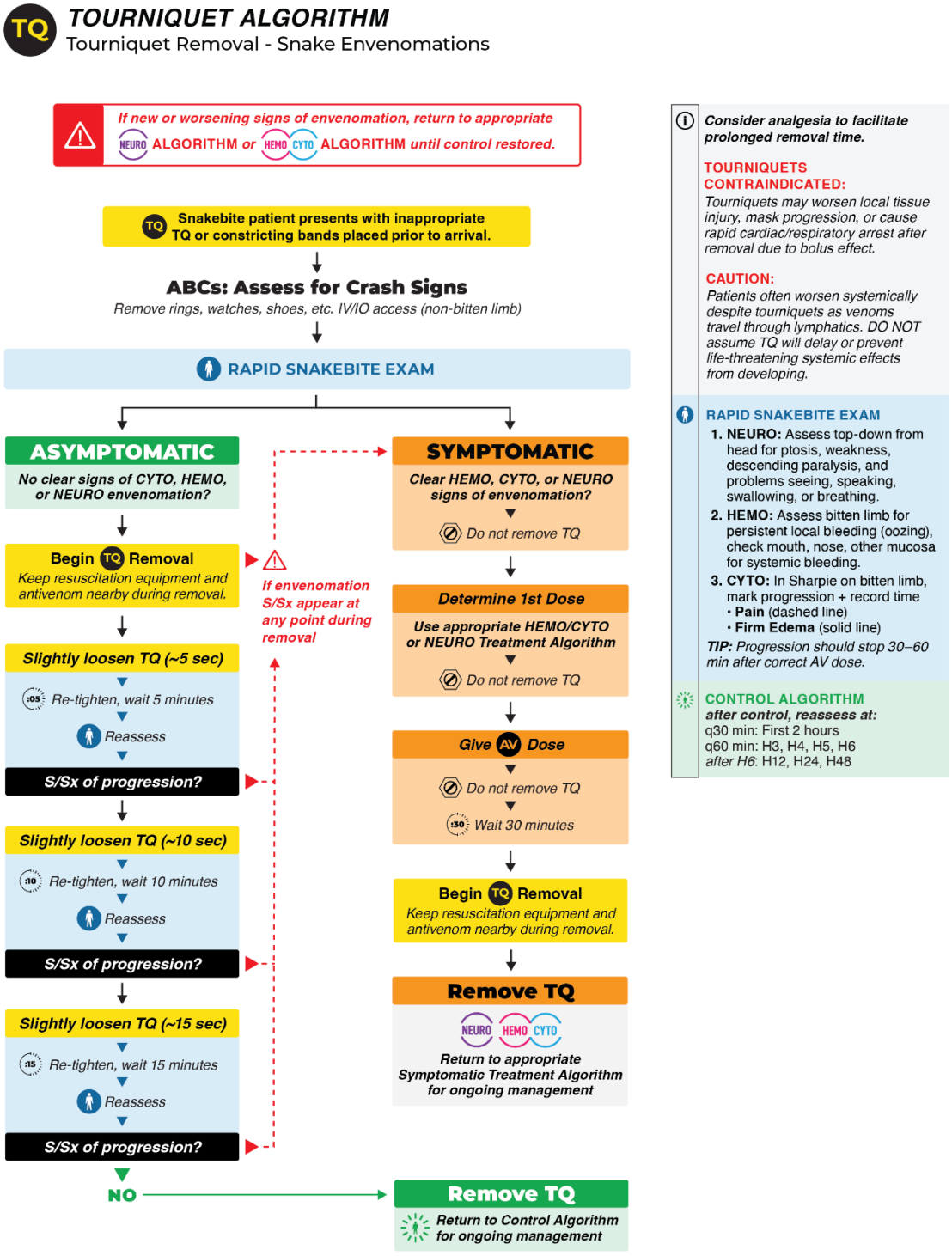
Note on Snake ID: *Snake ID is not recommended or required for treatment. However, when evidence is available, expert identification confirming a non-venomous species can permit early return-to-duty prior to Hour 48. Always consult DoD ADVISOR line (+1-833-238-7756) for clearance in these cases.*

HEMO DISPOSITION:
Patients with coagulopathy and/or systemic bleeding will require 2 weeks of bleeding precautions & serial labs prior to clearance for full return to duty as per unified treatment algorithm (US standards).

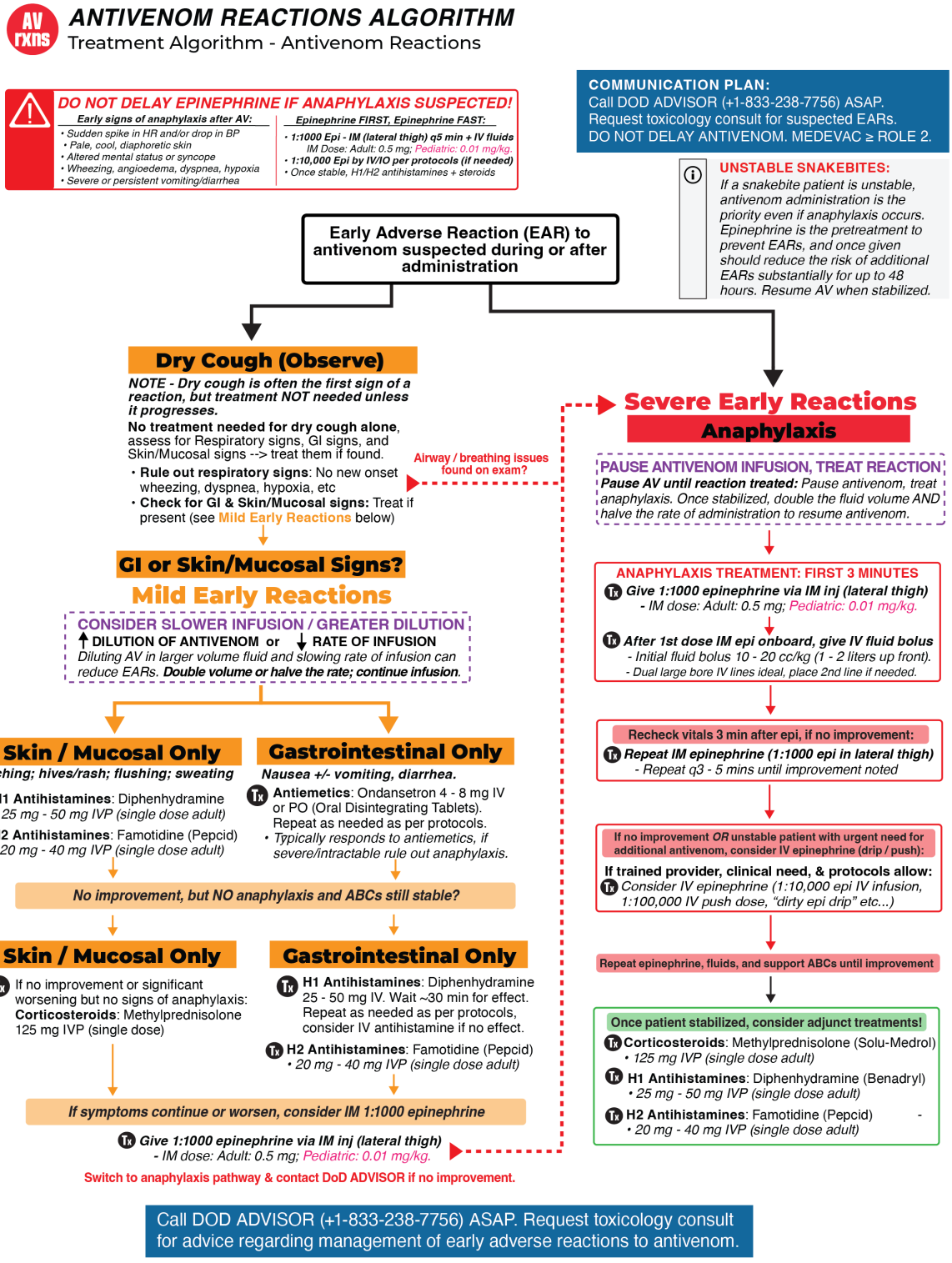
CAUTION - Polyphasic Recurrence and Venom Depot Effect
In some cases, initial control may be lost as additional venom is released from depots in tissue compartments. The risk is highest in the first 6 hours after control but may occur more than 24 hours later. If recurrence occurs, return to the appropriate treatment algorithm and give additional AV doses until control is regained. ***Patient must remain in control for 48h without recurrence prior to disposition.***

Refer to ***Fig. 4 - Defining Initial Control by Syndrome (p. 21)*** *for control criteria by syndrome.*

TOURNIQUET ALGORITHM



ANTIVENOM REACTIONS ALGORITHM



APPENDIX B: AFRICOM TREATMENT GUIDELINES

Safe and effective broad-spectrum, field-stable antivenoms are available for all three syndromes of snake envenomation in this AOR and treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is recommended for AFRICOM due to prolonged evacuation times, high incidence of snakebites, and the high risk of death or permanent disability from many venomous snakes in the AOR if early antivenom treatment is not available.

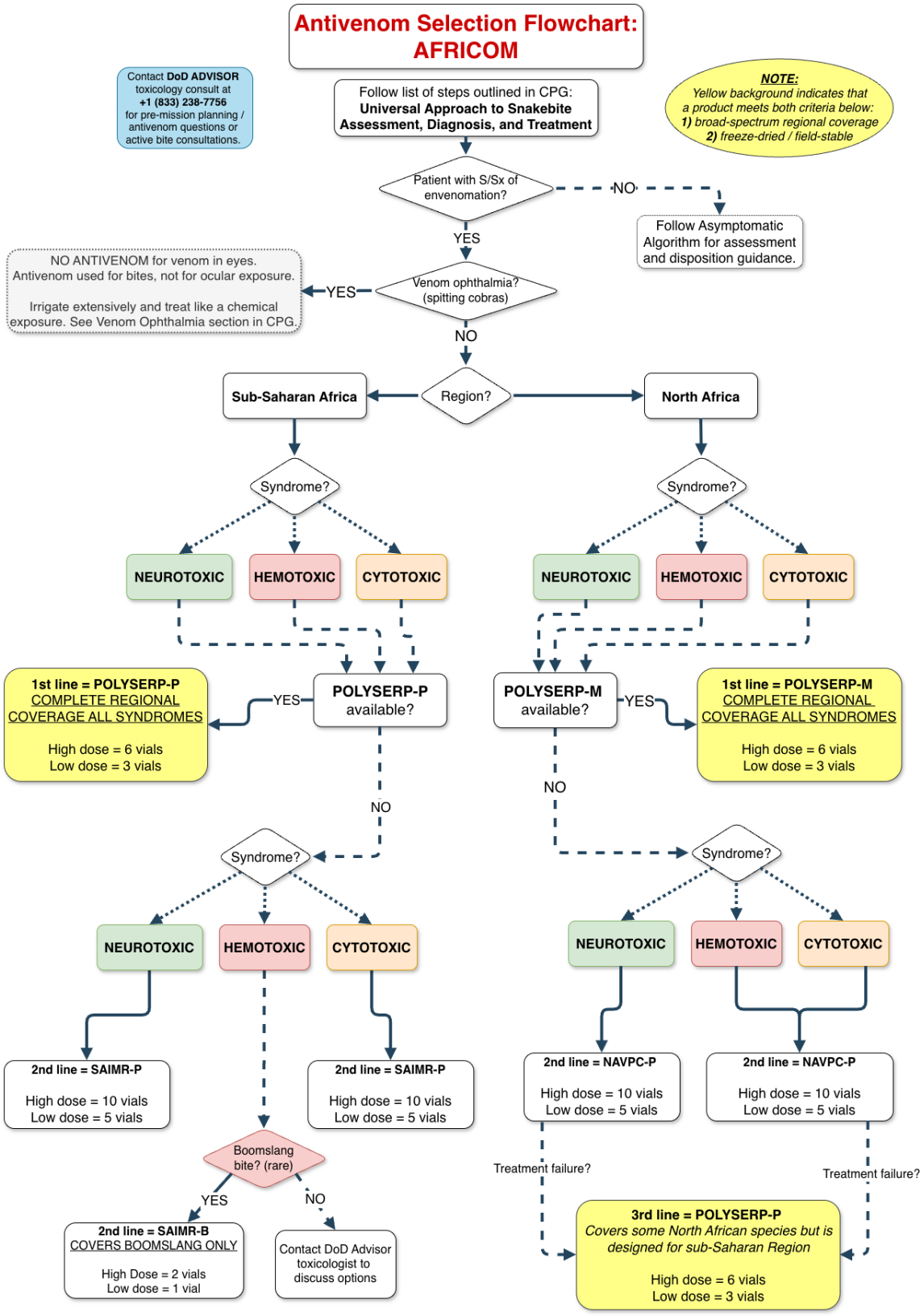
Adverse Reaction Management

- If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed. Refer to management of adverse reactions for specific instructions.
- If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the **antivenom reactions algorithm** listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

AFRICOM - First Line Antivenoms

First Line Antivenoms for AFRICOM	
AFRICOM **1st Line Antivenoms**	**First Line Antivenoms with Regional Coverage against All Three Major Syndromes (Neurotoxic/Hemotoxic/Cytotoxic)** **Sub-Saharan Africa:** Broad-spectrum coverage for all neurotoxic/hemotoxic/cytotoxic snakebite syndromes by known or unknown species - *POLYSERP-P: HIGH DOSE = 6 vials / LOW DOSE = 3 vials* **North Africa:** Broad-spectrum coverage for all neurotoxic/hemotoxic/cytotoxic snakebite syndromes by known or unknown species - *POLYSERP-M: HIGH DOSE = 6 vials / LOW DOSE = 3 vials*
AFRICOM Abbreviations	**POLYSERP-P** = POLYSERP PAN-AFRICA **POLYSERP-M** = POLYSERP MENA

AFRICOM ANTIVENOM SELECTION FLOWCHART



AFRICOM - Short Form Antivenom Guide

Short Name *Full Name* [Field Stability]	**COCOM** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
POLYSERP P *POLYSERP PAN-AFRICA* FREEZE-DRIED FIELD-STABLE	AFRICOM ***Sub-Saharan Africa*** 1st line - all critical threat species / syndromes. Covers *Atractaspis* and Boomslangs.	AFRICOM ***North Africa*** 2nd line - all critical threat species / syndromes. Covers Atractaspis (no boomslang in N. Africa).	H *High Dose = 6 vials* L *Low Dose = 3 vials*	NEURO HEMO CYTO
POLYSERP M *POLYSERP MENA* FREEZE-DRIED FIELD-STABLE	AFRICOM CENTCOM ***North Africa / Middle East*** 1st line - all critical threat species / syndromes.	AFRICOM ***Sub-Saharan Africa*** 2nd line - all critical threat species / syndromes.	H *High Dose = 6 vials* L *Low Dose = 3 vials*	NEURO HEMO CYTO
SAIMR P *SAVP SAIMR Polyvalent* REFRIGERATION REQUIRED	AFRICOM ***Sub-Saharan Africa*** 2nd line - all critical threat species / syndromes. In South Africa consider SAIMR-P due to native fauna specificity if not in austere setting. Otherwise use POLYSERP-P. HIGH RISK ANAPHYLAXIS PRETREAT (*1:1000 epi*)		H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO HEMO CYTO
Inoserp P *Inoserp Pan-Africa* FREEZE-DRIED FIELD-STABLE	AFRICOM ***Sub-Saharan Africa*** 2nd line - all critical threat species / syndromes in sub-Saharan Africa.		H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO HEMO CYTO
SAIMR B *SAVP SAIMR Boomslang* REFRIGERATION REQUIRED Snake ID may be needed!	AFRICOM ***Sub-Saharan Africa*** 2nd line – Monovalent; boomslang envenomations only (HEMO). Purely hemotoxic venom, toxicity may be delayed 24+ hours HIGH RISK ANAPHYLAXIS PRETREAT (*1:1000 epi*)		H *High Dose = 2 vials* L *Low Dose = 1 vials*	HEMO
NAVPCP *NAVPC (Saudi Arabia) Polyvalent* REFRIGERATION REQUIRED	AFRICOM CENTCOM ***North Africa / Middle East*** 2nd line - all critical threat species / syndromes. CONSIDER PRETREATMENT ↑ *risk anaphylaxis (Epi 1:1000)*		H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO HEMO CYTO

AFRICOM – LONG FORM ANTIVENOM GUIDE

Sub-Saharan Africa/North Africa

FIRST LINE

POLYSERP PAN-AFRICA (POLYSERP-P)

Freeze Dried/Unrefrigerated[1,106,161–164]

Field-stable at temperatures >100º F for at least 180 days without loss of efficacy

High Dose: 6 vials

Low Dose: 3 vials

Reconstitution and Administration Instructions: Reconstitute 2 vials in 10mL NS syringe and administer via slow IV/IO push over 2 minutes OR mix in 50-100mL isotonic fluid administered via IV/IO infusion over 5-10 minutes. If a reaction occurs, stop the push, treat the reaction, reassess response to treatment criteria. Dilute remaining dose in a 100 mL bag of isotonic fluids and administer via slow IV or IO infusion over 30 mins if needed.

Adverse Reactions: Very low (0.2%) incidence of serious adverse reactions based on publications and author experience with Inoserp-500.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Broad-spectrum coverage for 24+ species Cyto/Hemo/Neuro. Single-source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in sub-Saharan Africa when the causative species is either unknown or among the 24 snakes for which this product is directly indicated. Covers boomslangs and mole viper envenomations. Directly or indirectly covers all WHO category 1 and category 2 snakes in this region for which antivenom currently exists. Polyserp is a brand-name formulation of higher-potency Inoserp Pan-Africa, which was previously studied under the name Inoserp Pan-Africa 500. It is now available only as Polyserp-P with the higher neutralization potency and the generic Inoserp 500 has been removed from the market.

Additional Information: Special operations and conventional units deploying to austere operational environments and areas with critical threat venomous species should carry 6 vials per medic / 12 per team. It is recommended that a reserve quantity is stocked in all role 2 and role 3 facilities in AFRICOM in case additional antivenom is needed upon arrival, and to restock field medics that have used their supply.

NORTH AFRICA

FIRST LINE

POLYSERP MENA Polyvalent (POLYSERP-M)

Freeze Dried/Unrefrigerated [156-172]
Field-stable at temperatures >100º F for at least 180 days without loss of efficacy

High Dose: 6 vials

Low Dose: 3 vials

Reconstitution and Administration Instructions: Reconstitute 2 vials in 10mL NS syringe and administer via slow IV/IO push over 2 minutes OR mix in 50-100mL isotonic fluid administered via IV/IO infusion over 5-10 minutes.

If a reaction occurs, stop the push, treat the reaction, reassess response to treatment criteria. Dilute remaining dose in a 100 mL bag of isotonic fluids and administer via slow IV or IO infusion over 30 mins if needed.

Adverse Reactions: Low incidence (1%) of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs

Broad-spectrum coverage for 27+ species Cyto/Hemo/Neuro. Single-source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in North Africa (Algeria, Egypt, Libya, Morocco, Tunisia, Western Sahara) when the causative species is either unknown or among the 27 snakes for which this product is directly indicated. Directly or indirectly covers all the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists, except for Gloydius halys, which is covered by Shanghai SIOBP-G or Iranian RAZI-P. Paraspecific neutralization against Gloydius unknown but not anticipated.

Additional Information: Special operations and conventional units deploying to austere operational environments and areas with critical threat venomous species should carry 6 vials per medic / 12 per team. It is recommended that a reserve quantity is stocked in all role 2 and role 3 facilities in AFRICOM in case additional antivenom is needed upon arrival, and to restock field medics that have used their supply.

SUB SAHARAN AFRICA

SECOND LINE

INOSERP PAN-AFRICA (INOSERP-P)

Freeze Dried/Unrefrigerated[1,106,161–164]
Field-stable at temperatures >100º F for at least 180 days without loss of efficacy

High Dose: 10 vials

Low Dose: 5 vials

Reconstitution and Administration Instructions: Reconstitute every 2 vials in 10mL NS syringe and administer via slow IV/IO push over 2 minutes OR mix full dose in 50-100mL isotonic fluid administered via IV/IO infusion over 5-15 minutes.

If a reaction occurs, stop the push, treat the reaction, reassess response to treatment criteria. Dilute remaining dose in a 100 mL bag of isotonic fluids and administer via slow IV or IO infusion over 30 mins if needed.

Adverse Reactions: Very low (0.2%) incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Broad-spectrum coverage for 24+ species Cyto/Hemo/Neuro. Lower neutralizing potency per vial than POLYSERP necessitates higher doses making it less practical than POLYSERP for operational settings; however, it is an acceptable single-source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in sub-Saharan Africa when the causative species is either unknown or among the 24 snakes for which this product is directly indicated. Directly or indirectly covers all WHO category 1 and category 2 snakes in this region for which antivenom currently exists.

Additional Information: Special operations and conventional units deploying to austere operational environments and areas with critical threat venomous species should carry 10 vials per medic / 20 per team. It is recommended that a reserve quantity is stocked in all role 2 and role 3 facilities in AFRICOM in case additional antivenom is needed upon arrival, and to restock field medics that have used their supply.

SECOND LINE

NEURO HEMO CYTO

South African Vaccine Producers
SAIMR Polyvalent Snake Antivenom (SAIMR-P)

Liquid/Refrigerated[50,173-181,294]
Not field-stable – Requires cold-chain refrigeration

H High Dose — High Dose 10 vials

L Low Dose — Low Dose 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Very high rates of anaphylaxis ranging from 25% - 75% have been documented in multiple publications.

HIGH RISK ANAPHYLAXIS
PRETREAT (*1:1000 epi*)

Pretreatment Recommendations: Recommended for this antivenom. Administer 0.25 mg epinephrine injected SQ prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric epinephrine dose is weight based (0.01 mg/kg).

Neurotoxic and cytotoxic envenomations by 10 different species of African snakes. Southern Africa: Directly or indirectly covers all WHO category 1 and category 2 species for which an antivenom currently exists. East/Central/West Africa: Covers many cytotoxic and neurotoxic snakes in West, Central, and East Africa but has major coverage gaps with no efficacy against all WHO category 1 or category 2 hemotoxic snake species.
The product has been used successfully to treat additional species of African snakes through paraspecific neutralization, but research in this area is limited and most experiences are anecdotal.

Additional Information: Not recommended for operational settings. Recommend storing small quantities at strategically located Role 2 & 3 facilities in AFRICOM AOR.

SECOND LINE

HEMO

South African Vaccine Producers
SAIMR Boomsang Monovalent (SAIMR-B)

Species Specific – This antivenom is only effective for bites by Boomslang

Liquid/Refrigerated[173-181,294]
Not field-stable – Requires cold-chain refrigeration

Monovalent

H High Dose — High Dose: 2 vials

L Low Dose — Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: No clinical trials but effective anecdotally and in case reports. High rates of anaphylaxis are anticipated based on limited case reports of patients treated with SAIMR-B.

HIGH RISK ANAPHYLAXIS PRETREAT (*1:1000 epi*)

Pretreatment Recommendations: Recommended for this antivenom. Administer 0.25 mg epinephrine injected SQ prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.

Confirmed or suspected boomslang bite with no indications of improvement after 10 vials of POLYSERP-P. Monovalent that can only be used to treat the WHO category 2 boomslang. Does not provide coverage against any other WHO category 1 or category 2 species.

Additional Information: Not recommended for operational settings. Requires cold chain refrigeration. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in sub-Saharan Africa.

North Africa

SECOND LINE

National Antivenom & Vaccine Production Center Polyvalent Snake Antivenom (NAVPC-P)

Liquid/Refrigerated[182-186]

Not field-stable – Requires cold-chain refrigeration

High Dose: 10 vials

Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Insufficient evidence to determine risk of adverse reactions currently.

Pretreatment Recommendations: Recommended for this antivenom due to insufficient evidence for determining risk of EARs. Administer 0.25 mg epinephrine injected IM prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.

Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in this region for which antivenom currently exists.

This polyvalent can be used to treat neurotoxic and cytotoxic envenomations by 6 different species of Middle Eastern, North African, and Central Asian snakes; NEURO (Egyptian cobra, Desert Blacksnake) + some HEMO/CYTO (*Bitis, Echis, Cerastes* spp. It may be able to neutralize venom from additional species through paraspecific neutralization but this has not been researched.[187–192]

Additional Information: Not recommended for operational settings. Requires refrigeration, moderate to high rates of adverse reactions are anticipated. Better alternatives exist. If purchased, it should be kept at Role 2 & 3 facilities in the Arabian Peninsula.

APPENDIX C: CENTCOM TREATMENT GUIDELINES

Safe and effective broad-spectrum, field-stable antivenoms are available for all three syndromes of snake envenomation in this AOR and treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is recommended for CENTCOM due to potential for prolonged evacuation times, high incidence of snakebites, and the high risk of death or permanent disability from many venomous snakes in the AOR if early antivenom treatment is not available.

Adverse Reaction Management

- If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
- If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

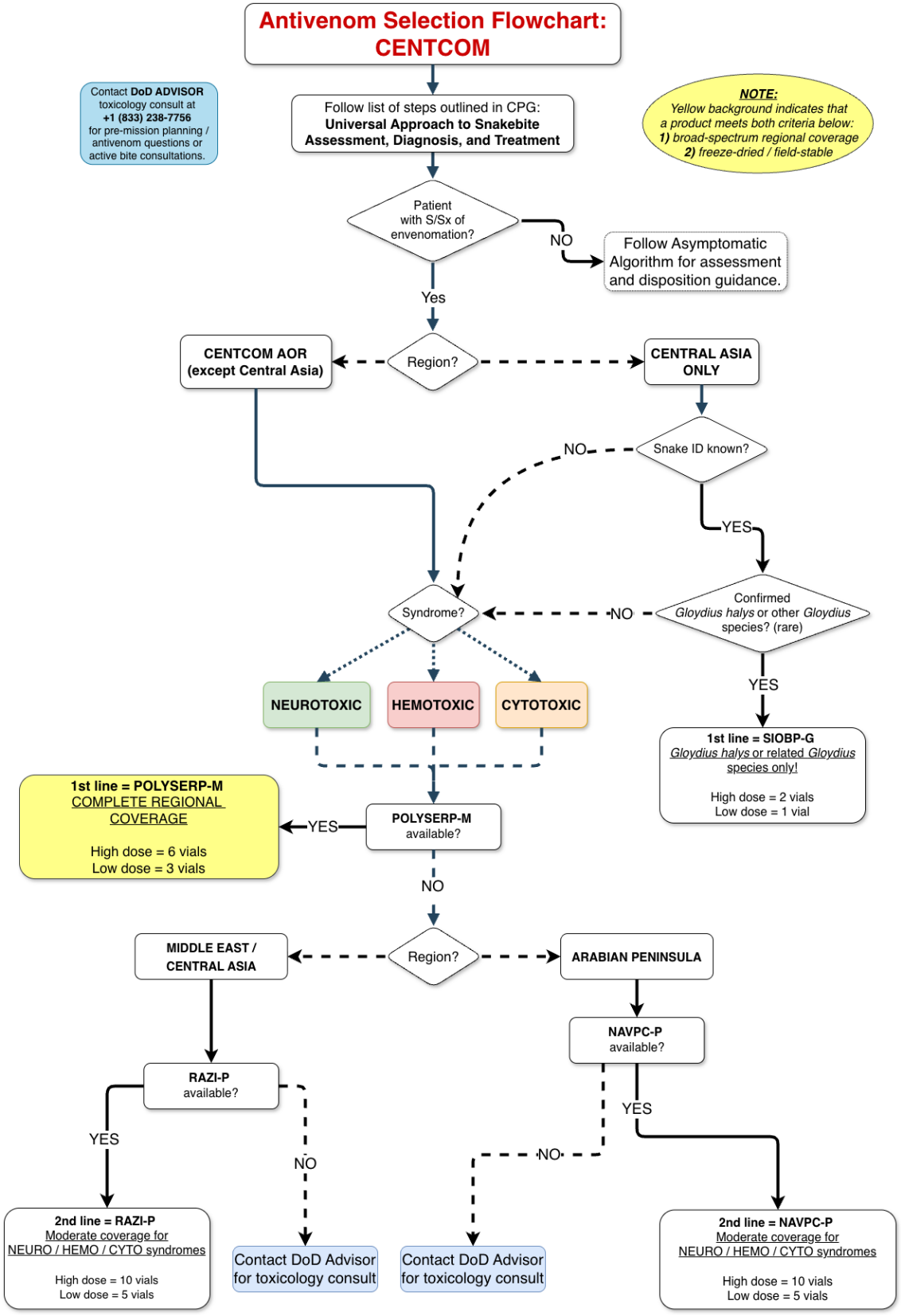
CENTCOM - First Line Antivenoms

First Line Antivenoms for CENTCOM	
CENTCOM **1st Line Antivenoms**	**First Line Antivenoms with Regional Coverage against All Three Major Syndromes (Neurotoxic/Hemotoxic/Cytotoxic)** **CENTCOM**: Broad-spectrum coverage for all neurotoxic/hemotoxic/cytotoxic snakebite syndromes by known* or unknown species - *POLYSERP-M: HIGH DOSE = 6 vials / LOW DOSE = 3 vials* **CENTRAL ASIA**: *If patient has a confirmed *Gloydius halys* bite (rare!), use SIOBP-G as 1st line if available. If unavailable or unconfirmed ID give POLYSERP-M - SIOBP-G: *HIGH DOSE = 2 vials / LOW DOSE = 1 vial*
CENTCOM **Abbreviations**	**POLYSERP-M** = POLYSERP MENA **SIOPB-G** = *Gloydius halys* monovalent

CONTACT

For emergency consultations, or additional information about snake bite management or this CPG, call the ADVISOR telemedicine hotline 833-ADVSRLN (833-238-7756) / DSN: 312-429-9089 and select toxicology from the phone menu.

CENTCOM ANTIVENOM SELECTION FLOWCHART



CENTCOM- SHORT FORM ANTIVENOM GUIDE

Short Name *Full Name* [Field Stability]	**COCOM** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
POLYSERP-M *POLYSERP MENA* FREEZE-DRIED FIELD-STABLE	AFRICOM CENTCOM ***North Africa / Middle East*** 1st line - all critical threat species / syndromes.	AFRICOM ***Sub-Saharan Africa*** 2nd line - all critical threat species / syndromes.	H *High Dose = 6 vials* L *Low Dose = 3 vials*	NEURO HEMO CYTO
NAVPC-P *NAVPC (Saudi Arabia) Polyvalent* REFRIGERATION REQUIRED	AFRICOM CENTCOM ***North Africa / Middle East*** 2nd line - all critical threat species / syndromes. CONSIDER PRETREATMENT ↑ *risk anaphylaxis (Epi 1:1000)*		H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO HEMO CYTO
SIOBP-G *Shanghai Institute of Biological Products – Gloydius Monovalent* REFRIGERATION REQUIRED Snake ID may be needed!	CENTCOM ***Middle East / Central Asia*** 1st / 2nd line - confirmed *Gloydius halys* bite. If unavailable, use POLYSERP-M. If no response to 2x high dose of POLYSERP-M and HEMO/CYTO dominant within Gloydius range, consider treatment with SIOBP-G.		H *High Dose = 2 vials* L *Low Dose = 1 vials*	HEMO CYTO
RAZI-P *RAZI Polyvalent Snake Antivenom* REFRIGERATION REQUIRED	CENTCOM ***Middle East / Central Asia*** 2nd Line - Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 12 vials of POLYSERP-M.		H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO HEMO CYTO

CENTCOM-LONG FORM ANTIVENOM GUIDE

Middle East/Central Asia

FIRST LINE

POLYSERP MENA Polyvalent (POLYSERP-M)

Freeze Dried/Unrefrigerated [156-172]
Field-stable at temperatures >100º F for at least 180 days without loss of efficacy

High Dose: 6 vials

Low Dose: 3 vials

Reconstitution and Administration Instructions: Reconstitute 2 vials in 10mL NS syringe and administer via slow IV/IO push over 2 minutes OR mix in 50-100mL isotonic fluid administered via IV/IO infusion over 5-10 minutes.

If a reaction occurs, stop the push, treat the reaction, reassess response to treatment criteria. Dilute remaining dose in a 100 mL bag of isotonic fluids and administer via slow IV or IO infusion over 30 mins if needed.

Adverse Reactions: Low incidence (1%) of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs

Broad-spectrum coverage for 27+ species Cyto/Hemo/Neuro. Single-source treatment option for all neurotoxic, hemotoxic, and cytotoxic snake envenomations in the Arabian Peninsula, the Middle East, and Central Asia when the causative species is either unknown or among the 27 snakes for which this product is directly indicated. Directly or indirectly covers all the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists

Additional Information: Special operations and conventional units deploying to austere operational environments and areas with critical threat venomous species should carry 8 vials per medic. It is recommended that a reserve quantity is stocked in all role 2 and role 3 facilities in CENTCOM in case additional antivenom is needed upon arrival, and to restock field medics that have used their supply.

ARABIAN PENINSULA

SECOND LINE

National Antivenom & Vaccine Production Center Polyvalent Snake Antivenom (NAVPC-P)

Liquid/Refrigerated[182-186]
Not field-stable – Requires cold-chain refrigeration

High Dose: 10 vials

Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Insufficient evidence to determine risk of adverse reactions currently.

Pretreatment Recommendations: Recommended for this antivenom due to insufficient evidence for determining risk of EARs. Administer 0.25 mg epinephrine injected IM prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.

Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Only for Arabian Peninsula, very limited utility further East. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.
This polyvalent can be used to treat neurotoxic and cytotoxic envenomations by 6 different species of Middle Eastern, North African, and Central Asian snakes. It may be able to neutralize venom from additional species through paraspecific neutralization, but this has not been researched.[187–192]

Additional Information: Not recommended for operational settings. Requires refrigeration, moderate to high rates of adverse reactions are anticipated. Better alternatives exist. If purchased, it should be kept at Role 2 & 3 facilities in the Arabian Peninsula.

FIRST LINE – Species Specific

HEMO CYTO

Shanghai Institute of Biological Products

Gloydius halys Monovalent (SIOPB-G)

Species Specific – First line for confirmed Gloydius halys bite (rare!) second line for unknown cytotoxic and/or hemotoxic envenomation in Middle East or Central Asia with no signs of improvement after 10 vials of POLYSERP-M

Liquid/Refrigerated[194-196]

Not field-stable: Requires cold chain refrigeration

H High Dose High Dose: 2 vials

L Low Dose Low Dose:1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low to moderate rates of EARs and serum sickness are anticipated but clinical evidence is limited.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met.

Indicated as first line only for confirmed envenomation by Gloydius halys or related Gloydius species. Monovalent for the WHO category 2 species Gloydius halys. Does not provide coverage against any other WHO category 1 or category 2 species.

Additional Information: Not recommended in operational environments. Recommend storing small quantities at strategically located Role 2 & 3 facilities in CENTCOM AOR.

This product is listed as Agkistrodon halys on the SIOBP website and product packaging but the taxonomy for this species has changed. Agkistrodon halys was moved to the genus Gloydius and should be listed as Gloydius halys as it is listed elsewhere. The product is abbreviated as SIOBP-G in the CPGs to account for this correction.

MIDDLE EAST/CENTRAL ASIA

SECOND LINE

Razi Serum and Vaccine Research Institute Polyvalent Snake Antivenom (RAZI-P)

Liquid/Refrigerated [198-205]

Not field-stable – Requires cold-chain refrigeration.

High Dose: 10 vials

Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Limited evidence but appears to be low based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met.

Neurotoxic and cytotoxic envenomations by 6 different species of Middle Eastern, North African, and Central Asian snakes. Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 10 vials of POLYSERP-M. Directly or indirectly covers all WHO category 1 species in the region. Directly or indirectly covers some of the WHO category 1 and category 2 snakes in this region for which an antivenom currently exists.

Additional Information: Not recommended for operational settings. Recommend storing small quantities at strategically located Role 2 & 3 facilities in CENTCOM AOR or selecting alternative second line from this CPG.

APPENDIX D: EUCOM TREATMENT GUIDELINES

Safe and effective broad-spectrum, refrigerated antivenoms are available for all three syndromes of snake envenomation due to European viper species in this AOR and treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is not routinely recommended for EUCOM. This section provides specifics about antivenoms use in this region.

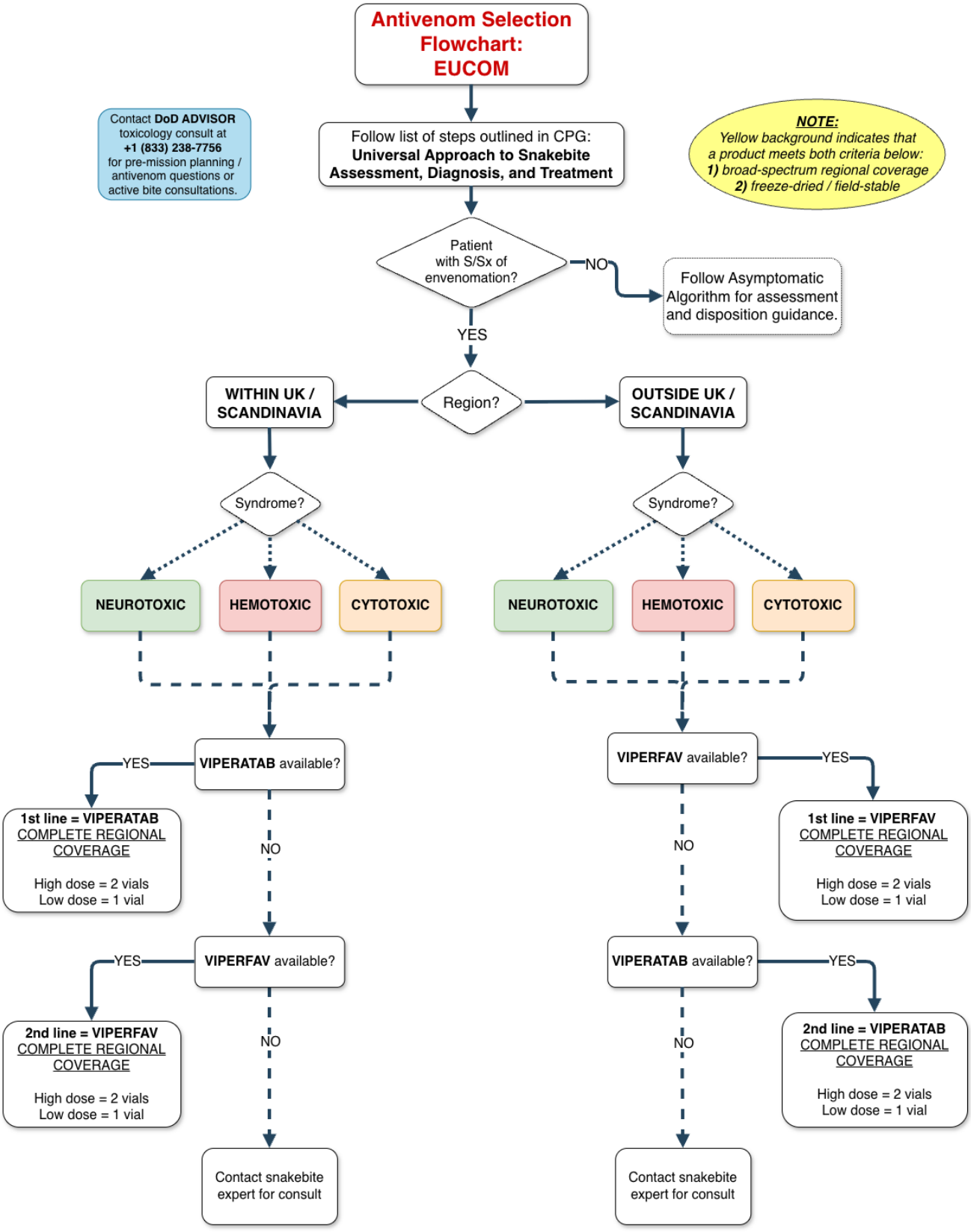
Adverse Reaction Management

- If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
- If a severe reaction such as anaphylaxis occurs, stop the infusion and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

EUCOM - First Line Antivenoms

First Line Antivenoms for EUCOM	
EUCOM 1st Line Antivenoms	**First Line Antivenoms with Regional Coverage Against All Three Major Syndromes (Neurotoxic/Hemotoxic/Cytotoxic)** **UK or Scandinavia**: Broad-spectrum coverage all neurotoxic/hemotoxic/cytotoxic syndromes from European *Vipera* species - *VIPERATAB (1st line): HIGH DOSE = 2 vials (one box), LOW DOSE = 1 vial* - *VIPERFAV (2nd line): HIGH DOSE = 2 vials / LOW DOSE = 1 vial* **Outside UK/Scandinavia**: Broad-spectrum coverage all neurotoxic/hemotoxic/cytotoxic syndromes from European *Vipera* species - *VIPERFAV (1st line): HIGH DOSE = 2 vials / LOW DOSE = 1 vial* - *VIPERATAB (2nd line): HIGH DOSE = 2 vials (one box), LOW DOSE = 1 vial*
EUCOM Abbreviations	**VIPERFAV** = VIPERFAV **VIPERATAB** = ViperaTAb

EUCOM ANTIVENOM SELECTION ALGORITHM



EUCOM – SHORT FORM ANTIVENOM GUIDE

Short Name *Full Name* [Field Stability]	**COCOM** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
VIPERFAV *Viperfav* *(Sanofi-Pasteur)* REFRIGERATION REQUIRED	**EUCOM** ***Outside UK / Scandinavia*** 1st line – European adder bites outside of UK / Scandinavia causing NEURO or HEMO/CYTO symptoms.	H *High Dose = 2 vials* L *Low Dose = 1 vials*	NEURO HEMO CYTO
VIPERATAB *ViperaTAb* *(MicroPharm)* REFRIGERATION REQUIRED	**EUCOM** ***Within UK / Scandinavia*** 1st line – European adder bites outside of UK / Scandinavia causing NEURO or HEMO/CYTO symptoms.	H *High Dose = 2 vials* L *Low Dose = 1 vials*	NEURO HEMO CYTO

EUCOM –Long Form Antivenom Guide

Outside UK or Scandinavia

FIRST LINE

Sanofi-Pasteur VIPERFAV

Freeze-dried/Refrigerated[206-212]
Not field-stable – Requires cold-chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF).

High Dose: 2 vials

Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by Vipera berus, V. aspis, V. ammodytes. Has demonstrated efficacy against other species of European vipers (genus Vipera) as well.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

UK OR SCANDINAVIA

SECOND LINE

Sanofi-Pasteur VIPERFAV

Freeze-dried/Refrigerated[206-212]

Not field-stable – Requires cold-chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF).

High Dose: 2 vials

Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by Vipera berus, V. aspis, V. ammodytes. Has demonstrated efficacy against other species of European vipers (genus Vipera) as well.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

UK OR SCANDINAVIA

FIRST LINE

Micropharm VIPERATAB (ViperaTAb)

Freeze Dried/Refrigerated[206,210,213-215]

Not field-stable – Requires cold-chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF).

High Dose: 2 vials

Low Dose: 1 vial

Reconstitution and Administration Instructions: Each box of VIPERATAB comes with two 4 mL vials of antivenom (one box = one dose). Dilute the entire dose of antivenom in a single 100 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by Vipera berus. Has demonstrated efficacy against other species of European vipers (V. aspis, V. ammodytes) as well but is not directly indicated for these species.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

OUTSIDE UK OR SCANDINAVIA

SECOND LINE

Micropharm VIPERATAB (ViperaTAb)

Freeze Dried/Refrigerated[206,210,213-215]

Not field-stable – Requires cold-chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF).

High Dose: 2 vials

Low Dose: 1 vial

Reconstitution and Administration Instructions: Each box of VIPERATAB comes with two 4 mL vials of antivenom (one box = one dose). Dilute the entire dose of antivenom in a single 100 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Neurotoxic, hemotoxic, and cytotoxic envenomation syndromes caused by Vipera berus. Has demonstrated efficacy against other species of European vipers (V. aspis, V. ammodytes) as well but is not directly indicated for these species.

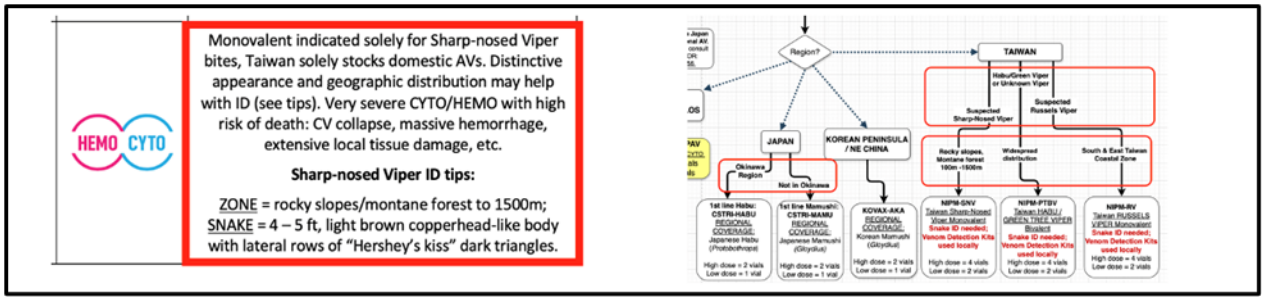
Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

APPENDIX E: INDOPACOM TREATMENT GUIDELINES

Snakebite management in Asia is complicated by a high diversity of venomous snakes, many narrow-spectrum local antivenoms that require snake ID and cold-chain storage, and only two broad-spectrum, field-stable polyvalents (TRC-NPAV and TRC-HPAV) which provide only partial coverage outside of Southeast Asia. Critically, TRC-HPAV and TRC-NPAV fail to cover many of the highest threat venomous snakes in Taiwan, Japan, the Korean Peninsula, China, and several other areas.[277-292] As a result, in these areas providers may need to make an educated guess as to the genus or species responsible. Refer to the **Appendix: Snake Identification (ID) Tips – INDOPACOM** for more detailed guidance on snake identification. Always start with the Antivenom Selection Flowchart: INDOPACOM and Antivenom Dosing by Product Table in Appendix H, which are designed to help you through this process with excerpted images below and detailed explanation in appendix. For rapid bedside decision making support when antivenom selection depends on snake ID, reference the Bedside Snake ID Workflow.

INDOPACOM Snake ID Legend

(L) - Antivenom Dosing by Product (R) - Antivenom Selection Flowchart: INDOPACOM



Adverse Reaction Management

- If a mild or moderate reaction occurs, slow the infusion and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed. Refer to the Antivenom Reactions Algorithm.
- If a severe reaction such as anaphylaxis occurs, stop the infusion, and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

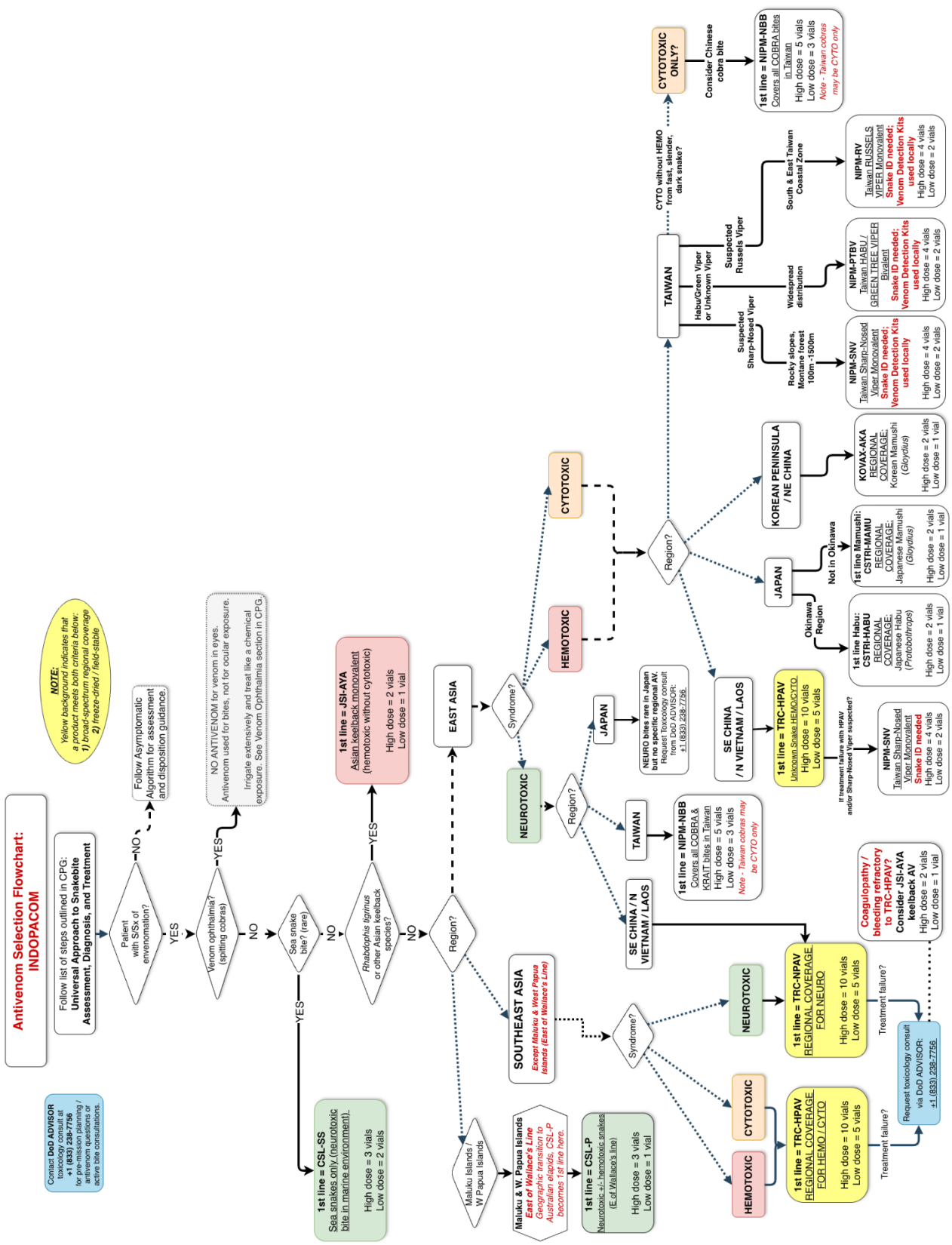
CONTACT

For emergency consultations, or additional information about snake bite management or this CPG, call the ADVISOR telemedicine hotline 833-ADVSRLN (833-238-7756) / DSN: 312-429-9089 and select toxicology from the phone menu.

INDOPACOM – FIRST LINE ANTIVENOMS

First Line Antivenoms - INDOPACOM		
INDOPACOM 1st Line Antivenoms	**First Line Antivenoms with Regional Coverage Against Neurotoxic Syndrome** **Southeast Asia**: Broad-spectrum for all neurotoxic *TRC-NPAV: HIGH DOSE = 10 vials / LOW DOSE = 5 vials* - TRC-*NPAV* is the 1st line for all neurotoxic bites in SE Asia outside of the circumstances listed below: **Marine environments**: Sea snake envenomations *- CSL-SS: HIGH DOSE = 3 vials / LOW DOSE = 1 vial* **Maluku/West Papua islands**: Neurotoxic *- CSL-P: HIGH DOSE = 3 vials / LOW DOSE = 1 vial* **Eastern China/Taiwan**: Neurotoxic *- NIPM-NBB: HIGH DOSE = 5 vials / LOW DOSE = 3 vials*	**First Line Antivenoms with Regional Coverage against Hemotoxic and/or Cytotoxic Syndromes** **Southeast Asia**: Broad-spectrum for all hemotoxic/cytotoxic (1st line in SE Asia) *TRC-HPAV: HIGH DOSE = 10 vials / LOW DOSE = 5 vials* TRC-HPAV is the 1st line for all hemotoxic/cytotoxic bites in SE Asia outside of circumstances listed below: **Korean Peninsula/Eastern China**: Viper envenomations (Cytotoxic +/- Hemotoxic) Korean Mamushi species (*Gloydius brevicaudus, G. ussuriensis, G. intermedius*) - KOVAX-AKA*: HIGH DOSE = 2 vials, LOW DOSE = 1 vial* **Taiwan / Se China / N Vietnam / Laos:** Sharp-nosed viper (*Deinagkistrodon acutus*) - NIPB-SNV*: HIGH DOSE = 4 vials / LOW DOSE = 2 vial* **Japan**: Viper envenomations (Cytotoxic +/- Hemotoxic) If Japanese HABU (*Protobothrops spp.)* envenomation: - CSTRI-HABU*: HIGH DOSE = 2 vials / LOW DOSE = 1 vial* If Japanese Mamushi (*Gloydius blomhoffii*) envenomation: - CSTRI-MAMU*: HIGH DOSE = 2 vials / LOW DOSE = 1 vial* **Japan/China/ N & S Korea/Vietnam/E Russia**: *Rhabdophis spp*. - Hemotoxic without Cytotoxic Spontaneous bleeding develops within several days of bite without cytotoxicity. - *JSI-AYA: HIGH DOSE = 2 vials / LOW DOSE = 1 vial* **Taiwan:** Habu / Green Bamboo Viper *(Protobothrops / Trimeresurus)* Bivalent - NIPM-SNV*: HIGH DOSE = 4 vials / LOW DOSE = 2 vials* **Taiwan:** Russell's Viper (*Daboia siamensis*) monovalent - NIPM-RV*: HIGH DOSE = 4 vials / LOW DOSE = 2 vials*
INDOPACOM Abbreviations	**TRC-NPAV** = Neuro Polyvalent Antivenom **CSL-P** = CSL Polyvalent **CSL-SS** = CSL Sea Snake **NIPM-NBB** = Taiwan CDC Naja atra - Bungarus multicinctus Bivalent	**TRC-HPAV** = Hemato Polyvalent Antivenom **KOVAX-AKA** = Agkistrodon Mamushi Antivenom **JSI-AYA** = Anti-Yamakagashi Antivenom **CSTRI-HABU** = Kaketsuken Habu Antivenom **CSTRI-MAMU** = Kaketsuken Mamushi Antivenom **NIPM-SNV** = Taiwan CDC Sharp-nosed Viper Monovalent **NIPM-PTBV** = Taiwan CDC Protobothrops / Trimeresurus Bivalent (Habu / Green Viper) **NIPM-RV** = Taiwan CDC Russell's Viper Monovalent

INDOPACOM ANTIVENOM SELECTION FLOWCHART



INDOPACOM - SHORT FORM ANTIVENOM GUIDE

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
TRC-NPAV *Thai Red Cross Neuro Polyvalent* FREEZE-DRIED FIELD-STABLE	**INDOPACOM** ***Southeast Asia [NEURO]*** 1st line – Broadest-spectrum NEURO polyvalent available for most of Asia. Best 1st line option in most cases of suspected Cobra / Krait envenomation.	H High Dose = 10 vials L Low Dose = 5 vials	NEURO
TRC-HPAV *Thai Red Cross Hemato Polyvalent* FREEZE-DRIED FIELD-STABLE	**INDOPACOM** ***Southeast Asia [HEMO/CYTO]*** 1st line – Broadest-spectrum HEMO/CYTO polyvalent available for most of Asia. Best 1st line option in most cases of suspected viperid envenomation. Does not cover *Rhabdophis* (NFFC HEMO only, rare).	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
CSL-SS CSL Sea Snake REFRIGERATION REQUIRED	**INDOPACOM** ***Sea Snake Envenomations [Marine]*** 1st line – sea snake envenomations in Indo-Pacific region. Characterized by neurotoxicity + myotoxicity (rhabdo) and nephrotoxicity (direct AKI). CONSIDER PRETREATMENT ↑risk anaphylaxis (Epi 1:1000) Sea snakes: bite rare, generally fishermen cutting out of nets/provoking	H High Dose = 3 vials L Low Dose = 2 vials	NEURO *NEURO + Myotoxicity & Nephrotoxicity*
CSL-P CSL Polyvalent REFRIGERATION REQUIRED	**INDOPACOM** ***SE of Wallace's Line (Maluku, W. Papua, Australasia)*** 1st line – NEURO/HEMO envenomations in Indo-Pacific region SE of Wallace's Line & Australasia. All elapids with mixed NEURO/HEMO syndrome. CONSIDER PRETREATMENT ↑risk anaphylaxis (Epi 1:1000)	H High Dose = 3 vials L Low Dose = 2 vials	NEURO HEMO CYTO *NEURO / HEMO dominant syndrome*
CSTRI-HABU *Kaketsuken Habu* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** ***Japan (Habu Monovalent)*** 1st line – HEMO/CYTO envenomations in Japan from Habu (*Protobothrops*). For Taiwanese, recommended local antivenom instead (unknown coverage)	H High Dose = 2 vials L Low Dose = 1 vials	HEMO CYTO
CSTRI-MAMU *Kaketsuken Mamushi Antivenom* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** ***Japan (Mamushi Monovalent)*** 1st line – HEMO/CYTO envenomations in Japan from Short-tailed Mamushi (*Gloydius blomhoffi*).	H High Dose = 2 vials L Low Dose = 1 vials	HEMO CYTO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
JSI-AYA *Anti-Yamakagashi* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Japan/China/Koreas/Vietnam/E Russia** 1st Line – HEMO keelback monovalent (*Rhabdophis tigrinus*) (Asian boomslang equivalent). **Consider as 2nd line if bleeding / clotting issues persist after 2x high doses of HPAV.**	H High Dose = 2 vials L Low Dose = 1 vials	HEMO CYTO
KOVAX-AKA *Agkistrodon Mamushi* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Korea (*Gloydius* Monovalent)** – Koreas / E. China (*Gloydius brevicaudus*) Korean Mamushi (For Japanese use CSTRI-MAMU)	H High Dose = 2 vials L Low Dose = 1 vials	HEMO CYTO
NIPM-NBB *Naja atra – Bungarus multicinctus* Bivalent REFRIGERATION REQUIRED	**INDOPACOM** **Taiwan / East China [NEURO] + [Cobras: Cyto +++ in region]** 1st line Bivalent indicated for all Cobra and Krait envenomations in Taiwan. Venom Detection Kits used locally for snake ID at bedside. **NOTE – Taiwanese Cobra bites present as CYTO dominant +/- neurotoxicity. Use for all suspected Cobra & Krait bites in Taiwan.** In China, use TRC-NPAV as 1st line NEURO, NIPM-NBB may be 2nd line. **Taiwan Cobra ID Tips**: Fast moving, shiny dark snake +/- white bands, may or may not raise head / open hood, many bites at night.	H High Dose = 5 vials L Low Dose = 3 vials	NEURO CYTO
NIPM-SNV *National Institute Preventative Medicine* (NIPM) *Sharp-nosed Viper Monovalent* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Taiwan, SE China, N. Vietnam, Laos** 1st line – Narrow-spectrum monovalent indicated solely for suspected sharp-nosed viper or failure of 2 high doses HPAV. Expect rapid CV collapse, bleeding, extensive tissue destruction. **Sharp-nosed Viper ID tips:** ZONE = rocky slopes/montane forest to 1500m; SNAKE = 4 – 5 ft, light brown copperhead-like body with lateral rows of "Hershey's kiss" dark triangles. Large triangular head, prominent elongated, up-sloping snout. "Hundred Pacer."	H High Dose = 4 vials L Low Dose = 2 vials	HEMO CYTO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
NIPM-PTBV *NIPM Protobothrops / Trimeresurus Bivalent* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Taiwan: Entire Island; unknown HEMO/CYTO viper bite OR snake ID (Habu or Green Pit Viper).** 1st line Taiwan – Bivalent for suspected habu / green pit viper **or unknown HEMO/CYTO dominant viper bite**. Venom Detection Kits used locally for snake ID at bedside. **Taiwan Habu / Green Viper ID Tips**: Most bites in Taiwan! Habu: 3 – 5 ft slender viper with long lance-shaped head. Brown body with variable blotched pattern. Widely distributed across Taiwan. Green Pit Viper (Bamboo Viper, Tree Viper): 1 - 3 ft long, green body, red eyes, whiteish belly. Often found in low vegetation.	H *High Dose = 4 vials* L *Low Dose = 2 vials*	HEMO CYTO
NIPM-RV *NIPM Russell's Viper Monovalent* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Taiwan: South / East Coastal Zones** 1st line Taiwan – Monovalent indicated for Russell's viper (*Daboia siamensis)* bites. Venom Detection Kits used locally for snake ID at bedside. **Taiwan Russell's Viper ID Tips:** ZONE: South & East coasts below 500m; SNAKE = Brown snake, fat body 3 – 5 ft long with 3 rows of oval spots along back [*black & white border, brownish center*], triangular head.	H *High Dose = 4 vials* L *Low Dose = 2 vials*	HEMO CYTO

CPG Revision: Approach to Snakebite in Asia

The CPG revision approaches snakebite management in Asia by prioritizing coverage against highest threat species causing the most bites and the species which are most likely to cause severe injury and death. We have selected antivenoms with favorable efficacy, safety, and sourcing that give the broadest species coverage with the fewest possible products. Taking the species and the antivenoms into account, we have subdivided Asia into the following regions: 1) Southeast Asia, 2) Southeast China/Northern Laos/Northern Vietnam, 3) Taiwan, 4) Japan, and 5) Korean Peninsula/Northeast China.

Venomous Asian snakes fall into 2 broad categories, **elapids** (primarily neurotoxic), and **vipers** (primarily hemotoxic/cytotoxic). Exceptions exist, however, and the most notable is that several Asian cobras (elapids) cause primarily cytotoxic effects with minimal neurotoxicity. Other Asian cobras, however, are severely neurotoxic. The available neuro antivenom products, such as Thai Red Cross Neuro Polyvalent (**TRC-NPAV**), and Taiwan Neuro Polyvalent (**NIPM-NBB**) are **indicated for both** neurotoxic **and** cytotoxic cobra syndromes. The primary clinical implication of this is that a patient presenting with a neurotoxic bite or a cytotoxic cobra bite (severe pain, signs of tissue damage, absence of hemorrhage) **should receive a neuro polyvalent antivenom.** In general, the Thai polyvalent antivenoms provide excellent coverage for most of the venomous snakes found in SE Asia (Thailand, Myanmar, Cambodia, Laos, Vietnam, Malaysia, Indonesia, and Brunei). As such, monovalent antivenoms are not needed in this region.

CPG Revision: East Asia (China, Japan, Korean Peninsula, Borders)

SE China, Northern Laos, and Northern Vietnam:

The venomous snake fauna in this region is very similar to Taiwan. A notable exception is the presence of the king cobra in China and adjacent southern countries. King cobras are large elapids that produce a mixed clinical syndrome of severe neurotoxicity (main life threat) and cytotoxic tissue damage; which is covered by **TRC-NPAV.** The Thai polyvalent antivenoms are indicated in this region but notably do not cover other important snakes like the Habu (*Protobothrops*) and the Sharp-nosed viper (*Deinagkistrodon*). These special cases are addressed with the Taiwan antivenoms (**NIPM-PTBV and NIPM-SNV**) in the algorithm.

Japan, Korean Peninsula, NE China:

The venomous snakes of Japan, the Korean Peninsula, and NE China are similar and vipers like the Mamushi (*Gloydius* spp.) predominate.[284-292] Japanese and Korean antivenoms provide good coverage for these snakes. An exception is the Okinawa region and adjacent smaller southern Japanese islands, where the Habu (*Protobothrops*) is found.[283] This is also addressed in the algorithm with Japanese Habu antivenom (**CSTRI-HABU**).

Sea Snake Envenomation:

Finally, sea snakes are present throughout the Indo-Pacific region in oceans and aquatic coastal regions. These snakes can produce severe neurotoxic effects. **Bites are extremely rare from sea snakes** and usually only occur to fishermen removing the snakes from their nets. Australia produces the only antivenom for sea snakes (**CSL-SS**) and this is reflected as a special case in the algorithm. In cases where the clinical envenomation syndrome is unclear and/or the culprit snake is in question, the clinician should contact the **DOD Advisor Line.**

INDOPACOM - LONG FORM ANTIVENOM GUIDE

Southeast Asia

FIRST LINE

NEURO

Thai Red Cross
Neuro Polyvalent Antivenom (TRC-NPAV)

Freeze-dried/Unrefrigerated[62,196,217,219-221]
Field-stable at ambient tropical temperatures of ≤ 25º C / 77º F - likely stable for several months at higher temps based on data from similar products

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

King cobra (O. hannah) *bites likely to require much higher doses of antivenom due to massive venom yield; it is not unusual to require dozens of vials in these cases.*

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Broad-spectrum treatment option for all neurotoxic snake envenomations by known or unknown species in Southeast Asia. Polyvalent antivenom directly indicated for the treatment of neurotoxic envenomation syndromes caused by *Ophiophagus hannah, Naja kaouthia, Bungarus candidus,* and *B. fasciatus candidus*. Has demonstrated efficacy against other related species of Asian cobras and kraits; is not directly indicated for these species but is the best neurotoxic polyvalent in the region and should be tried as the first line in most cases. If suspected keelback (*Rhabdophis*) bite with pure HEMO (no CYTO) and slower onset, consider JSI-AYA monovalent.

Additional Information: Recommended for operational settings. Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at strategically located Role 2 & 3 facilities in INDOPACOM AOR.

SOUTHEAST ASIA

FIRST LINE

HEMO CYTO

Thai Red Cross

Hemato Polyvalent Antivenom (TRC-HPAV)

Freeze-dried/Unrefrigerated[62,196,197,216-218,279-282]

Field-stable - likely retains stability at higher temperatures for short excursions (likely up to several months)

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Broad-spectrum treatment option for all hemotoxic and cytotoxic snake envenomations by known or unknown species in Southeast Asia. Directly indicated for the treatment of envenomation syndromes caused by Calloselasma rhodostoma, Trimeresurus albolabris, and Daboia russelli siamensis. Has demonstrated efficacy against other related species of Asian vipers within the same genera (Crytelytrops, Popeia, Daboia, etc.); is not directly indicated for these species but is the best hemotoxic / cytotoxic polyvalent in the region and should be tried as first line in most cases. If suspected keelback (*Rhabdophis*) bite with pure HEMO (no CYTO) and slower onset, consider JSI-AYA monovalent.

Additional Information: Recommended for operational settings. Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at strategically located Role 2 & 3 facilities in INDOPACOM AOR.

MARINE ENVIRONMENTS

FIRST LINE – Species Specific

Commonwealth Serum Laboratories – Sea Snake (CSL-SS)

NEURO

Species Specific – First line for Indo-Pacific sea snake bite (rare!)

Liquid/Refrigerated[231-245]
Not field-stable - Requires cold chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF). Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

H High Dose — High Dose: 3 vials

L Low Dose — Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: High rates of anaphylaxis have been reported with other CSL products in Papua New Guinea.[293]

HIGH RISK ANAPHYLAXIS PRETREAT (*1:1000 epi*)

Pretreatment Recommendations: Consider pretreatment as high rates of anaphylaxis have been reported with other CSL products in Papua New Guinea.[293]

Indicated as first line for envenomation by neurotoxic envenomation by sea snakes or unknown species occurring in a strictly marine environment. It is effective against envenomations by most major species of sea snakes in Australasia. Typical syndrome includes both neurotoxicity and direct myotoxicity causing myalgias, rhabdomyolysis, myoglobinuria, nephrotoxicity.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

MALUKU/WEST PAPUA ISLANDS

FIRST LINE

Commonwealth Serum Laboratories Polyvalent (CSL-P)

NEURO HEMO CYTO

Liquid/Refrigerated[61,241,245-248]
Not field-stable – Requires cold chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF); Likely to retain efficacy during short excursion at higher temperatures for several weeks in the field but should be disposed of and replaced afterwards.

H High Dose — High Dose: 3 vials

L Low Dose — Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Bites are rare but high rates of anaphylaxis have been reported with other CSL products in Papua New Guinea.[293]

⚠ Elevated Risk Anaphylaxis PRETREAT (1:1000 Epi)

Pretreatment Recommendations: Consider pretreatment as high rates of anaphylaxis have been reported with other CSL products in Papua New Guinea.[293]

Neurotoxic/hemotoxic dominant envenomation by Australasian elapids or unknown species occurring East of the biogeographic boundary Wallace's line (East of Bali; East of Makassar Strait; South/East of Celebes Sea). This polyvalent can be used to treat neurotoxic envenomations by the most medically significant species of Australasian elapid snakes found East of Wallace's line. Pain likely present but CYTO effects otherwise generally minimal with NEURO/HEMO dominance.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

JAPAN (OKINAWA REGION)

FIRST LINE – Species Specific

Chemo-Sero Theraputic Research Institute Kaketsuken Habu Antivenom (CSTRI-HABU)

Species Specific – First line for Japanese Habu species

Freeze-dried/Refrigerated[231-235,277,283,284]

Not field-stable - Requires cold chain refrigeration below 10ºC (50 ºF); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration.

High Dose: 2 vials

Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely Indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met; however, total reactions (~11% overall; ~25% serum sickness) higher than other regional products. Consider pretreatment on an individual basis.

Species specific for hemotoxic/cytotoxic envenomation syndromes caused by Japanese Habu (Protobothrops [Trimeresurus] flavoviridis) but can treat without confirmed ID. Not indicated for neurotoxic syndromes. Neurotoxic bites are rare in Japan but no specific regional antivenom currently exists.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

JAPAN (NOT IN OKINAWA REGION)

FIRST LINE – Species Specific

HEMO CYTO

Chemo-Sero Theraputic Research Institute Kaketsuken Mamushi Antivenom (CSTRI-MAMU)

Species Specific – First line for Japanese Mamushi species

Freeze-dried/Refrigerated[231-235,284,286]
Not field-stable - Requires cold chain refrigeration below 10ºC (50 ºF); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration.

H High Dose: 2 vials

L Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Species specific for hemotoxic/cytotoxic envenomation syndromes caused by Japanese Mamushi (Gloydius blomhoffi) but can treat without confirmed ID. Not indicated for neurotoxic syndromes. Neurotoxic bites are rare in Japan but no specific regional antivenom currently exists.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

JAPAN/CHINA/N KOREA/VIETNAM/E RUSSIA

FIRST LINE – Species Specific

HEMO CYTO

Japan Snake Institute Anti-Yamakagashi Antivenom (JSI-AYA)

Species Specific – First line for Asian Keelback Species, primarily Tiger Keelback (Rhabdophis tigrinus)

Freeze-dried/Refrigerated[231-233]
Not field-stable - Requires cold chain refrigeration below 10ºC (50 ºF); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration

H High Dose High Dose: 2 vials

L Low Dose Low Dose:1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

First line treatment option for hemotoxic and cytotoxic envenomation syndromes caused by the Tiger Keelback (*Rhabdophis tigrinus*) and other East Asian keelback species. Not indicated for neurotoxic envenomations.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

KOREAN PENINSULA/NE CHINA

FIRST LINE – Species Specific

HEMO CYTO

Korea Vaccine
Agkistrodon Mamushi Antivenom (KOVAX-AKA)

Species Specific – First line for Korean Mamushi species

Freeze-dried/Refrigerated[234-240,289-292]
Not field-stable - Requires cold chain refrigeration below 10ºC (50 ºF); likely to retain efficacy for short excursions lasting several weeks in the field but should be disposed of and replaced after extended time outside refrigeration.

H High Dose High Dose: 2 vials

L Low Dose Low Dose: 1 vial

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by the major species of Mamushi in the Korean Peninsula (Gloydius brevicaudus, G. ussuriensis, G. intermedius). May neutralize other related species. Not indicated for neurotoxic envenomation syndromes.

Additional Information: Not recommended for operational settings. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities.

TAIWAN

FIRST LINE

NEURO CYTO

National Institute of Preventative Medicine Naja atra/Bungarus multicinctus Bivalent (NIPM-NBB)

Freeze-dried/Refrigerated[222-230]
Liquid, Field-stable for short excursions; requires cold chain refrigeration below 10ºC (50 ºF); however, testing by Taiwanese CDC showed no loss of potency after 30 days of incubation at 35º C / 95º F or after it was returned to refrigerated storage for 4 months thereafter.

H High Dose — High Dose: 5 vials

L Low Dose — Low Dose: 3 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 100 – 500 mL bag of isotonic solution and administer by intravenous infusion over 10 – 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Broad-spectrum coverage for multiple species of neurotoxic envenomations including cobra and krait in East Asia. Bivalent antivenom directly indicated for the treatment of neurotoxic envenomation syndromes caused by Naja atra and Bungarus multicinctus. Has demonstrated efficacy against other related species of Asian cobras and kraits but is not directly indicated for these species. Not indicated for hemo or cytotoxic syndromes.

Additional Information: Conditionally recommended for operational settings during short excursions. Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at regional Role 2 & 3 facilities.

EAST ASIA: SE CHINA, N VIETNAM, LAOS
TAIWAN: ROCKY SLOPES, MONTANE FOREST 100M-1500M

FIRST LINE – Species Specific

HEMO CYTO

National Institute Preventative Medicine (NIPM-PTBV)

SNAKE ID NEEDED: Species Specific – Habu/Green Viper
Venom Detection Kits Used Locally

Freeze-dried/Refrigerated[223,235-240,277-278]
Field-stable for short-periods - Requires cold chain refrigeration below 10ºC (50 ºF); however, testing by Taiwanese CDC showed no loss of potency after 30 days of incubation at 35º C / 95º F and also after it was returned to refrigerated storage for 4 months thereafter.

H High Dose: 4 vials

L Low Dose: 2 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

SOUTH AND EAST TAIWAN: COASTAL ZONE

FIRST LINE – Species Specific

HEMO CYTO

National Institute Preventative Medicine (NIPM-RS/RV)

SNAKE ID NEEDED: Species Specific – Russell's Viper
Venom Detection Kits Used Locally

Freeze-dried/Refrigerated[223,235-240]
Field-stable for short-periods - Requires cold chain refrigeration below 10ºC (50 ºF); however, testing by Taiwanese CDC showed no loss of potency after 30 days of incubation at 35º C / 95º F and after it was returned to refrigerated storage for 4 months thereafter.

H High Dose — High Dose: 4 vials

L Low Dose — Low Dose: 2 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low incidence of serious adverse reactions based on current publications.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Directly indicated for the treatment of hemotoxic and cytotoxic envenomation syndromes caused by the sharp-nosed viper (Deinagkistrodon acutus). Also indicated for unknown bites in SE China, N Vietnam, and Laos after treatment failure with NIPM-HPAV. Not indicated for neurotoxic envenomation syndromes.

Additional Information: Conditionally recommended for operational settings during short excursions. Recommend carrying full dose into field on extended operations in austere environments and storing larger quantities at regional Role 2 and 3 facilities.

INDOPACOM – SNAKE IDENTIFICATION TIPS

In some parts of Asia, bedside antivenom selection sometimes depends on a presumptive snake ID. When ID is required, the objective is not perfect certainty - it is to make a timely and evidence-based "best guess" that allows treatment to proceed. Do not delay lifesaving antivenom in pursuit of 100% certainty**. Providers are advised to contact the DoD ADVISOR line and request a toxicology consult as soon as possible.**

DoD ADVISOR: +1 (833) 238-7756 / DSN: (312) 429-9089 |Request Toxicology Consult

Core principles

- **Safety first**: Never encourage patients, bystanders, or staff to chase, capture, kill, or handle a snake to aid identification. **Even a severed head can reflex bite and inject venom for hours.** Treat any snake—alive or dead—as capable of causing envenomation.
- **If photos or a specimen available:** contact DoD advisor toxicologist for ID assist.
- **Don't let ID delay care.** Stabilize airway, breathing, and circulation; start syndrome guided management; and use the regional algorithm. Reassess the presumptive ID as new information emerges.
- **Use a weighted evidence approach**. When photos or a specimen are not available, combine: (1**) place** (geography, habitat, elevation), (2) **snake description/behavior** if seen, (3) **circumstances of the bite**, and (4) **clinical syndrome at the bedside**. The combination is usually more reliable than any single element.
- Start with the info embedded in the **AV Rapid Reference table** and the regional **Antivenom Algorithm: INDOPACOM AOR** within the CPG (see next section for details and screenshots).

CPG REVISION: DEDICATED COVERAGE PATHWAYS FOR TAIWAN

Dedicated Coverage Paths: The following species cause nearly all snake envenomations in Taiwan: Chinese cobra (*Naja atra* - cytotoxic), many-banded krait (*Bungarus multicinctus* -severely neurotoxic), Habu (*Protobothrops mucrosquamatus* - hemotoxic/cytotoxic), green tree viper (*Trimeresurus stejnegeri* - hemotoxic/cytotoxic), sharp-nosed viper (*Deinagkistrodon acutus* - hemotoxic/cytotoxic), and eastern Russell's viper (*Daboia siamensis* - hemotoxic/cytotoxic). Photographs of these snakes are included below.

Four different antivenom products are produced in Taiwan, two are polyvalent and two are monovalent. All are effective for their covered species. The polyvalent neuro product (**NIPM-NBB**) covers kraits and cobras, and the bivalent hemorrhagic product (**NIPM-PTBV**) covers the Habu and green pit viper. Monovalent products cover the sharp-nosed viper (**NIPM-SNV**) and Russell's viper (**NIPM-RV**).

How to Use Taiwanese Antivenoms

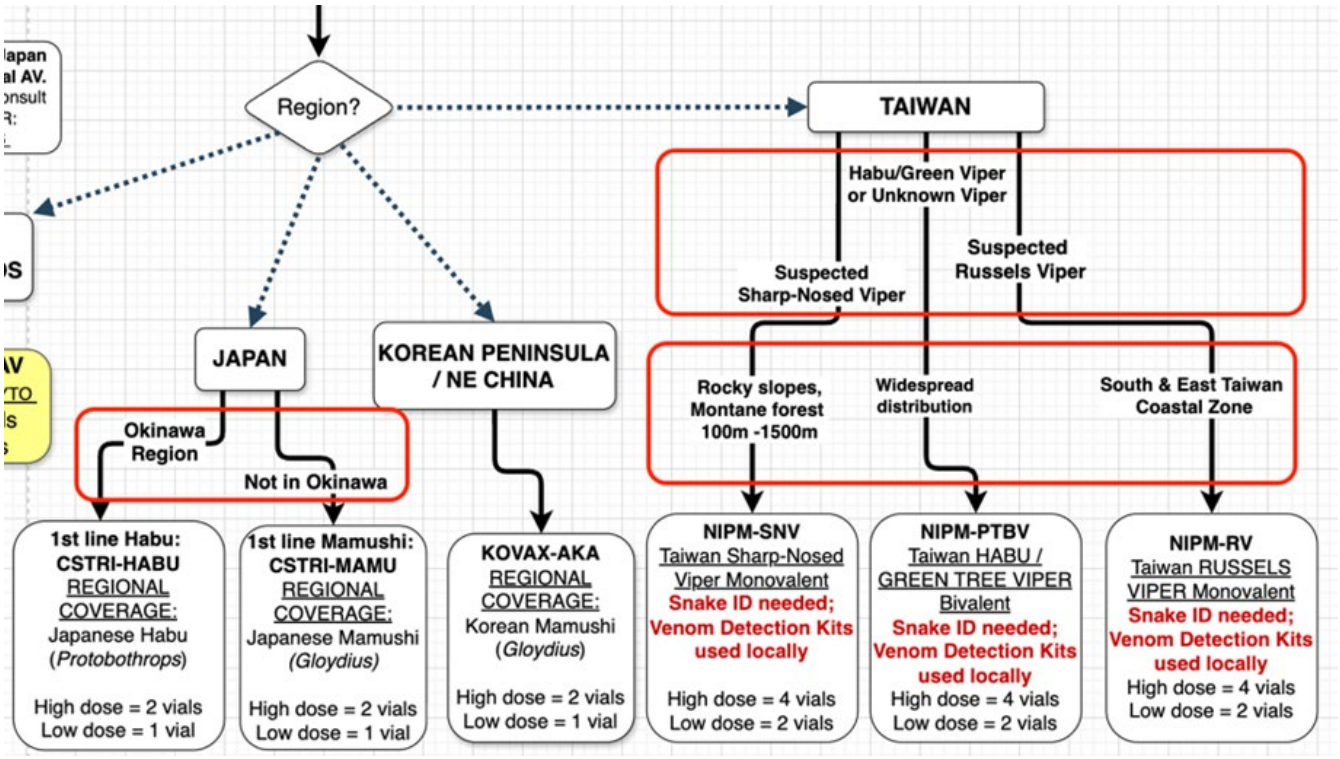
Taiwan's multi-antivenom approach relies on knowing the species responsible for the bite. Identifying the culprit species in Asia is more useful than in any other region. Taiwanese clinicians use snake-identification posters and venom detection kits to help choose the proper antivenom. A detailed history from the victim regarding the behavior and appearance of the snake is important. Description of the habitat (mountainous, coastal flats, agricultural, etc.) is also important and can help identify the culprit. For assistance in identifying Taiwan venomous snakes, refer to the above images.

The Taiwan bivalent viper antivenom (**NIPM-PTBV**) will likely be used most frequently, followed by the Taiwan neuro bivalent (**NIPM-NBB**; **indicated not only for neurotoxic krait bites but also cytotoxic cobra bites**). The monovalent antivenoms will be needed for bites from suspected sharp-nosed vipers (**NIPM-SNV**) and Russell's vipers (**NIPM-RV**) and this is addressed in the algorithm.

Start at Regional Antivenom Flowchart: INDOPACOM and Antivenom Dosing By Product Table (in CPG)

Because broad-spectrum, field stable polyvalents (**TRC-NPAV and TRC-HPAV**) have **gaps outside Southeast Asia**, the CPG includes **region tailored decision points for Taiwan, Japan, the Korean Peninsula, East China, and other areas** where local monovalents or mixed coverage strategies may be required. In these subsections, **location/elevation/habitat plus syndrome** often narrows to a logical presumptive ID **even when the snake was not seen**. Use those boxes first when working in these areas.

INDOPACOM AOR ANTIVENOM ALGORITHM



INDOPACOM AV RAPID REFERENCE GUIDE

NIPM-SNV *National Institute Preventative Medicine* (NIPM) *Sharp-nosed Viper Monovalent* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM - Taiwan** **Taiwan, SE China, N. Vietnam, Laos** 1st line – Narrow-spectrum monovalent indicated solely for suspected sharp-nosed viper or failure of 2 high doses HPAV. Expect rapid CV collapse, bleeding, extensive tissue destruction.	H *High Dose = 4 vials* L *Low Dose = 2 vials*	HEMO CYTO	Monovalent indicated solely for Sharp-nosed Viper bites, Taiwan solely stocks domestic AVs. Distinctive appearance and geographic distribution may help with ID (see tips). Very severe CYTO/HEMO with high risk of death: CV collapse, massive hemorrhage, extensive local tissue damage, etc. **Sharp-nosed Viper ID tips:** ZONE = rocky slopes/montane forest to 1500m; SNAKE = 4 – 5 ft, light brown copperhead-like body with lateral rows of "Hershey's kiss" dark triangles.

BEDSIDE SNAKE ID WORKFLOW (WHEN ANTIVENOM CHOICE DEPENDS ON ID)

1. **Stabilize ABCs**; start syndrome guided care (airway equipment ready for neurotoxicity; pressure immobilization only when indicated; analgesia).
2. **If snake photos (or dead snake) AVAILABLE:**
   a. Contact DoD Advisor at +1 (833) 238-7756, request toxicology, tell them you have photos or a dead snake with the patient.
   b. Ideally, photos show the full body/pattern as well as several clear angles of the head (top, front, sides). Ventral side photos can be helpful but dorsal more important.
   c. ***DO NOT take risks to obtain photos!*** *Never touch the head with your hands - even a decapitated snake head can bite and inject venom >24 hours after the bite.*
3. **If snake photos (or dead snake) NOT AVAILABLE:**
   a. Ask the patient about where the bite occurred (location / estimated elevation), what type of habitat it was (e.g., dry rocky hillside, wading through creek), what the patient was doing when the bite occurred, what the snake looked like, and if they remember anything about how it behaved (e.g., rose up and hooded its neck).
   b. **Review ID tips (habitat/location) in Antivenom Algorithm: INDOPACOM AOR** in the CPG regional pages for INDOPACOM. Review the location/habitat text on the sub-regional arrows for your area, this may provide an answer.
   c. **Review snake description and habitat/location tips in the AV RAPID REFERENCE table in the CPG**: Antivenoms that require species ID have tips for identification based on location/habitat and **snake description.**
   d. **Classify the syndrome(s):** NEURO, HEMO, CYTO, or mixed (e.g. HEMO/CYTO). If mixed, identify the dominant syndrome.
   e. **Scan history / description for strong signals** (hooding/spitting; sea exposure; nocturnal bed bite with minimal local signs).
4. **Make a presumptive ID → Select antivenom per regional algorithm** for the most likely group **→ treat without delay.**
5. **Reassess frequently**: If the clinical course and labs do not improve after adequate dosing, **reopen the differential** and switch antivenom per algorithm or after DoD ADVISOR consultation.
6. **Sometimes, it may be necessary to try more than one antivenom in these cases** – this is often done in Taiwanese hospitals.

APPENDIX F: NORTHCOM TREATMENT GUIDELINES

Safe and effective antivenoms are available for all neurotoxic/hemo/cytotoxic pit viper envenomations and for neurotoxic coral snake envenomations in this AOR. Treatment does not require identification of the species responsible. Snakebite treatment at the point of injury is not routinely recommended for NORTHCOM.

For all NORTHCOM antivenoms, refer to the package insert in the antivenom box for specific usage instructions as per FDA regulations for domestically approved products. Also see Unified treatment algorithm for the management of crotaline snakebite in the U.S. (Lavonas et al. 2011) for dosing and management guidelines on pit viper bites.[101] This section provides specifics about antivenoms use in this region.

Adverse Reaction Management

- If a mild or moderate reaction occurs, slow the infusion, and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
- If a severe reaction such as anaphylaxis occurs, stop the infusion, and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

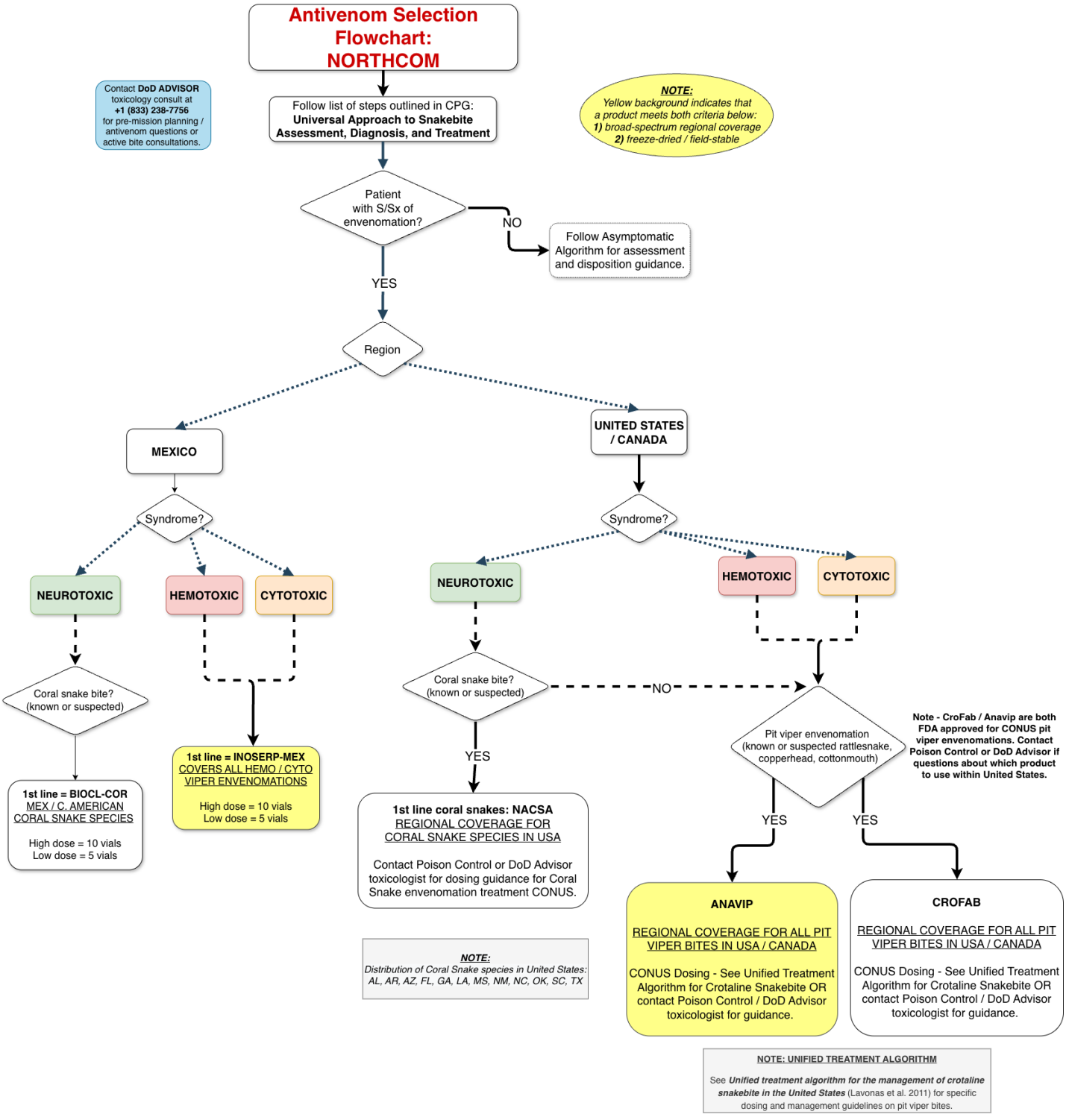
CONTACT

For emergency consultations, or additional information about snake bite management or this CPG, call the ADVISOR telemedicine hotline 833-ADVSRLN (833-238-7756) / DSN: 312-429-9089 and select toxicology from the phone

FIRST LINE ANTIVENOMS – NORTHCOM

First Line Antivenoms NORTHCOM		
NORTHCOM 1st Line Antivenoms	**First Line Antivenoms with Regional Coverage Against Neurotoxic Syndrome** **United States**: Coral snake envenomations *Contact local poison control or DoD ADVISOR for NASCA dosing recommendations.* --- **Mexico:** Neurotoxic polyvalent *BIOCL-COR: HIGH DOSE = 10 vials / LOW DOSE = 5 vials*	**First Line Antivenoms with Regional Coverage against Hemotoxic and/or Cytotoxic Syndromes** **United States/Canada**: Broad spectrum coverage all hemotoxic/cytotoxic syndromes* Any pit viper envenomation (rattlesnake, copperhead, cottonmouth): *Contact local poison control or DoD ADVISOR or follow Unified Treatment Algorithm for the Management of Crotaline Snakebite in the United States* (Lavonas et al. 2011) for specific dosing and management guidelines on pit viper bites CONUS. --- **Mexico:** Broad spectrum coverage all hemotoxic/cytotoxic syndromes* Any pit viper envenomation (rattlesnake, copperhead, cottonmouth): - *INOSERP-MEX: HIGH DOSE = 10 vials / LOW DOSE = 5 vials*
NORTHCOM Abbreviations	**NACSA** = North American Coral Snake Antivenin **BIOCL-COR** = CORALMYN	**CROFAB** = CroFab **ANAVIP** = ANAVIP --- **INOSERP-MEX** = Inoserp Mexico

NORTHCOM ANTIVENOM SELECTION FLOWCHART



NORTHCOM – SHORT FORM ANTIVENOM GUIDE

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
CROFAB REFRIGERATION REQUIRED	**NORTHCOM** **USA & Canada** 1st line – broad-spectrum indicated for all viper envenomations in USA & Canada. **Not indicated for Mexico.**		*Refer to Unified Treatment Algorithm (CONUS)*	HEMO CYTO
ANAVIP FREEZE-DRIED FIELD-STABLE	**NORTHCOM** **USA & Canada** 1st line – broad-spectrum indicated for all viper envenomations in USA & Canada. **Not indicated for Mexico.**		*Refer to Unified Treatment Algorithm (CONUS)*	HEMO CYTO
NACSA *North American Coral Snake Antivenin* REFRIGERATION REQUIRED	**NORTHCOM** **USA** 1st line – CORAL SNAKES ONLY (NEURO). Indicated for all coral snake envenomations. **Not indicated for Mexico.** **Contact Poison Control to obtain 1(800)-222-1222.**		Call poison control for dosing (CONUS)	NEURO
INOSERP-MEX *Inoserp Mexico* FREEZE-DRIED FIELD-STABLE	**NORTHCOM** **Mexico** 1st line - all viper envenomations in Mexico	**SOUTHCOM** **Belize, Guatemala, Honduras, El Salvador, Nicaragua** 1st line – all viper envenomations in Northern Central America. **Costa Rica, Panama, South America** 2nd line - all viper bites from Costa Rica southwards.	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
BIOCL-AVT *Antivipmyn-Tri (Instituto Bioclon, Mexico)* FREEZE-DRIED FIELD-STABLE	**SOUTHCOM** **Costa Rica, Panama, South America** 1st line – all viper bites from Costa Rica southwards.	**NORTHCOM** **Mexico** 2nd line - all viper envenomations in Mexico.	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
BIOCL-COR CORALMYN (Instituto Bioclon, Mexico) FREEZE-DRIED FIELD-STABLE REFRIGERATION REQUIRED	**SOUTHCOM** **Central America** 1st line - all coral snakes in Mexico & Central America.	**SOUTHCOM** **South America** 2nd line – all coral snakes in South America. Can be found in freeze-dried or liquid (refrigerated) forms.	H High Dose = 10 vials L Low Dose = 5 vials	NEURO

NORTHCOM –Long Form Antivenom Guide

United States & Canada

FIRST LINE

HEMO CYTO

BTG Therapeutics CROFAB - CroFab

Freeze-dried/Refrigerated[94, 95, 101,249-250]

Requires refrigeration but one study has demonstrated that it will maintain efficacy under field conditions for ≥ 90 days if needed

H High Dose — High Dose: 8 - 12 vials (follow unified treatment algorithm or contact poison control / DoD advisor)

L Low Dose — Low Dose: 4-6 vials (follow unified treatment algorithm or contact poison control / DoD advisor)

Administration Instructions: Follow the Unified Treatment Algorithm for North America

Envenomation by all Pit Viper species (rattlesnakes, copperheads, cottonmouths) in North America.

Additional Information: Follow the Unified Treatment Algorithm for North America

If Alpha-Gal syndrome suspected (patient from high prevalence area, suspicious medical Hx, etc); consider CroFab as first line if available due to possible lower risk of reaction. Unproven but compelling evidence, further study needed.

UNITED STATES & CANADA

FIRST LINE

HEMO CYTO

RDT/Instituto Bioclon ANAVIP

Freeze-dried/Unrefrigerated[92]
Field-stable at room temperature of 25º C / 77º F

High Dose Initial Dose: 10 vials (10 vials as per FDA, to max of 20 with repeated dosing – contact poison control or DoD advisor for specific guidance)

Low Dose Initial Dose: 10 vials (10 vials as per FDA, to max of 20 with repeated dosing – contact poison control or DoD advisor for specific guidance)

Administration Instructions: Follow the Unified Treatment Algorithm for North America

Envenomation by all Pit Viper species (rattlesnakes, copperheads, cottonmouths) in North America

Additional Information: Follow the Unified Treatment Algorithm for North America
if Alpha-Gal syndrome suspected (patient from high prevalence area, suspicious medical Hx, etc); consider CroFab as first line if available due to possible lower risk of reaction. Unproven but compelling evidence, further study needed.

UNITED STATES & CANADA (USA: AL, AR, AZ, FL, GA, LA, MS, NM, NC, OK, SC, TX)

FIRST LINE – Species Specific

NEURO

North American Coral Snake Antivenin (NACSA)

Freeze-dried/Refrigerated[251]
Store between 2 – 8º C / 35.6 - 46.4 ºF; however, likely retains stability for short excursions in the field.

High Dose Initial Dose: 3-5 vials, but contact poison control or DoD Advisor for definitive dosing

Low Dose Initial Dose: 3-5 vials, but contact poison control or DoD Advisor for definitive dosing

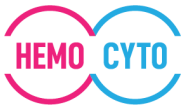
Administration Instructions: Follow the Unified Treatment Algorithm for North America

Neurotoxic envenomations by North American coral snake (NACSA) species in the United States including Eastern coral snake (Micrurus fulvius) and Texas coral snake (Micrurus tener).

Additional Information: Follow the Unified Treatment Algorithm for North America
Difficult to obtain, must contact poison control or Miami-Dade Fire Rescue Venom One for sourcing questions.

MEXICO

FIRST LINE



Inosan Biopharma/Sanfer
Inoserp Mexico (INOSERP-MEX)

Freeze-dried/Unrefrigerated
Field-stable at temperatures >100º F for at least 180 days without loss of efficacy

High Dose: 10 vials

Low Dose: 5 vials

Reconstitution and Administration Instructions: May be given by slow direct IV/IO push or reconstituted and mixed in a single 100 - 250 mL bag of 0.9% NS bag and given by rapid IV/IO infusion over 5 – 10 minutes. If direct push, may dilute up to two vials in the same 10 cc syringe of NS or sterile water and administer over 2 – 3 minutes per syringe IV/IO (slow direct push).

Adverse Reactions: Low rates of reactions anticipated.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Indicated for all HEMO/CYTO viper envenomations in Mexico and N. Central America (Belize, Guatemala, Honduras, El Salvador, and Nicaragua). Directly or indirectly covers over 40 species of vipers including all or most of the WHO category 1 and category 2 snakes in this region.[272] Does not cover coral snakes (Micrurus spp.).

Additional Information: Lyophilized product recommended for use in operational settings and designed for low resource environments. Broad coverage and simple dosing enable administration in the field for any symptomatic snakebite by unknown species in this region. Broader immunizing mixture than ANTIVIPMYN likely translates to higher neutralization against critical threat species in the region.

MEXICO

SECOND LINE

HEMO CYTO

Instituto Bioclon – ANTIVIPMYN-TRI (BIOCL-AVT)

Freeze-dried/Unrefrigerated[251-255]
Field-stable at ambient tropical temperatures of ≤ 37º C / 98.6º F.

H High Dose High Dose: 10 vials

L Low Dose Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low rates of reactions anticipated.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met.

Indicated for Hemotoxic and cytotoxic envenomations by more than 14 different species of Mexican viperids. Directly or indirectly covers most of the WHO category 1 and category 2 snakes in this region. NOTE – may be sold as "Antivipmyn" in Mexico rather than Antivipmyn-Tri in Mexico without Lachesis coverage; "Tri" indicates Lachesis coverage. Does not cover coral snakes (Micrurus spp.).

Additional Information: Recommended for operational settings. Lyophilized product that likely retains stability at higher temperatures for short excursions. Recommend carrying full dose or loading dose (≥ 5 vials) into field on extended operations in austere environments and storing larger quantities at strategically located Role 2 & 3 facilities in SOUTHCOM AOR.

MEXICO

FIRST LINE

Instituto Bioclon / Laboratorios Silanes, Mexico CORALMYN (BIOCL-COR)

NEURO

Liquid/Refrigerated AND Freeze-dried/Unrefrigerated formulations exist[256-262]
Field-stable if freeze-dried formulation; Liquid requires cold chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF)

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low rates of reactions anticipated.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Neurotoxic envenomations by most major species of Mexican and Central American coral snakes from the genus Micrurus. It may be used as a second line for many species of South American coral snake if first line unavailable.

Additional Information: Comes in both liquid (refrigerated) and freeze-dried (field stable) formulations! Freeze-dried formulation recommended for operational environments; Liquid formulation not recommended for operational environments. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in Central & South America. If liquid, likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

APPENDIX G: SOUTHCOM TREATMENT GUIDELINES

Safe and effective antivenoms are available for all hemo/cytotoxic pit viper envenomations and for neurotoxic coral snake envenomations in this AOR. Treatment does not require identification of the species responsible but does require identification of the syndrome. Snakebite treatment at the point of injury is recommended for SOUTHCOM. This section provides specifics about antivenoms use in this region.

Adverse Reaction Management

- If a mild or moderate reaction occurs, slow the infusion, and treat symptomatically with antihistamines, steroids, and/or antiemetics as needed.
- If a severe reaction such as anaphylaxis occurs, stop the infusion, and treat according to the anaphylaxis protocol listed elsewhere in the CPG. Reassess the patient once the reaction has been controlled and resume the infusion at a slower rate if any of the specific criteria for antivenom treatment listed elsewhere in the CPG have not completely resolved.

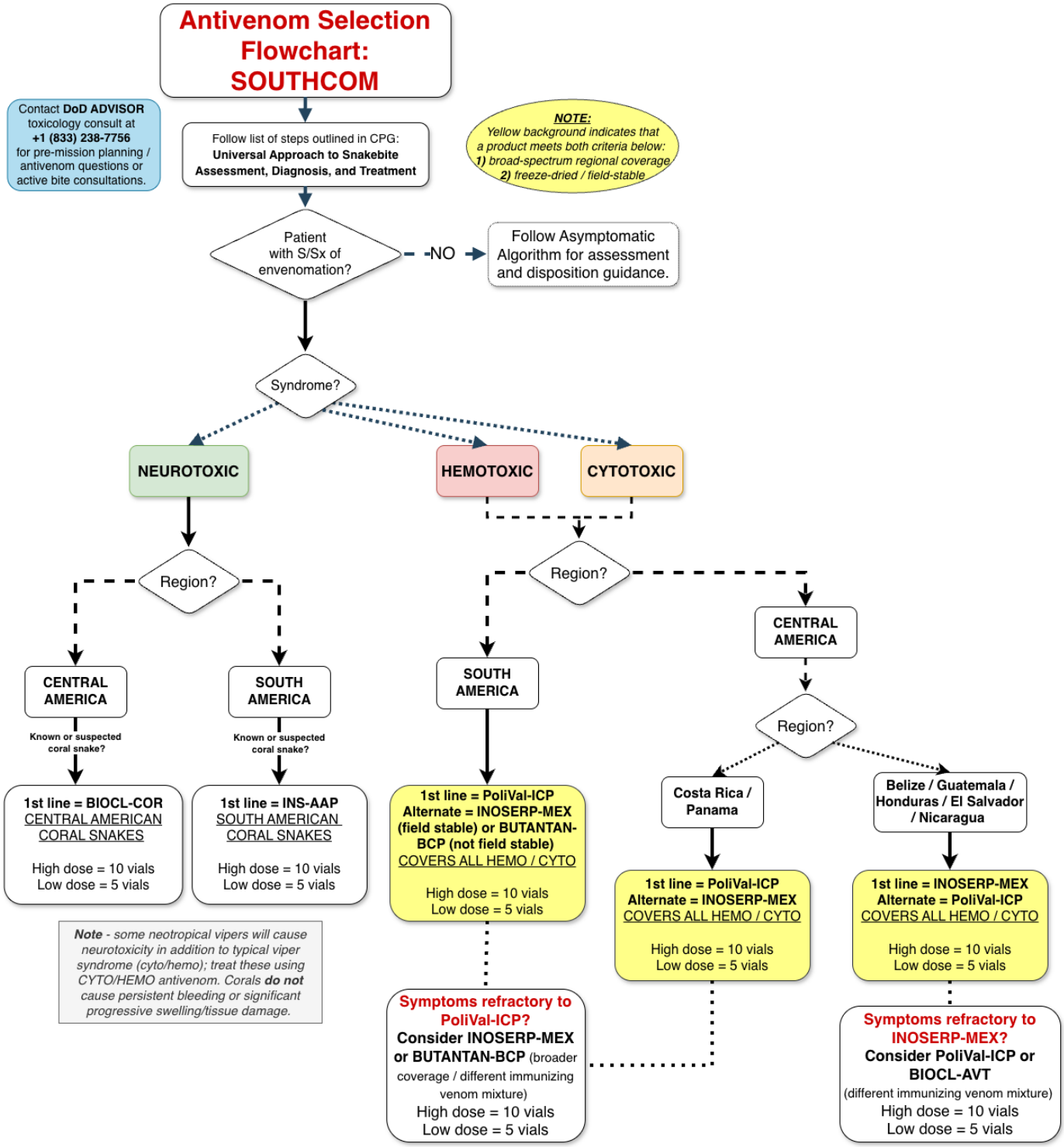
SOUTHCOM First Line Antivenoms

First Line Antivenoms – SOUTHCOM		
SOUTHCOM 1st Line Antivenoms	**First Line Antivenoms with Regional Coverage Against Neurotoxic Syndrome** **Central America:** Neurotoxic polyvalent - *BIOCL-COR: HIGH DOSE = 10 vials / LOW DOSE = 5 vials* **South America**: Neurotoxic polyvalent - *INS-AAP: HIGH DOSE = 10 vials / LOW DOSE = 5 vials*	**First Line Antivenoms with Regional Coverage Against Hemotoxic and/or Cytotoxic Syndromes** **Central and South America**: Broad-spectrum all hemotoxic/cytotoxic syndromes - *INOSERP-MEX: HIGH DOSE = 10 vials / LOW DOSE = 5 vials* - *PoliVal-ICP: HIGH DOSE = 10 vials / LOW DOSE = 5 vials*
SOUTHCOM Abbreviations	**BIOCL-COR** = CORALMYN **INS-AAP** = Antiveneno Anticoral Polivalente **PoliVal-ICP** = Antiveneno Ofídico Polivalente ICP **BUTANTAN-BCR** = Soro Antibotrópico-Crotálico **INOSERP-MEX** = Inoserp Mexico	

CONTACT

For emergency consultations, or additional information about snake bite management or this CPG, call the ADVISOR telemedicine hotline 833-ADVSRLN (833-238-7756) / DSN: 312-429-9089 and select toxicology from the phone

SOUTHCOM – ANTIVENOM SELECTION FLOWCHART



SOUTHCOM – SHORT FORM ANTIVENOM GUIDE

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
INOSERP-MEX *Inoserp Mexico* FREEZE-DRIED FIELD-STABLE	**NORTHCOM** **Mexico** 1st line - all viper envenomations in Mexico	**SOUTHCOM** **Belize, Guatemala, Honduras, El Salvador, Nicaragua** 1st line – all viper envenomations in Northern Central America. **Costa Rica, Panama, South America** 2nd line - all viper bites from Costa Rica southwards.	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
PoliVal-ICP *Antiveneno Antiofídico Polivalente (Instituto Clodomiro Picado, Costa Rica)* FREEZE-DRIED FIELD-STABLE REFRIGERATION REQUIRED	**SOUTHCOM** **Costa Rica, Panama, South America** 1st line - all viper bites from Costa Rica southwards. Pretreat with epi. CONSIDER PRETREATMENT ↑risk anaphylaxis (Epi 1:1000) *NOTE – Comes in both lyophilized/field-stable and liquid/refrigerated formulations.*	**SOUTHCOM** **Belize, Guatemala, Honduras, El Salvador, Nicaragua** 2nd line – all viper envenomations in Northern Central America. Pretreat with epi. CONSIDER PRETREATMENT ↑risk anaphylaxis (Epi 1:1000) *NOTE – Comes in both lyophilized/field-stable and liquid/refrigerated formulations.*	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
BUTANTAN-BCP *Soro Antibotrópico-Crotálico (Instituto Butantan, Brazil)* REFRIGERATION REQUIRED	**SOUTHCOM** **South America** Alternative 2nd line – all viper bites in South America. Only available as a refrigerated liquid formulation, store at 2 – 8 ºC (DO NOT FREEZE). Moderately high rates of reaction anticipated, pretreat with epi. Reasonable alternative for treatment refractory viper bites that fail to respond to PoliVal-ICP and/or INOSERP-MEX in South America. CONSIDER PRETREATMENT ↑risk anaphylaxis (Epi 1:1000)		H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
BIOCL-COR *CORALMYN* *(Instituto Bioclon, Mexico)* FREEZE-DRIED FIELD-STABLE REFRIGERATION REQUIRED	SOUTHCOM **Central America** 1st line – all coral snakes in Mexico & Central America.	SOUTHCOM **South America** 2nd line – all coral snakes in South America. *Can be found in freeze-dried or liquid (refrigerated) forms.*	H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO
INS-AAP *Antiveneno Anticoral Polivalente* *(Brazil)* REFRIGERATION REQUIRED	SOUTHCOM **South America** 1st line – all coral snakes in South America.	SOUTHCOM **Central America** 2nd line – all coral snakes in Central America.	H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO

SOUTHCOM – LONG FORM ANTIVENOM

First Line Northern Central America

Second Line Southern Central America/South America

FIRST LINE \ SECOND LINE

HEMO CYTO

Inosan Biopharma/Sanfer Inoserp Mexico (INOSERP-MEX)

Freeze-dried/Unrefrigerated
Field-stable at temperatures >100º F for at least 180 days without loss of efficacy

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

Reconstitution and Administration Instructions: May be given by slow direct IV/IO push or reconstituted and mixed in a single 100 - 250 mL bag of 0.9% NS bag and given by rapid IV/IO infusion over 5 – 10 minutes. If direct push, may dilute up to two vials in the same 10 cc syringe of NS or sterile water and administer over 2 – 3 minutes per syringe IV/IO (slow direct push).

Adverse Reactions: Low rates of reactions anticipated.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Viper envenomations (HEMO/CYTO) in Central America & South America. Broad immunizing mixture should provide enhanced coverage versus many of the common viper bites in this region. For suspected *Lachesis* (bushmaster) bites, use PoliVal-ICP first if available. Best fit for most operational settings in Central and South America due to broad coverage, low risk of EARs among other platform products, high purity, and temperature stability in extended expeditionary excursions. Not indicated for coral snake envenomations. Reasonable alternative for primary coverage in Southern Central America and South America; greater coverage against common viperids and lower expected rates of adverse reactions compared to PoliVal-ICP (primary difference is no coverage vs *Lachesis*).

Additional Information: Recommended for use in operational settings and designed for low resource settings. Broad coverage and simple dosing enable administration in the field for any symptomatic snakebite by unknown species in this region.

First Line Southern Central America/South America
Second Line Northern Central America

FIRST LINE \ SECOND LINE

HEMO CYTO

Instituto Clodomiro Picado, Costa Rica

PoliVal ICP (PoliVal-ICP)

Liquid/Refrigerated AND Freeze-dried/Unrefrigerated formulations exist[256-262]

Field-stable if freeze-dried formulation; Liquid requires cold chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF)

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Moderate rates of reactions anticipated (11 – 28% EARs including anaphylaxis); pretreatment recommended in most cases.

CONSIDER PRETREATMENT
↑ *risk anaphylaxis (Epi 1:1000)*

Pretreatment Recommendations: Recommended for this antivenom due to insufficient evidence for determining risk of EARs. Administer 0.25 – 0.5 mg epinephrine injected IM prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.

Viper envenomations (HEMO/CYTO) in Southern Central America & South America. Direct or indirect coverage against most viperid envenomations causing HEMO/CYTO syndromes in Latin America and first line for all suspected *Lachesis* (bushmaster) bites due to direct neutralization. Highly effective but higher rates of reaction documented so pretreatment should be considered prior to administration. Not indicated for coral snake envenomations.

Additional Information: Freeze-dried formulation recommended for operational environments; Liquid formulation not recommended for operational environments. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in Central & South America. If liquid, likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

Second Line South America

FIRST LINE

HEMO CYTO

Instituto Butantan, Brazil

Soro Antibotrópico-Crotálico (BUTANTAN-BCP)

Liquid/Refrigerated

Requires cold chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF)

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Moderate rates of reaction anticipated due to residual albumin and other proteins. Pretreatment recommended.

⚠ CONSIDER PRETREATMENT
↑ *risk anaphylaxis (Epi 1:1000)*

Pretreatment Recommendations: Recommended for this antivenom due to risk of EARs. Administer 0.25 – 0.5 mg epinephrine injected IM prior to beginning antivenom infusion to reduce the risk of a serious reaction. Pediatric doses should be weight based at a dose of 0.01 mg/kg, up to 0.25 mg.

Indicated for hemotoxic and cytotoxic envenomations by South American species from the genus Bothrops and Crotalus. Directly or indirectly covers most of the WHO category 1 and category 2 snakes in this region. Does not cover coral snakes (Micrurus spp.).

Additional Information: Not recommended for operational settings. Liquid formulation that requires continuous refrigeration; DO NOT FREEZE. May be most useful in the setting of refractory viper envenomations in South America that fail to respond to PoliVal-ICP or INOSERP-MEX.

FIRST LINE CENTRAL AMERICA, SECOND LINE SOUTH AMERICA

FIRST LINE \ SECOND LINE

NEURO

Instituto Bioclon / Laboratorios Silanes, Mexico CORALMYN (BIOCL-COR)

Liquid/Refrigerated AND Freeze-dried/Unrefrigerated formulations exist[256-262]
Field-stable if freeze-dried formulation; Liquid requires cold chain refrigeration between 2 - 8 ºC (35.6 - 46.4 ºF)

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low rates of reactions anticipated.

Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

Neurotoxic envenomations by most major species of Mexican and Central American coral snakes from the genus Micrurus. It may be used as a **second line treatment option for coral snake / unknown neurotoxic envenomation in South America if first line (INS-AAP) is not available.**

Additional Information: Freeze-dried formulation recommended for operational environments; Liquid formulation not recommended for operational environments. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in Central & South America. If liquid, likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

First Line South America, Second Line Central America

FIRST LINE \ SECOND LINE

Instituto Nacional de Salud, Colombia
Antiveneno Anticoral Polivalente (INS-AAP)

NEURO

Liquid/Refrigerated [260-2]

Not field-stable - requires cold chain refrigeration between 4 - 8 ºC / 39.2 - 46.4 ºF

H High Dose — High Dose: 10 vials

L Low Dose — Low Dose: 5 vials

Reconstitution and Administration Instructions: Dilute the entire dose of antivenom in a single 250 - 500 mL bag of isotonic solution and administer by intravenous infusion over 10 - 30 minutes.

Adverse Reactions: Low rates of reactions anticipated.

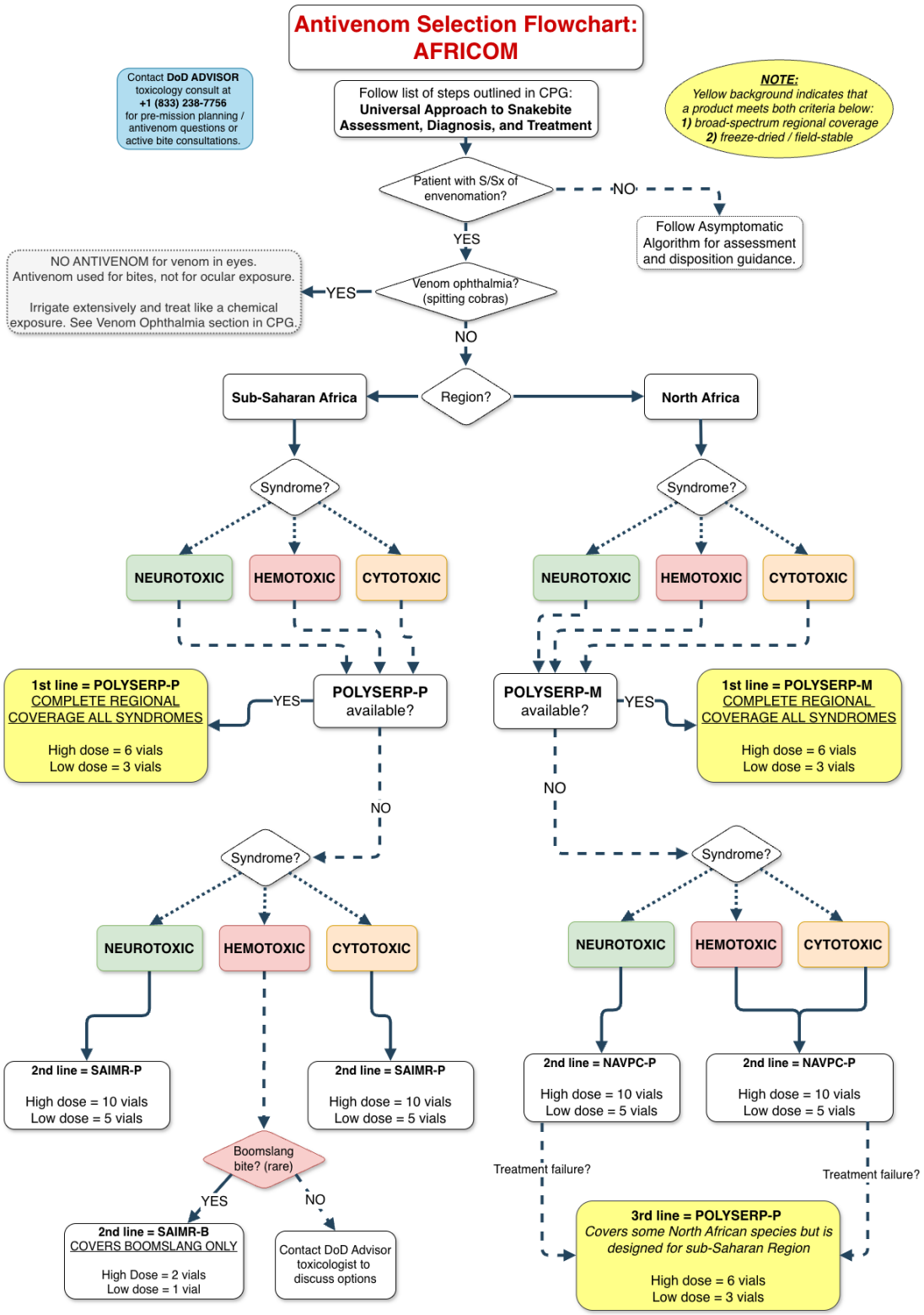
Pretreatment Recommendations: Not routinely indicated unless patient is unstable, asthmatic/atopic, known hypersensitivity or other pretreatment criteria met. Low risk of severe allergic reactions and other EARs.

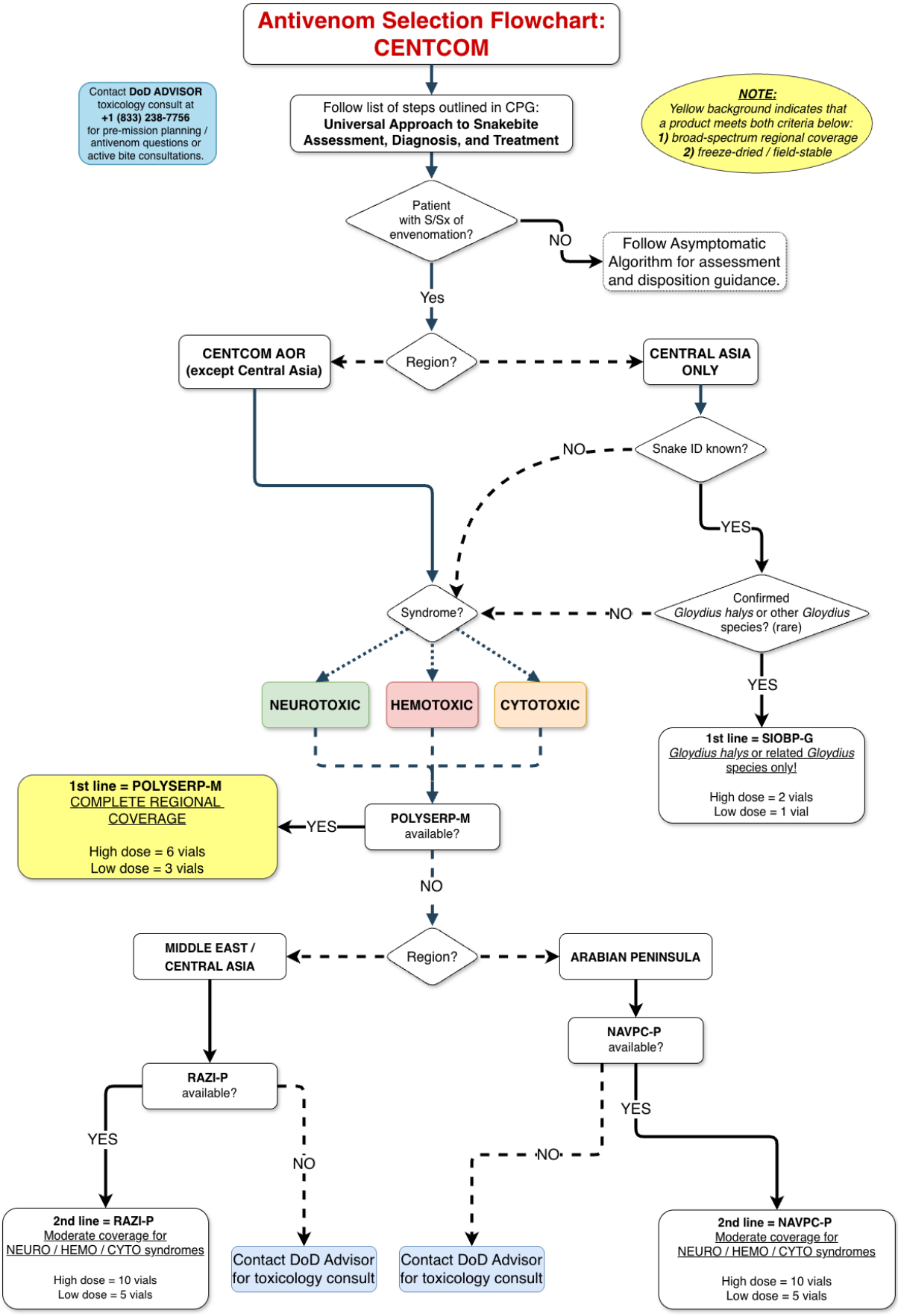
Neurotoxic envenomation in South America by coral snakes or unknown species (coral snakes are only strictly neurotoxic snakes in SOUTHCOM AOR). This polyvalent can be used to treat neurotoxic envenomations by most major species of South American coral snakes from the genus Micrurus as well as some Central American species.

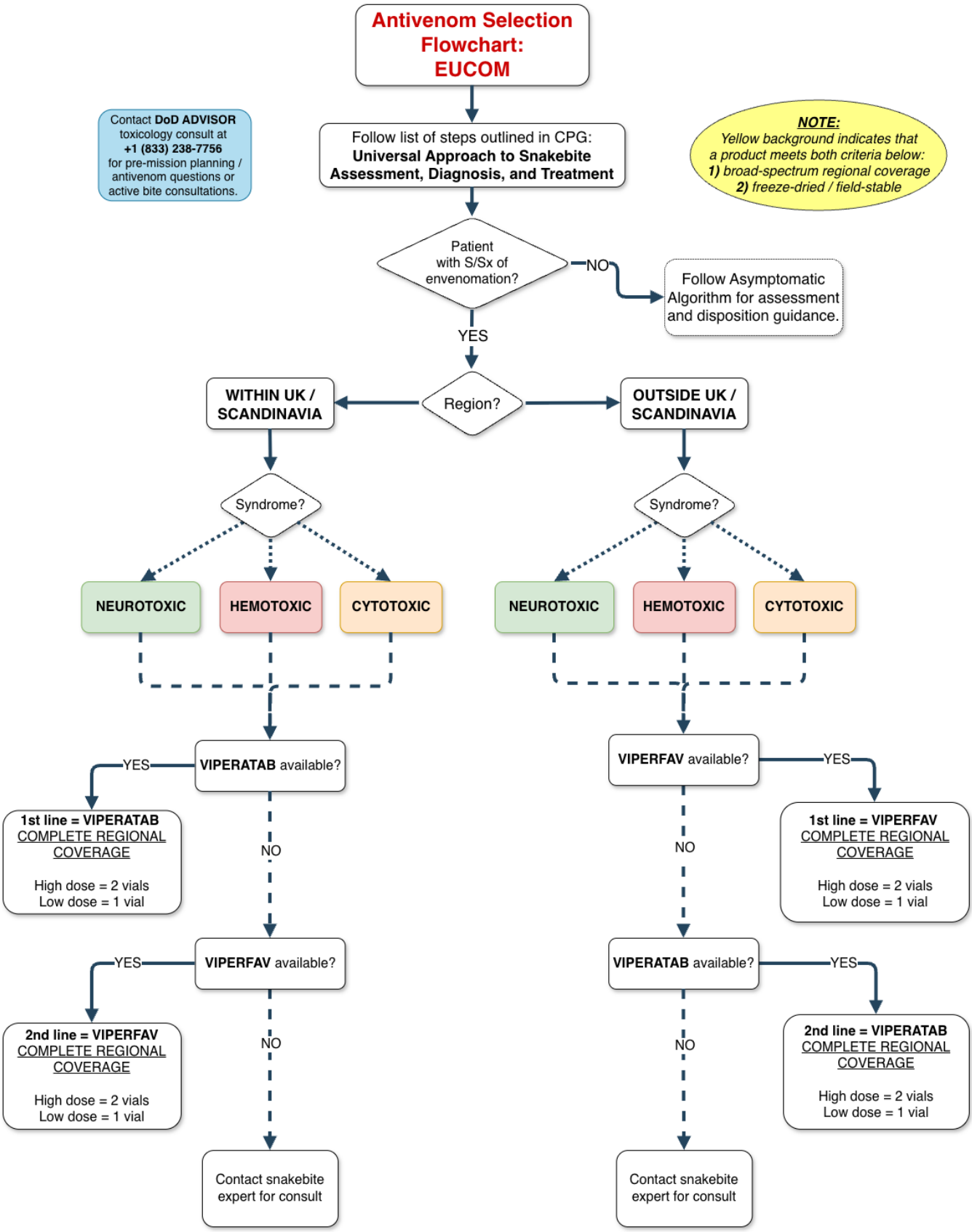
Additional Information: Not recommended for operational settings. Liquid product that requires refrigeration. Recommend storing several vials at a small number of strategically located Role 2 & 3 facilities in South America. Likely to retain efficacy for several weeks in the field but should be disposed of after that duration of time outside refrigeration.

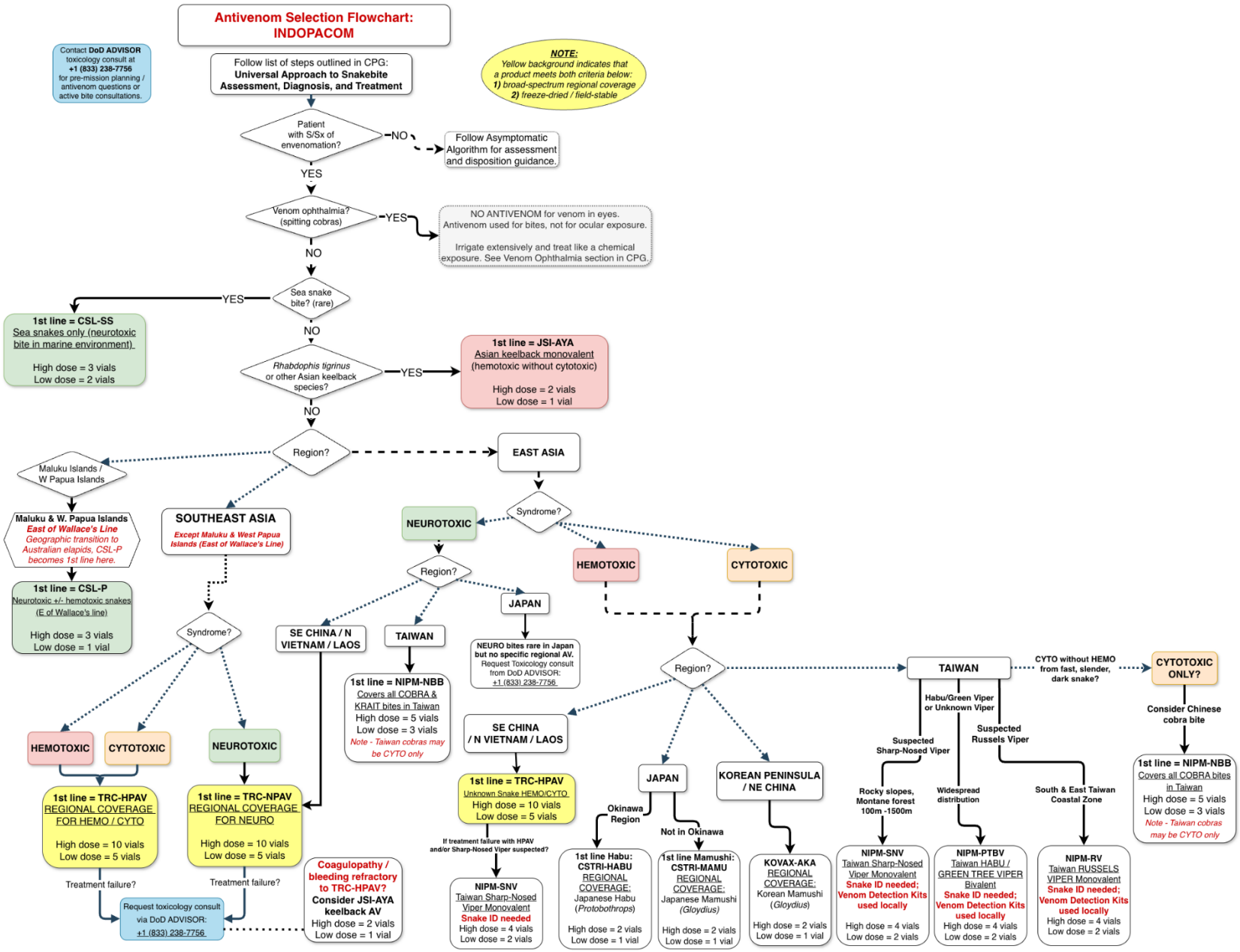
APPENDIX H: REGIONAL ANTIVENOM SELECTION FLOWCHARTS & ANTIVENOM DOSING BY PRODUCT

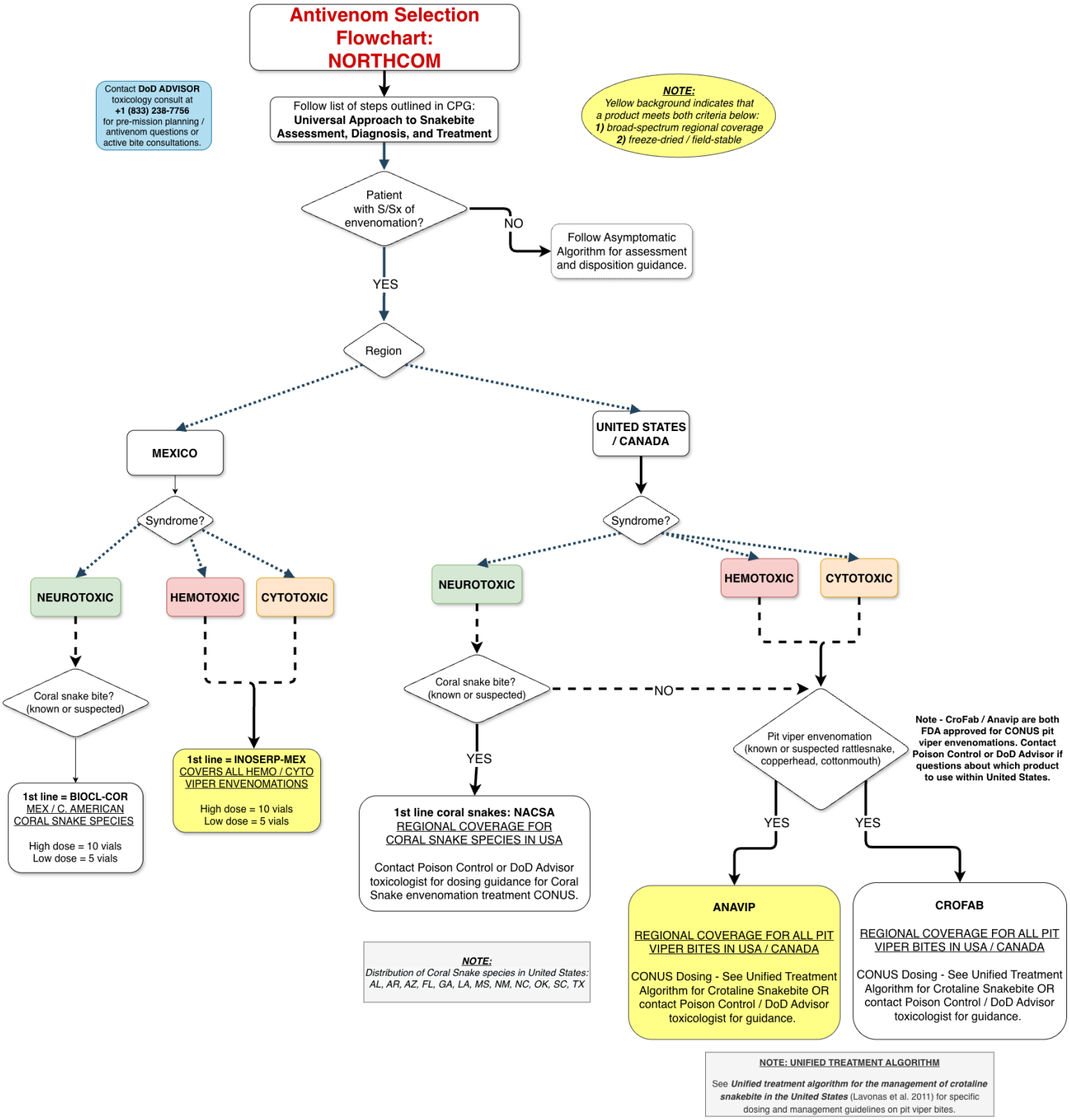
APPENDIX H – REGIONAL ANTIVENOM SELECTION FLOWCHARTS

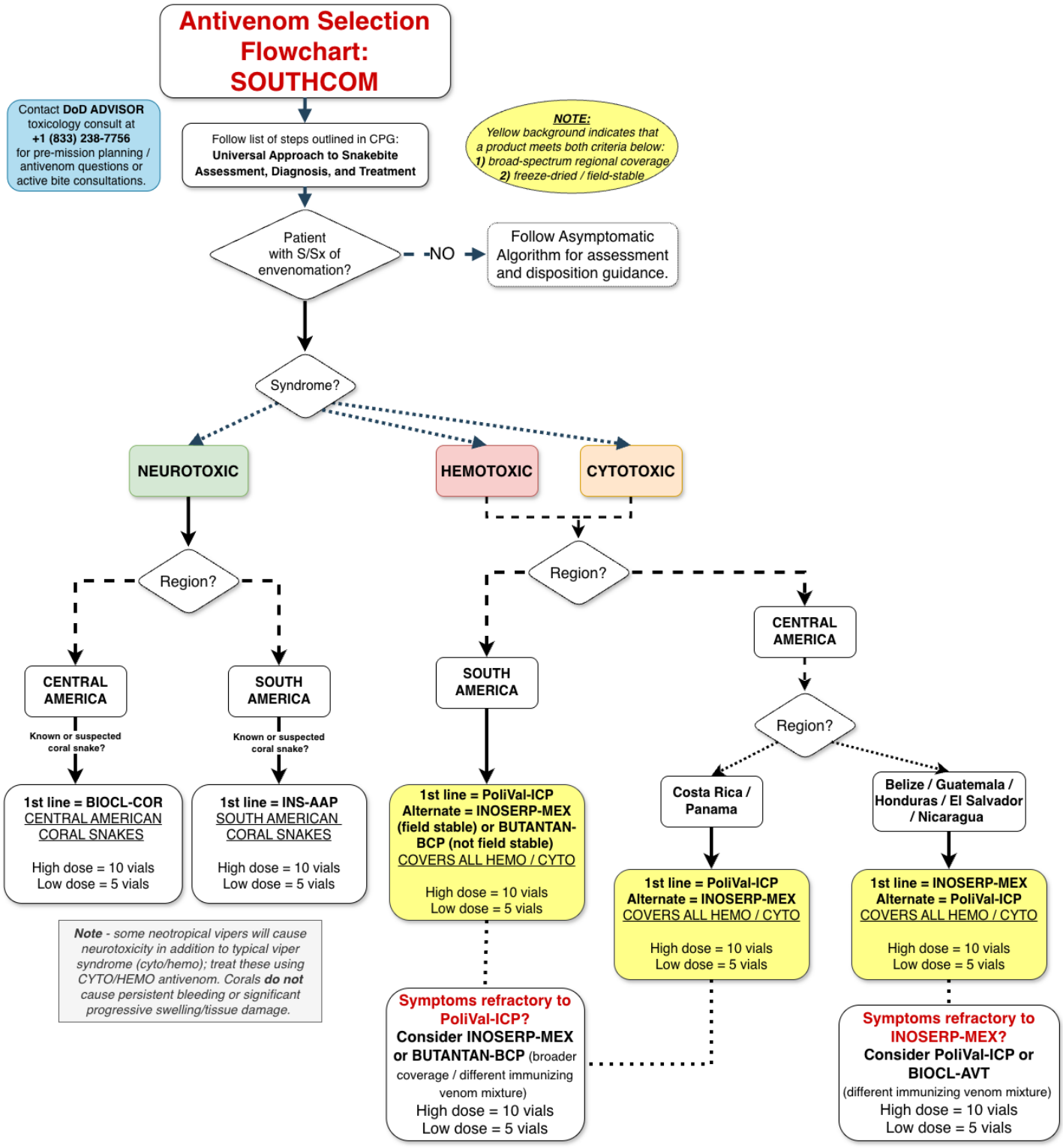



Antivenom Selection Flowchart: CENTCOM
Contact DoD ADVISOR toxicology consult at +1 (833) 238-7756 for pre-mission planning / antivenom questions or active bite consultations.
Follow list of steps outlined in CPG: Universal Approach to Snakebite Assessment, Diagnosis, and Treatment
NOTE: Yellow background indicates that a product meets both criteria below: 1) broad-spectrum regional coverage 2) freeze-dried / field-stable
Patient with S/Sx of envenomation?
NO
Follow Asymptomatic Algorithm for assessment and disposition guidance.
Yes
Region?
CENTCOM AOR (except Central Asia)
CENTRAL ASIA ONLY
Snake ID known?
NO
YES
Syndrome?
NO
Confirmed Gloydius halys or other Gloydius species? (rare)
YES
NEUROTOXIC
HEMOTOXIC
CYTOTOXIC
1st line = SIOBP-G
Gloydius halys or related Gloydius species only!
High dose = 2 vials
Low dose = 1 vial
1st line = POLYSERP-M
COMPLETE REGIONAL COVERAGE
High dose = 6 vials
Low dose = 3 vials
YES
POLYSERP-M available?
NO
Region?
MIDDLE EAST / CENTRAL ASIA
ARABIAN PENINSULA
NAVPC-P available?
RAZI-P available?
YES
NO
YES
NO
2nd line = RAZI-P
Moderate coverage for NEURO / HEMO / CYTO syndromes
High dose = 10 vials
Low dose = 5 vials
Contact DoD Advisor for toxicology consult
Contact DoD Advisor for toxicology consult
2nd line = NAVPC-P
Moderate coverage for NEURO / HEMO / CYTO syndromes
High dose = 10 vials
Low dose = 5 vials


Antivenom Selection Flowchart: EUCOM
Contact DoD ADVISOR toxicology consult at +1 (833) 238-7756 for pre-mission planning / antivenom questions or active bite consultations.
Follow list of steps outlined in CPG: Universal Approach to Snakebite Assessment, Diagnosis, and Treatment
NOTE: Yellow background indicates that a product meets both criteria below: 1) broad-spectrum regional coverage 2) freeze-dried / field-stable
Patient with S/Sx of envenomation?
NO
Follow Asymptomatic Algorithm for assessment and disposition guidance.
YES
Region?
WITHIN UK / SCANDINAVIA
OUTSIDE UK / SCANDINAVIA
Syndrome?
Syndrome?
NEUROTOXIC
HEMOTOXIC
CYTOTOXIC
NEUROTOXIC
HEMOTOXIC
CYTOTOXIC
VIPERATAB available?
YES
1st line = VIPERATAB COMPLETE REGIONAL COVERAGE
High dose = 2 vials
Low dose = 1 vial
NO
VIPERFAV available?
YES
2nd line = VIPERFAV COMPLETE REGIONAL COVERAGE
High dose = 2 vials
Low dose = 1 vial
NO
Contact snakebite expert for consult
VIPERFAV available?
YES
1st line = VIPERFAV COMPLETE REGIONAL COVERAGE
High dose = 2 vials
Low dose = 1 vial
NO
VIPERATAB available?
YES
2nd line = VIPERATAB COMPLETE REGIONAL COVERAGE
High dose = 2 vials
Low dose = 1 vial
NO
Contact snakebite expert for consult


Antivenom Selection Flowchart: INDOPACOM
Contact DoD ADVISOR toxicology consult at +1 (833) 238-7756 for pre-mission planning / antivenom questions or active bite consultations.
Follow list of steps outlined in CPG: Universal Approach to Snakebite Assessment, Diagnosis, and Treatment
NOTE: Yellow background indicates that a product meets both criteria below: 1) broad-spectrum regional coverage 2) freeze-dried / field-stable
Patient with S/Sx of envenomation?
NO
Follow Asymptomatic Algorithm for assessment and disposition guidance.
YES
Venom ophthalmia? (spitting cobras)
YES
NO ANTIVENOM for venom in eyes. Antivenom used for bites, not for ocular exposure.
Irrigate extensively and treat like a chemical exposure. See Venom Ophthalmia section in CPG.
NO
Sea snake bite? (rare)
YES
1st line = CSL-SS
Sea snakes only (neurotoxic bite in marine environment)
High dose = 3 vials
Low dose = 2 vials
NO
Rhabdophis tigrinus or other Asian keelback species?
YES
1st line = JSI-AYA
Asian keelback monovalent
(hemotoxic without cytotoxic)
High dose = 2 vials
Low dose = 1 vial
NO
Region?
EAST ASIA
Maluku Islands / W Papua Islands
Maluku & W. Papua Islands
East of Wallace's Line
Geographic transition to Australian elapids, CSL-P becomes 1st line here.
1st line = CSL-P
Neurotoxic +/- hemotoxic snakes (E of Wallace's line)
High dose = 3 vials
Low dose = 1 vial
SOUTHEAST ASIA
Except Maluku & West Papua Islands (East of Wallace's Line)
Syndrome?
HEMOTOXIC
CYTOTOXIC
NEUROTOXIC
1st line = TRC-HPAV
REGIONAL COVERAGE FOR HEMO / CYTO
High dose = 10 vials
Low dose = 5 vials
1st line = TRC-NPAV
REGIONAL COVERAGE FOR NEURO
High dose = 10 vials
Low dose = 5 vials
Treatment failure?
Treatment failure?
Request toxicology consult via DoD ADVISOR: +1 (833) 238-7756
Coagulopathy / bleeding refractory to TRC-HPAV?
Consider JSI-AYA keelback AV
High dose = 2 vials
Low dose = 1 vial
Syndrome?
NEUROTOXIC
Region?
SE CHINA / N VIETNAM / LAOS
TAIWAN
JAPAN
1st line = NIPM-NBB
Covers all COBRA & KRAIT bites in Taiwan
High dose = 5 vials
Low dose = 3 vials
Note - Taiwan cobras may be CYTO only
NEURO bites rare in Japan but no specific regional AV.
Request Toxicology consult from DoD ADVISOR: +1 (833) 238-7756
HEMOTOXIC
CYTOTOXIC
Region?
SE CHINA / N VIETNAM / LAOS
1st line = TRC-HPAV
Unknown Snake HEMO/CYTO
High dose = 10 vials
Low dose = 5 vials
If treatment failure with HPAV and/or Sharp-Nosed Viper suspected?
NIPM-SNV
Taiwan Sharp-Nosed Viper Monovalent
Snake ID needed
High dose = 4 vials
Low dose = 2 vials
JAPAN
Okinawa Region
Not in Okinawa
1st line Habu: CSTRI-HABU
REGIONAL COVERAGE:
Japanese Habu (Protobothrops)
High dose = 2 vials
Low dose = 1 vial
1st line Mamushi: CSTRI-MAMU
REGIONAL COVERAGE:
Japanese Mamushi (Gloydius)
High dose = 2 vials
Low dose = 1 vial
KOREAN PENINSULA / NE CHINA
KOVAX-AKA
REGIONAL COVERAGE:
Korean Mamushi (Gloydius)
High dose = 2 vials
Low dose = 1 vial
TAIWAN
Habu/Green Viper or Unknown Viper
Suspected Sharp-Nosed Viper
Suspected Russels Viper
Rocky slopes, Montane forest 100m -1500m
Widespread distribution
South & East Taiwan Coastal Zone
NIPM-SNV
Taiwan Sharp-Nosed Viper Monovalent
Snake ID needed; Venom Detection Kits used locally
High dose = 4 vials
Low dose = 2 vials
NIPM-PTBV
Taiwan HABU / GREEN TREE VIPER Bivalent
Snake ID needed; Venom Detection Kits used locally
High dose = 4 vials
Low dose = 2 vials
NIPM-RV
Taiwan RUSSELS VIPER Monovalent
Snake ID needed; Venom Detection Kits used locally
High dose = 4 vials
Low dose = 2 vials
CYTO without HEMO from fast, slender, dark snake?
CYTOTOXIC ONLY?
Consider Chinese cobra bite
1st line = NIPM-NBB
Covers all COBRA bites in Taiwan
High dose = 5 vials
Low dose = 3 vials
Note - Taiwan cobras may be CYTO only


Antivenom Selection Flowchart: NORTHCOM
Contact DoD ADVISOR toxicology consult at +1 (833) 238-7756 for pre-mission planning / antivenom questions or active bite consultations.
Follow list of steps outlined in CPG: Universal Approach to Snakebite Assessment, Diagnosis, and Treatment
NOTE: Yellow background indicates that a product meets both criteria below: 1) broad-spectrum regional coverage 2) freeze-dried / field-stable
Patient with S/Sx of envenomation?
NO
Follow Asymptomatic Algorithm for assessment and disposition guidance.
YES
Region
MEXICO
UNITED STATES / CANADA
Syndrome?
Syndrome?
NEUROTOXIC
HEMOTOXIC
CYTOTOXIC
NEUROTOXIC
HEMOTOXIC
CYTOTOXIC
Coral snake bite? (known or suspected)
Coral snake bite? (known or suspected)
NO
YES
1st line = BIOCL-COR MEX / C. AMERICAN CORAL SNAKE SPECIES High dose = 10 vials Low dose = 5 vials
1st line = INOSERP-MEX COVERS ALL HEMO / CYTO VIPER ENVENOMATIONS High dose = 10 vials Low dose = 5 vials
1st line coral snakes: NACSA REGIONAL COVERAGE FOR CORAL SNAKE SPECIES IN USA Contact Poison Control or DoD Advisor toxicologist for dosing guidance for Coral Snake envenomation treatment CONUS.
Pit viper envenomation (known or suspected rattlesnake, copperhead, cottonmouth)
Note - CroFab / Anavip are both FDA approved for CONUS pit viper envenomations. Contact Poison Control or DoD Advisor if questions about which product to use within United States.
YES
YES
ANAVIP REGIONAL COVERAGE FOR ALL PIT VIPER BITES IN USA / CANADA CONUS Dosing - See Unified Treatment Algorithm for Crotaline Snakebite OR contact Poison Control / DoD Advisor toxicologist for guidance.
CROFAB REGIONAL COVERAGE FOR ALL PIT VIPER BITES IN USA / CANADA CONUS Dosing - See Unified Treatment Algorithm for Crotaline Snakebite OR contact Poison Control / DoD Advisor toxicologist for guidance.
NOTE: Distribution of Coral Snake species in United States: AL, AR, AZ, FL, GA, LA, MS, NM, NC, OK, SC, TX
NOTE: UNIFIED TREATMENT ALGORITHM
See Unified treatment algorithm for the management of crotaline snakebite in the United States (Lavonas et al. 2011) for specific dosing and management guidelines on pit viper bites.


Antivenom Selection Flowchart: SOUTHCOM
Contact DoD ADVISOR toxicology consult at +1 (833) 238-7756 for pre-mission planning / antivenom questions or active bite consultations.
Follow list of steps outlined in CPG: Universal Approach to Snakebite Assessment, Diagnosis, and Treatment
NOTE: Yellow background indicates that a product meets both criteria below: 1) broad-spectrum regional coverage 2) freeze-dried / field-stable
Patient with S/Sx of envenomation?
NO
Follow Asymptomatic Algorithm for assessment and disposition guidance.
Syndrome?
NEUROTOXIC
HEMOTOXIC
CYTOTOXIC
Region?
Region?
CENTRAL AMERICA
SOUTH AMERICA
Known or suspected coral snake?
Known or suspected coral snake?
1st line = BIOCL-COR CENTRAL AMERICAN CORAL SNAKES
High dose = 10 vials
Low dose = 5 vials
1st line = INS-AAP SOUTH AMERICAN CORAL SNAKES
High dose = 10 vials
Low dose = 5 vials
Note - some neotropical vipers will cause neurotoxicity in addition to typical viper syndrome (cyto/hemo); treat these using CYTO/HEMO antivenom. Corals do not cause persistent bleeding or significant progressive swelling/tissue damage.
SOUTH AMERICA
1st line = PoliVal-ICP Alternate = INOSERP-MEX (field stable) or BUTANTAN-BCP (not field stable) COVERS ALL HEMO / CYTO
High dose = 10 vials
Low dose = 5 vials
Symptoms refractory to PoliVal-ICP? Consider INOSERP-MEX or BUTANTAN-BCP (broader coverage / different immunizing venom mixture)
High dose = 10 vials
Low dose = 5 vials
CENTRAL AMERICA
Region?
Costa Rica / Panama
Belize / Guatemala / Honduras / El Salvador / Nicaragua
1st line = PoliVal-ICP Alternate = INOSERP-MEX COVERS ALL HEMO / CYTO
High dose = 10 vials
Low dose = 5 vials
1st line = INOSERP-MEX Alternate = PoliVal-ICP COVERS ALL HEMO / CYTO
High dose = 10 vials
Low dose = 5 vials
Symptoms refractory to INOSERP-MEX? Consider PoliVal-ICP or BIOCL-AVT (different immunizing venom mixture)
High dose = 10 vials
Low dose = 5 vials

APPENDIX H, TABLE 1 –ANTIVENOM DOSING BY PRODUCT

JTS recommended HIGH/LOW doses are listed in this table and supersede any package inserts or dosing provided by the manufacturer.

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
POLYSERP-P *POLYSERP PAN-AFRICA* FREEZE-DRIED FIELD-STABLE	**AFRICOM** ***Sub-Saharan Africa*** 1st line - all critical threat species / syndromes. Covers *Atractaspis* and Boomslangs.	**AFRICOM** ***North Africa*** 2nd line - all critical threat species / syndromes. Covers Atractaspis (no boomslang in N. Africa).	H High Dose = 6 vials L Low Dose = 3 vials	NEURO HEMO CYTO
POLYSERP-M *POLYSERP MENA* FREEZE-DRIED FIELD-STABLE	**AFRICOM** **CENTCOM** ***North Africa / Middle East*** 1st line - all critical threat species / syndromes.	**AFRICOM** ***Sub-Saharan Africa*** 2nd line - all critical threat species / syndromes.	H High Dose = 6 vials L Low Dose = 3 vials	NEURO HEMO CYTO
SAIMR-P *SAVP SAIMR Polyvalent* REFRIGERATION REQUIRED	**AFRICOM** ***Sub-Saharan Africa*** 2nd line - all critical threat species / syndromes. In South Africa consider SAIMR-P due to native fauna specificity if not in austere setting. Otherwise use POLYSERP-P. HIGH RISK ANAPHYLAXIS PRETREAT (*1:1000 epi*)		H High Dose = 10 vials L Low Dose = 5 vials	NEURO HEMO CYTO
Inoserp P *Inoserp Pan-Africa* FREEZE-DRIED FIELD-STABLE	**AFRICOM** ***Sub-Saharan Africa*** 2nd line - all critical threat species / syndromes in sub-Saharan Africa.		H High Dose = 10 vials L Low Dose = 5 vials	NEURO HEMO CYTO
SAIMR-B *SAVP SAIMR Boomslang* REFRIGERATION REQUIRED Snake ID may be needed!	**AFRICOM** ***Sub-Saharan Africa*** 2nd line – Monovalent; boomslang envenomations only (HEMO). Purely hemotoxic venom, toxicity may be delayed 24+ hours HIGH RISK ANAPHYLAXIS PRETREAT (*1:1000 epi*)		H High Dose = 2 vials L Low Dose = 1 vials	HEMO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
NAVPC-P *NAVPC (Saudi Arabia) Polyvalent* REFRIGERATION REQUIRED	AFRICOM CENTCOM ***North Africa / Middle East*** 2nd line - all critical threat species / syndromes. CONSIDER PRETREATMENT ↑ *risk anaphylaxis (Epi 1:1000)*	H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO HEMO CYTO
SIOBP-G *Shanghai Institute of Biological Products – Gloydius Monovalent* REFRIGERATION REQUIRED Snake ID may be needed!	CENTCOM ***Middle East / Central Asia*** 1st / 2nd line - confirmed *Gloydius halys* bite. If unavailable, use POLYSERP-M. If no response to 2x high dose of POLYSERP-M and HEMO/CYTO dominant within Gloydius range, consider treatment with SIOBP-G.	H *High Dose = 2 vials* L *Low Dose = 1 vials*	HEMO CYTO
RAZI-P *RAZI Polyvalent Snake Antivenom* REFRIGERATION REQUIRED	CENTCOM ***Middle East / Central Asia*** 2nd Line - Unknown neurotoxic, hemotoxic, or cytotoxic envenomation with no indications of improvement after 12 vials of POLYSERP-M.	H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO HEMO CYTO
VIPERFAV *Viperfav (Sanofi-Pasteur)* REFRIGERATION REQUIRED	EUCOM ***Outside UK / Scandinavia*** 1st line – European adder bites outside of UK / Scandinavia causing NEURO or HEMO/CYTO symptoms.	H *High Dose = 2 vials* L *Low Dose = 1 vials*	NEURO HEMO CYTO
VIPERATAB *ViperaTAb (MicroPharm)* REFRIGERATION REQUIRED	EUCOM ***Within UK / Scandinavia*** 1st line – European adder bites outside of UK / Scandinavia causing NEURO or HEMO/CYTO symptoms.	H *High Dose = 2 vials* L *Low Dose = 1 vials*	HEMO CYTO
TRC-NPAV *Thai Red Cross Neuro Polyvalent* FREEZE-DRIED FIELD-STABLE	INDOPACOM ***Southeast Asia [NEURO]*** 1st line – Broadest-spectrum NEURO polyvalent available for most of Asia. Best 1st line option in most cases of suspected Cobra / Krait envenomation.	H *High Dose = 10 vials* L *Low Dose = 5 vials*	NEURO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
TRC-HPAV *Thai Red Cross Hemato Polyvalent* FREEZE-DRIED FIELD-STABLE	**INDOPACOM** ***Southeast Asia [HEMO/CYTO]*** 1st line – Broadest-spectrum HEMO/CYTO polyvalent available for most of Asia. Best 1st line option in most cases of suspected viperid envenomation. Does not cover *Rhabdophis* (NFFC HEMO only, rare).	H *High Dose = 10 vials* L *Low Dose = 5 vials*	HEMO CYTO
CSL-SS CSL Sea Snake REFRIGERATION REQUIRED	**INDOPACOM** ***Sea Snake Envenomations [Marine]*** 1st line – sea snake envenomations in Indo-Pacific region. Characterized by neurotoxicity + myotoxicity (rhabdo) and nephrotoxicity (direct AKI). CONSIDER PRETREATMENT ↑ *risk anaphylaxis (Epi 1:1000)* Seasnakes: bite rare, generally fishermen cutting out of nets/provoking	H *High Dose = 3 vials* L *Low Dose = 2 vials*	NEURO *NEURO + Myotoxic & Nephrotoxic*
CSL-P CSL Polyvalent REFRIGERATION REQUIRED	**INDOPACOM** ***SE of Wallace's Line (Maluku, W. Papua, Australasia)*** 1st line – NEURO/HEMO envenomations in Indo-Pacific region SE of Wallace's Line & Australasia. All elapids with mixed NEURO/HEMO syndrome. CONSIDER PRETREATMENT ↑ *risk anaphylaxis (Epi 1:1000)*	H *High Dose = 3 vials* L *Low Dose = 2 vials*	NEURO HEMO CYTO *NEURO / HEMO dominant syndrome*
CSTRI-HABU *Kaketsuken Habu Antivenom* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** ***Japan (Habu Monovalent)*** 1st line – HEMO/CYTO envenomations in Japan from Habu (*Protobothrops*). For Taianese, recommended local antivenom instead (unknown coverage).	H *High Dose = 2 vials* L *Low Dose = 1 vials*	HEMO CYTO
CSTRI-MAMU *Kaketsuken Mamushi Antivenom* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** ***Japan (Mamushi Monovalent)*** 1st line – HEMO/CYTO envenomations in Japan from Short-tailed Mamushi (*Gloydius blomhoffi*).	H *High Dose = 2 vials* L *Low Dose = 1 vials*	HEMO CYTO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
JSI-AYA *Anti-Yamakagashi Antivenom* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Japan/China/Koreas/Vietnam/E Russia** 1st Line – HEMO keelback monovalent (*Rhabdophis tigrinus*) (Asian boomslang equivalent). **Consider as 2nd line if bleeding / clotting issues persist after 2x high doses of HPAV.**	H High Dose = 2 vials L Low Dose = 1 vials	HEMO CYTO
KOVAX-AKA *Agkistrodon Mamushi Antivenom* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Korea (*Gloydius* Monovalent)** – Koreas / E. China (*Gloydius brevicaudus*) Korean Mamushi (For Japanese use CSTRI-MAMU)	H High Dose = 2 vials L Low Dose = 1 vials	HEMO CYTO
NIPM-NBB *Naja atra – Bungarus multicinctus* Bivalent REFRIGERATION REQUIRED	**INDOPACOM** **Taiwan / East China [NEURO] + [Cobras: Cyto +++ in region]** 1st line Bivalent indicated for all Cobra and Krait envenomations in Taiwan. Venom Detection Kits used locally for snake ID at bedside. **NOTE – Taiwanese Cobra bites present as CYTO dominant +/- neurotoxicity. Use for all suspected Cobra & Krait bites in Taiwan.** In China, use TRC-NPAV as 1st line NEURO, NIPM-NBB may be 2nd line. **Taiwan Cobra ID Tips**: Fast moving, shiny dark snake +/- white bands, may or may not raise head / open hood, many bites at night.	H High Dose = 5 vials L Low Dose = 3 vials	NEURO CYTO
NIPM-SNV *National Institute Preventative Medicine* (NIPM) *Sharp-nosed Viper Monovalent* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Taiwan, SE China, N. Vietnam, Laos** 1st line – Narrow-spectrum monovalent indicated solely for suspected sharp-nosed viper or failure of 2 high doses HPAV. Expect rapid CV collapse, bleeding, extensive tissue destruction. **Sharp-nosed Viper ID tips:** ZONE = rocky slopes/montane forest to 1500m; SNAKE = 4 – 5 ft, light brown copperhead-like body with lateral rows of "Hershey's kiss" dark triangles. Large triangular head, prominent elongated, up-sloping snout. "Hundred Pacer."	H High Dose = 4 vials L Low Dose = 2 vials	HEMO CYTO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications	**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
NIPM-PTBV *NIPM Protobothrops / Trimeresurus Bivalent* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Taiwan: Entire Island; unknown HEMO/CYTO viper bite OR snake ID** **(Habu or Green Pit Viper).** 1st line Taiwan – Bivalent for suspected habu / green pit viper **or unknown HEMO/CYTO dominant viper bite**. Venom Detection Kits used locally for snake ID at bedside. **Taiwan Habu / Green Viper ID Tips**: Most bites in Taiwan! Habu: 3 – 5 ft slender viper with long lance-shaped head. Brown body with variable blotched pattern. Widely distributed across Taiwan. Green Pit Viper (Bamboo Viper, Tree Viper): 1 - 3 ft long, green body, red eyes, whiteish belly. Often found in low vegetation.	H High Dose = 4 vials L Low Dose = 2 vials	HEMO CYTO
NIPM-RV *NIPM Russell's Viper Monovalent* REFRIGERATION REQUIRED Snake ID may be needed!	**INDOPACOM** **Taiwan: South / East Coastal Zones** 1st line Taiwan – Monovalent indicated for Russell's viper (*Daboia siamensis)* bites. Venom Detection Kits used locally for snake ID at bedside. **Taiwan Russell's Viper ID Tips:** ZONE: South & East coasts below 500m; SNAKE = Brown snake, fat body 3 – 5 ft long with 3 rows of oval spots along back [*black & white border, brownish center*], triangular head.	H High Dose = 4 vials L Low Dose = 2 vials	HEMO CYTO
CROFAB REFRIGERATION REQUIRED	**NORTHCOM** **USA & Canada** 1st line – broad-spectrum indicated for all viper envenomations in USA & Canada. **Not indicated for Mexico.**	*Refer to Unified Treatment Algorithm (CONUS)*	HEMO CYTO
ANAVIP FREEZE-DRIED FIELD-STABLE	**NORTHCOM** **USA & Canada** 1st line – broad-spectrum indicated for all viper envenomations in USA & Canada. **Not indicated for Mexico.**	*Refer to Unified Treatment Algorithm (CONUS)*	HEMO CYTO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
NACSA *North American Coral Snake Antivenin* REFRIGERATION REQUIRED	**NORTHCOM** **USA** 1st line – CORAL SNAKES ONLY (NEURO). Indicated for all coral snake envenomations. **Not indicated for Mexico. Contact Poison Control to obtain 1(800)-222-1222.**		Call poison control for dosing (CONUS)	NEURO
INOSERP-MEX *Inoserp Mexico (Inosan Biopharma, Mexico)* FREEZE-DRIED FIELD-STABLE	**NORTHCOM** **Mexico** 1st line - all viper envenomations in Mexico	**SOUTHCOM** **Belize, Guatemala, Honduras, El Salvador, Nicaragua** 1st line – all viper envenomations in Northern Central America. **Costa Rica, Panama, South America** 2nd line - all viper bites from Costa Rica southwards.	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
BIOCL-AVT *Antivipmyn-Tri (Instituto Bioclon / Laboratorios Silanes, Mexico)* FREEZE-DRIED FIELD-STABLE	**SOUTHCOM** **Costa Rica, Panama, South America** 1st line – all viper bites from Costa Rica southwards.	**NORTHCOM** **Mexico** 2nd line - all viper envenomations in Mexico.	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
PoliVal-ICP *Antiveneno Antiofídico Polivalente (Instituto Clodomiro Picado, Costa Rica)* FREEZE-DRIED FIELD-STABLE REFRIGERATION REQUIRED	**SOUTHCOM** **Costa Rica, Panama, South America** 1st line - all viper bites from Costa Rica southwards. Pretreat with epi. CONSIDER PRETREATMENT ↑ risk anaphylaxis (Epi 1:1000) *NOTE – Comes in both lyophilized/field-stable and liquid/refrigerated formulations.*	**SOUTHCOM** **Belize, Guatemala, Honduras, El Salvador, Nicaragua** 2nd line – all viper envenomations in Northern Central America. Pretreat with epi. CONSIDER PRETREATMENT ↑ risk anaphylaxis (Epi 1:1000) *NOTE – Comes in both lyophilized/field-stable and liquid/refrigerated formulations.*	H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO

Short Name *Full Name* [Field Stability]	**CCMD** **Regional Coverage** + Indications		**Algorithmic Dosing** *(High / Low)*	**Syndromes Covered**
BUTANTAN-BCP *Soro Antibotrópico-Crotálico (Instituto Butantan, Brazil)* REFRIGERATION REQUIRED	SOUTHCOM **South America** Alternative 2nd line – all viper bites in South America. Only available as a refrigerated liquid formulation, store at 2 – 8 ºC (DO NOT FREEZE). Moderately high rates of reaction anticipated, pretreat with epi. Reasonable alternative for treatment refractory viper bites that fail to respond to PoliVal-ICP and/or INOSERP-MEX in South America. CONSIDER PRETREATMENT ↑risk anaphylaxis (Epi 1:1000)		H High Dose = 10 vials L Low Dose = 5 vials	HEMO CYTO
BIOCL-COR *CORALMYN (Instituto Bioclon, Mexico)* FREEZE-DRIED FIELD-STABLE REFRIGERATION REQUIRED	SOUTHCOM **Central America** 1st line - all coral snakes in Mexico & Central America. *NOTE – Produced in both in freeze-dried field-stable or liquid (refrigerated) forms.*	SOUTHCOM **South America** 2nd line – all coral snakes in South America. *NOTE – Produced in both in freeze-dried field-stable or liquid (refrigerated) forms.*	H High Dose = 10 vials L Low Dose = 5 vials	NEURO
INS-AAP *Antiveneno Anticoral Polivalente (Brazil)* REFRIGERATION REQUIRED	SOUTHCOM **South America** 1st line – all coral snakes in South America.	SOUTHCOM **Central America** 2nd line - all coral snakes in Central America.	H High Dose = 10 vials L Low Dose = 5 vials	NEURO

APPENDIX I: CLASS VIII MEDICAL MATERIEL

1. Antivenom & Snakebite-Specific Medications

Primary therapeutic agents

- Antivenom - Minimum: 2 high doses
  OR 4 low doses per Antivenom needed.
- Epinephrine 2mg (1:1000 (IM anaphylaxis), 1:10,000 (IV))
- Atropine (Multidose vials 8mg/20mL, or 4x 1mg/mL vials)
- Neostigmine

Anaphylaxis medications:

- Epinephrine (1:1000 (IM anaphylaxis), 1:10,000 (IV))
- Corticosteroids (e.g., methylprednisolone or dexamethasone)
- H1 antihistamines (e.g., diphenhydramine)
- H2 antihistamines (e.g., famotidine)

Special ophthalmic medications (Spitting Cobra exposures)

- Tetracaine ophthalmic
- Phenylephrine 10% ophthalmic
- Antibiotic eye drops (e.g. oxfloxacin or moxifloxacin gtts)
- Lubricating eye drops

2. Adjunct Medications

- Ketamine
- Fentanyl
- Acetaminophen (PO/IV)
- Antibiotics (IV and ophthalmic as needed)
- Benzodiazepines (for seizures)
- Etomidate (If not using Ketamine)
- Paralytics (If considering RSI + Trained)
- Tetanus vaccine
- Antibiotics (IV and ophthalmic as needed)

3. Blood Products

- Whole Blood

4. Intravenous Fluids & Administration

- Normal Saline (preferred; flushes for rapid mix/push + bag for mixing & antivenom infusion, if given by infusion)
- Lactated Ringer's (alternative)
- Bag sizes: 250mL Preferred
  - Alternate: 100mL, or SIVP only if supplies are low.
  - 500 and 1000 mL, adds unneeded time and fluid, especially for pediatrics.
  - 10 cc syringes (or saline flushes) + fill needles

5. IV / IO Access Equipment

- Peripheral IV catheters - Various sizes (22–18g)
- IV start kits
- IO access kits
- Coban for IVs on diaphoretic patients
- Central line kits
- Tegaderm
- Medical tape
- Syringes – (1, 3, 5, 10, and 20 mL)
- Needles
- Tape

6. Airway & Ventilation Equipment

- Cricothyroidotomy kit
- Endotracheal tubes
- Supraglottic airway (iGel)
- Bag Valve Mask (BVM)
- PEEP valve
- Ventilator
- Oxygen supply (O2 tanks, Oxygen concentrator, and Masks/NRB)
- Laryngoscope (VL preferred)
- Powered suction unit
- Backup manual suction device
- Assorted suction catheters
- NG and OG tubes (various sizes)

7. Monitoring & Diagnostic Equipment

- Sharpies 2-3
- Pulse oximeter
- Non-invasive blood pressure monitor
- ECG monitor
- Temperature monitor
- Respiratory rate monitoring
- Capnography
- Peak flow meter
- Spirometer
- Glucometer

8. Laboratory Capability

- iSTAT system (CBC, CMP, Hemoglobin / Hematocrit, PT / PTT / INR, Fibrinogen, Creatine Kinase (CK)
- Test strips / lancets
- Vacutainer tubes (red-top)
- Clean, dry, 100% glass tubes for WBCT
- Blood draw needles

9. Ophthalmic Diagnostic Equipment

- Fluorescein stain kit
- Slit lamp (if available)
- Ophthalmoscope

10. Wound Care & Limb Management

- Bandages
- Sterile dressings
- Splints

For additional information including National Stock Number (NSN), please contact dha.ncr.med-log.list.lpr-cps@health.mil

DISCLAIMER: *This is not an exhaustive list. These are items identified to be important for the care of combat casualties.*

APPENDIX J: WHOLE BLOOD CLOTTING TEST

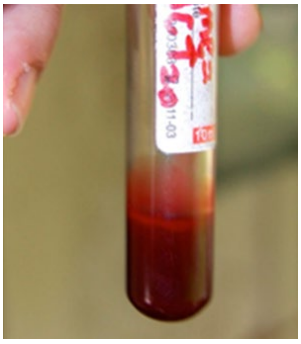
Whole Blood Clotting Test for Venom-Induced Consumptive Coagulopathies

The whole blood clotting test (WBCT) is a simple but critical bedside gross examination used in the assessment, diagnosis, and therapeutic monitoring of snakebite patients in the developing world and remote environments.[1-10] Refer to the diagram below regarding instructions for performing the test. At minutes 20 and 30, the tube is gently picked up and tilted 90 degrees; a stable solid clot retained within the tube is scored "Grade 0" and indicates normal coagulation. Abnormal results are scored "Grade 1" for a partial, semisolid clot that breaks apart and detaches from the glass tube shortly after it is turned or "Grade 2" for completely incoagulable liquid blood that pours out of the tube immediately. Attempting to score the test earlier than 20 minutes will not yield accurate results due to the consumptive mechanism of the coagulopathy. Using a healthy donor as a control is ideal to confirm questionable findings.

Continue WBCT testing throughout the course of care to monitor for secondary resumption of venom-induced consumptive coagulopathy.[11-13] After control of the envenomation has been achieved, reassess WBCT every 24 hours throughout the course of hospitalization. It is important to remember that the WBCT must be interpreted in the context of the larger clinical picture. If a patient has improved in all parameters except for a persistent abnormal WBCT, it may reflect an inertia in replenishment of depleted clotting factors after a severe hemotoxic envenomation.[1] If the venom is active then hematocrit should continue to decrease or signs of ongoing hemolysis or bleeding should be present.

Whole Blood Clotting Test (WBCT)

Draw 2 mL of venous blood and transfer directly into a clean and dry glass tube. Leave it upright, open, undisturbed for 20 and/or 30 minutes at room temp.



Collection: a blood sample for WBCT testing immediately after collection.

After exactly 20 minutes, pick up the tube and invert it. If a solid clot is retained, the test indicates normal coagulation.

Normal: a solid clot is retaining upon inversion of the tube at 20 or 30 minutes (Grade 0, no coagulopathy).

If clot breaks down quickly upon inversion of the tube or fails to coagulate, the test indicates a coagulopathy.

Abnormal: clot degrades rapidly (Grade 1, friable clot) or fails to coagulate whatsoever (Grade 2).

APPENDIX K: METHODOLOGY FOR CLINICAL & OPERATIONAL UPDATES

This revision of the Joint Trauma System (JTS) Snakebite Envenomation Clinical Practice Guidelines followed the established JTS framework for updating existing CPGs, with emphasis on operational relevance and improved bedside usability for providers at all levels across the continuum of care (prehospital through Role 3). The update was conducted as a focused, expert-driven revision of the original CPG ID 81 (2020) to achieve the following:

1. Improving bedside usability as a clinical reference tool and enabling rapid, time-critical decision-making through streamlined ACLS-style STAT treatment algorithms.
2. Enhancing operational relevance, pre-mission planning, and force health protection in deployed settings globally.
3. Simplified syndrome and severity-driven antivenom dosing guidance designed to reduce preventable deaths and disabilities through rapid initiation of treatment at the POI and early consultation with DoD Advisor toxicologists.
4. Printable rapid-reference tools optimized for austere and resource-limited environments including dosing tables, antivenom coverage algorithms, and suggested antivenom treatment packing checklist.
5. Expanded INDOPACOM algorithms with dedicated regional management pathways to address coverage gaps in Taiwan, Japan, the Korean Peninsula, China/East Asia, and other high-risk geographic regions.

Antivenom Recommendations

Antivenom selection was based on a combination of published evidence and expert experience. Authors prioritized antivenoms which offered broad-spectrum regional coverage of medically significant species, enabled syndromic treatment without reliance on species identification, could be carried for extended periods in field conditions without cold chain, and demonstrated low rates of adverse reactions in peer-reviewed studies or firsthand applications. Due to the lack of high quality studies on many antivenoms globally, whenever possible first line antivenoms were selected from manufacturer product platforms which have been used extensively by the authors in comparable operational environments. Strategic considerations, including supply chain reliability and security risks (e.g. deprioritization of products manufactured by adversarial states) were also considered.

APPENDIX L: SNAKEBITE CPG DEVELOPMENT PROCESS

This Clinical Practice Guideline (CPG) was developed to provide pragmatic clinical guidance for military medical providers managing snakebite envenomations in far-forward, expeditionary settings.

Recognizing the ethical and logistical challenges of conducting rigorous clinical trials for time-critical envenomations on the battlefield, the recommendations herein are based on the best available evidence. Where high-quality published data is limited, the guidance reflects a synthesis of available literature, author experience, and expert recommendations. The methodology incorporates SME opinion, operational experience, observational studies, and unpublished data to address gaps in military or civilian literature.

In line with Joint Trauma System (JTS) policy, this CPG prioritizes operational relevance, speed, and real-time performance improvement. Therefore, it does not adhere to all standards of the National Academy of Sciences, Engineering, and Medicine, such as formal strength-of-evidence grading. Final adjudication was achieved through a structured, iterative expert review and consensus of selected senior authors, rather than a formal Delphi methodology. While potentially useful for civilian providers in austere environments, this CPG is specifically tailored to the unique capabilities and needs of military medical personnel.

Roles & Responsibilities

The development and revision of this CPG were managed through a structured process involving a working group leader, section authors, and a senior author group.

- Working Group Leader: The first author (JM) led the JTS Snakebite Envenomation Working Group, defined the scope, provided revisions, and ensured compliance with JTS development standards.
- Senior Author Group: A senior group composed of JMB, BG, CD, EB, AF, and JM conducted a secondary review and iterative revisions of all draft sections. This group represented key stakeholders across the continuum of care, including conventional and special operations paramedics, emergency medicine physicians, toxicologists, and non-toxicologist experts in austere envenomations.
- Additional Subject Matter Experts: JMB and BG also consulted with DR, MC, JL, CP, NB, BW, KM, and SG as additional domain SMEs on specialized topics throughout the process.

The original CPG was divided into the following sections for initial review and revision:

Section	Assigned Authors
General Principles/Universal Approach/Special Situations	MK, DSM, NS, DR, MC, TW, CD, EB, AF, JL
STAT Treatment, Pre-Mission Planning, Appendixes	JMB, CD, EB, BG, AF, DR, MC, JL, CP, KM
AFRICOM	AF, DB, JMB, BG, MC, DR, CP
INDOPACOM	BG, JMB, NB, BW, SG, JL, MC, MK, CP
CENTCOM, EUCOM, NORTHCOM, SOUTHCOM	JMB, BG, DR, MC, JL, NB

Approval & Finalization

Draft sections were extensively reviewed by the senior author group to ensure clinical validity and operational feasibility. Once consensus was achieved, the recommendations were passed to the first author (JM) for final review. The consolidated document was then reviewed by designated DoD toxicology reviewers and advanced through the formal JTS review and approval pathway.

APPENDIX M: FUTURE SNAKEBITE THERAPIES IN R&D PIPELINE

Several investigational drugs currently under study for snakebite treatment have received significant public and media attention in recent years.[263,264] The most promising are small-molecule therapeutics (SMTs), notably the phospholipase A_2 (PLA_2) inhibitor varespladib and the snake-venom metalloprotease (SVMP) inhibitor marimastat. However, they have been frequently mischaracterized in press reports as "universal antivenoms" when they are neither universal nor antivenoms, leading to significant confusion among medical providers and policymakers. In some cases, this confusion has complicated the efforts of medical providers seeking to obtain CPG recommended antivenoms for deployments OCONUS, negatively impacting Force Health Protection. It is therefore critical to clarify the position of the Joint Trauma System on investigational drugs for snakebite treatment.

1. **The only definitive treatment for a snake envenomation is the timely administration of appropriate antivenom at the appropriate dose required to neutralize circulating venom compounds.** SMTs may eventually prove useful as adjunct therapies to be given in addition to recommended antivenoms, but not as replacements. Due to the complexity of snake venoms and envenomations, this is unlikely to change in the next 20+ years.
2. The utility of SMTs lies not in replacing antivenoms, but in supporting them as adjunct therapies much like TXA, either in prehospital settings when ALS-capable providers are not available to administer IV/IO antivenoms or, in some cases, potentially as co-administered medications given with antivenom to improve outcomes where coverage may be lacking. **In all cases, the best outcome depends on timely administration of the appropriate antivenom to the patient. Definitive treatment with antivenoms given at the earliest opportunity will remain the single most important factor in determining patient outcomes in these cases.**
3. While some SMTs have shown early promise, their safety, tolerability, and efficacy must be demonstrated in rigorous, peer-reviewed clinical trials before any consideration for inclusion in the Clinical Practice Guidelines can be made. This process will likely take years and the outcome is uncertain. The JTS Snakebite Envenomation Working Group will continue to monitor advances in snakebite therapies and will incorporate new treatments into the guidelines when it is appropriate to do so based on rigorous scientific evidence and clinical best practices.

APPENDIX N: FDA FORM 1572

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

STATEMENT OF INVESTIGATOR

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014
Expiration Date: September 30, 2026
See OMB Statement on Reverse.

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

Name of Clinical Investigator

Address 1		Address 2	
City	State/Province/Region	Country	ZIP or Postal Code

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS PROVIDED *(Select one of the following.)*

☐ Curriculum Vitae ☐ Other Statement of Qualifications

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED — CONTINUATION PAGE for Item 3

Name of Medical School, Hospital, or Other Research Facility

Address 1		Address 2	
City	State/Province/Region	Country	ZIP or Postal Code

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY — CONTINUATION PAGE for Item 4

Name of Clinical Laboratory Facility

Address 1		Address 2	
City	State/Province/Region	Country	ZIP or Postal Code

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES) — CONTINUATION PAGE for Item 5

Name of IRB

Address 1		Address 2	
City	State/Province/Region	Country	ZIP or Postal Code

6. NAMES OF SUBINVESTIGATORS *(If not applicable, enter "None")*

CONTINUATION PAGE – for Item 6

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR

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8. PROVIDE THE FOLLOWING CLINICAL PROTOCOL INFORMATION. *(Select one of the following.)*

☐ For Phase 1 investigations, a general outline of the planned investigation including the estimated duration of the study and the maximum number of subjects that will be involved.

☐ For Phase 2 or 3 investigations, an outline of the study protocol including an approximation of the number of subjects to be treated with the drug and the number to be employed as controls, if any; the clinical uses to be investigated; characteristics of subjects by age, sex, and condition; the kind of clinical observations and laboratory tests to be conducted; the estimated duration of the study; and copies or a description of case report forms to be used.

9. COMMITMENTS

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64. I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

INSTRUCTIONS FOR COMPLETING FORM FDA 1572
STATEMENT OF INVESTIGATOR

1. Complete all sections. Provide a separate page if additional space is needed.
2. Provide curriculum vitae or other statement of qualifications as described in Section 2.
3. Provide protocol outline as described in Section 8.
4. Sign and date below.
5. FORWARD THE COMPLETED FORM AND OTHER DOCUMENTS BEING PROVIDED TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.

10. DATE *(mm/dd/yyyy)*	11. SIGNATURE OF INVESTIGATOR Sign

(**WARNING**: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

The information below applies only to requirements of the Paperwork Reduction Act of 1995.

The burden time for this collection of information is estimated to average 100 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the address to the right:

Department of Health and Human Services
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Office of Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

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DO NOT SEND YOUR COMPLETED FORM TO THIS PRA STAFF EMAIL ADDRESS.

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AN=97769554&h=aCL3DOIU4Hd42wlqYcgdgZj%2FBGL85TNYqaRzpVEugU8VMNFsJPUh89ow7KIxuquHIM1uSTGZjlV9DyrrRuZQxw%3D%3D&crl=c.

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APPENDIX P: TELEMEDICINE / TELECONSULTATION

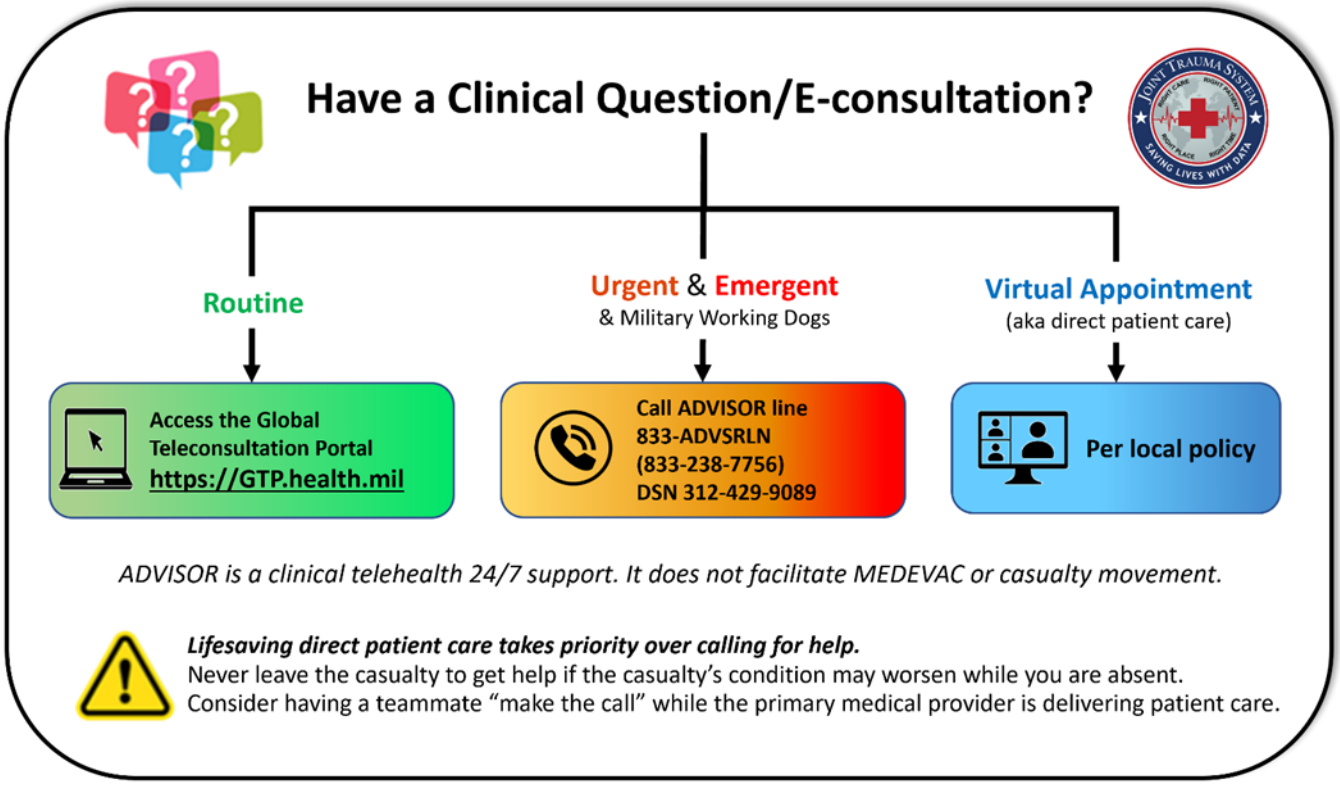

Illustration by Raymond Samonte

GTP: https://GTP.health.mil

Theater Patient Movement Requirements Center (TPMRC) to coordinate evacuation:

- *TPMRC-Americas (NORTHCOM & SOUTHCOM), 618-817-4200*
- *TPMRC- East (EUCOM, AFRICOM, CENTCOM), DSN 314-480-8040*
- *TPMRC- West (INDOPACOM), DSN 315-448-1062*

APPENDIX Q: INFORMATION REGARDING OFF-LABEL USES IN CPGS

PURPOSE

The purpose of this Appendix is to ensure an understanding of DoD policy and practice regarding inclusion in CPGs of "off-label" uses of U.S. Food and Drug Administration (FDA)–approved products. This applies to off-label uses with patients who are armed forces members.

BACKGROUND

Unapproved (i.e. "off-label") uses of FDA-approved products are extremely common in American medicine and are usually not subject to any special regulations. However, under Federal law, in some circumstances, unapproved uses of approved drugs are subject to FDA regulations governing "investigational new drugs." These circumstances include such uses as part of clinical trials, and in the military context, command required, unapproved uses. Some command requested unapproved uses may also be subject to special regulations.

ADDITIONAL INFORMATION REGARDING OFF-LABEL USES IN CPGS

The inclusion in CPGs of off-label uses is not a clinical trial, nor is it a command request or requirement. Further, it does not imply that the Military Health System requires that use by DoD health care practitioners or considers it to be the "standard of care." Rather, the inclusion in CPGs of off-label uses is to inform the clinical judgment of the responsible health care practitioner by providing information regarding potential risks and benefits of treatment alternatives. The decision is for the clinical judgment of the responsible health care practitioner within the practitioner-patient relationship.

ADDITIONAL PROCEDURES

Balanced Discussion

Consistent with this purpose, CPG discussions of off-label uses specifically state that they are uses not approved by the FDA. Further, such discussions are balanced in the presentation of appropriate clinical study data, including any such data that suggest caution in the use of the product and specifically including any FDA-issued warnings.

Quality Assurance Monitoring

With respect to such off-label uses, DoD procedure is to maintain a regular system of quality assurance monitoring of outcomes and known potential adverse events. For this reason, the importance of accurate clinical records is underscored.

Information to Patients

Good clinical practice includes the provision of appropriate information to patients. Each CPG discussing an unusual off-label use will address the issue of information to patients. When practicable, consideration will be given to including in an appendix an appropriate information sheet for distribution to patients, whether before or after use of the product. Information to patients should address in plain language: a) that the use is not approved by the FDA; b) the reasons why a DoD health care practitioner would decide to use the product for this purpose; and c) the potential risks associated with such use.