

# **CDC Resources Available for Evaluation and Management of Smallpox Vaccine Adverse Events**

**Smallpox Vaccine Adverse Event  
Workshop**

**January 22-23, 2003**



# Resources covered in session

- **Clinical Evaluation Tools**
  - dermatologic tools (3)
  - ocular
  - neurologic
- **VIG and Cidofovir**
  - VIG clinical evaluation tool
  - schematic of VIG release process
  - suggested clinical case definitions for clinical team consultation
- **VIG and Cidofovir: description of products and their INDs**

## Frequently Asked Questions and Answers

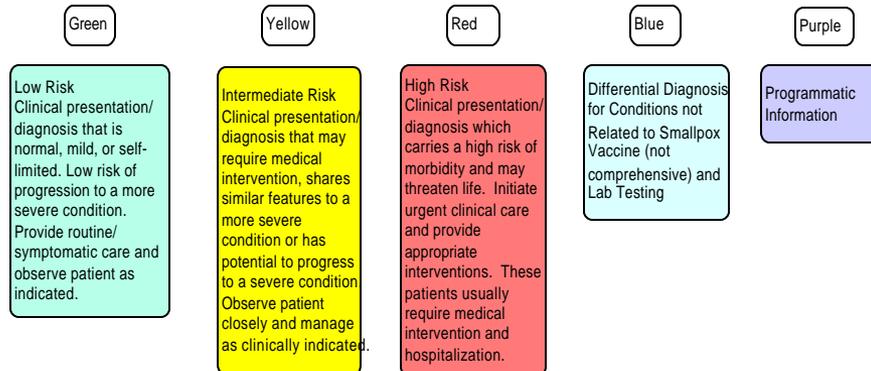
### How do I use the Clinical Evaluation Tools for Smallpox Vaccine Adverse Reactions?

The Clinical Evaluation Tools for Smallpox Vaccine Adverse Reactions are intended to be used by trained clinicians.

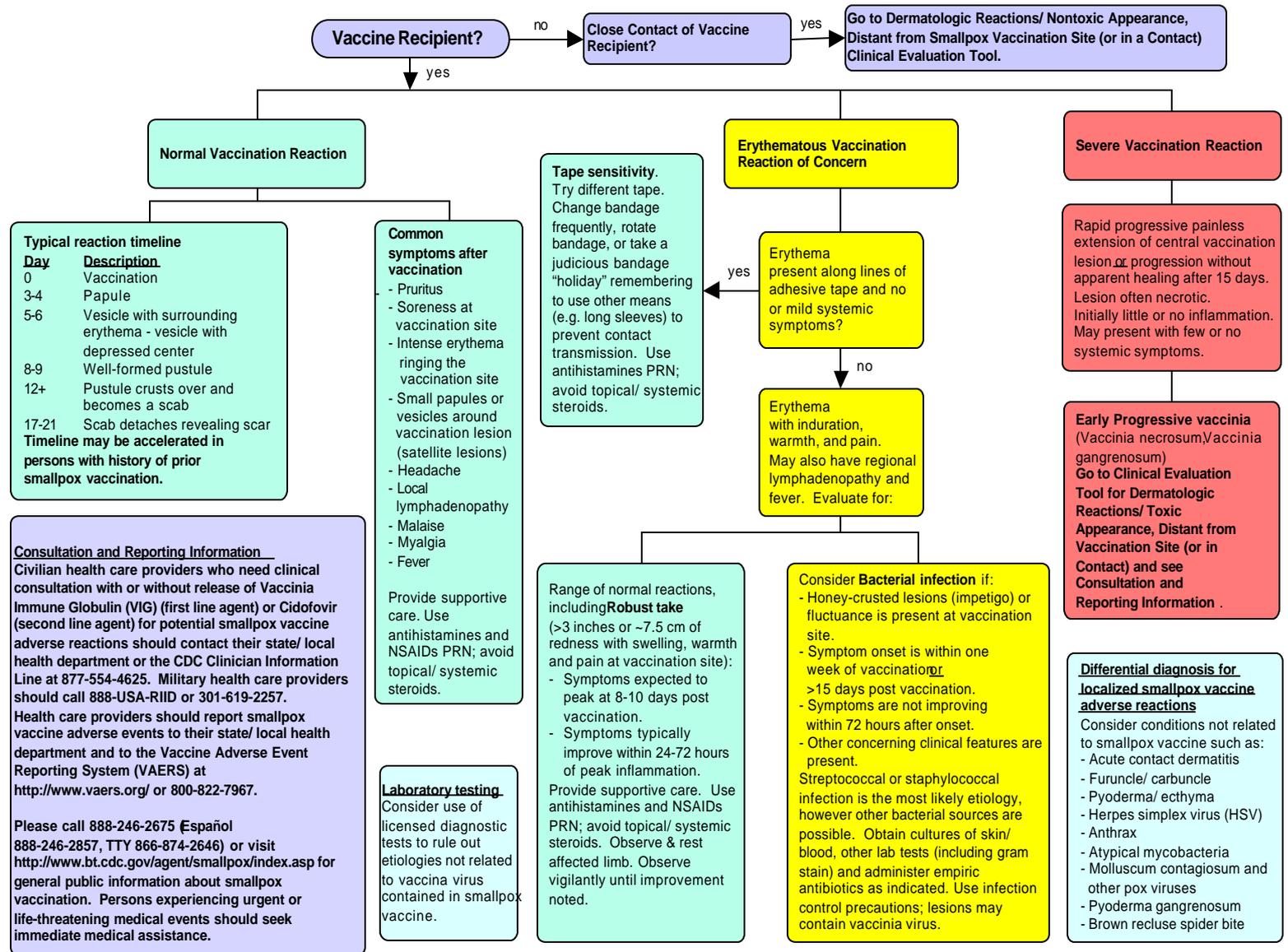
1. Choose the appropriate Clinical Evaluation Tool using the title as a guide.
2. Determine
  - the type of potential smallpox vaccine adverse reaction.
  - if the patient has a toxic or nontoxic appearance if applicable to the Tool (use both tools if toxicity is difficult to determine).
  - if the patient is a smallpox vaccine recipient (vaccinee) or a close contact of a smallpox vaccine recipient.
3. Work through the boxes in the Clinical Evaluation Tool to determine if your patient fits one or more of the descriptions.
4. Consider the differential diagnosis (not comprehensive) of conditions not related to the smallpox vaccine provided in each Clinical Evaluation Tool.
5. After narrowing the diagnostic considerations, read about the conditions in more detail (see question on more information about smallpox vaccine adverse reactions).
6. Review the diagnostic, treatment, and reporting information provided in the Clinical Evaluation Tool and contact your state/local health department and CDC as indicated.

### What do the colors mean in the Clinical Evaluation Tools?

Some of the Clinical Evaluation Tools are color coded to assist clinicians triage and manage patients. The legend is as follows:



**Clinical Evaluation Tool for Smallpox Vaccine Adverse Reactions**  
**Dermatologic Reactions/ Localized to Vaccination Site (1-20-2003 Version)**  
[www.bt.cdc.gov/agent/smallpox/vaccination/clinEval](http://www.bt.cdc.gov/agent/smallpox/vaccination/clinEval) **DRAFT DO NOT DISTRIBUTE**



**Typical reaction timeline**

Day	Description
0	Vaccination
3-4	Papule
5-6	Vesicle with surrounding erythema - vesicle with depressed center
8-9	Well-formed pustule
12+	Pustule crusts over and becomes a scab
17-21	Scab detaches revealing scar

**Timeline may be accelerated in persons with history of prior smallpox vaccination.**

**Common symptoms after vaccination**

- Pruritus
- Soreness at vaccination site
- Intense erythema ringing the vaccination site
- Small papules or vesicles around vaccination lesion (satellite lesions)
- Headache
- Local lymphadenopathy
- Malaise
- Myalgia
- Fever

Provide supportive care. Use antihistamines and NSAIDs PRN; avoid topical/ systemic steroids.

**Tape sensitivity.**  
 Try different tape. Change bandage frequently, rotate bandage, or take a judicious bandage "holiday" remembering to use other means (e.g. long sleeves) to prevent contact transmission. Use antihistamines PRN; avoid topical/ systemic steroids.

Range of normal reactions, including **Robust take** (>3 inches or ~7.5 cm of redness with swelling, warmth and pain at vaccination site):

- Symptoms expected to peak at 8-10 days post vaccination.
- Symptoms typically improve within 24-72 hours of peak inflammation.

Provide supportive care. Use antihistamines and NSAIDs PRN; avoid topical/ systemic steroids. Observe & rest affected limb. Observe vigilantly until improvement noted.

**Erythematous Vaccination Reaction of Concern**

Erythema present along lines of adhesive tape and no or mild systemic symptoms?

Erythema with induration, warmth, and pain. May also have regional lymphadenopathy and fever. Evaluate for:

Consider **Bacterial infection** if:

- Honey-crusted lesions (impetigo) or fluctuance is present at vaccination site.
- Symptom onset is within one week of vaccination or >15 days post vaccination.
- Symptoms are not improving within 72 hours after onset.
- Other concerning clinical features are present.

Streptococcal or staphylococcal infection is the most likely etiology, however other bacterial sources are possible. Obtain cultures of skin/ blood, other lab tests (including gram stain) and administer empiric antibiotics as indicated. Use infection control precautions; lesions may contain vaccinia virus.

**Severe Vaccination Reaction**

Rapid progressive painless extension of central vaccination lesion or progression without apparent healing after 15 days. Lesion often necrotic. Initially little or no inflammation. May present with few or no systemic symptoms.

**Early Progressive vaccinia** (Vaccinia necrosum, Vaccinia gangrenosum)  
**Go to Clinical Evaluation Tool for Dermatologic Reactions/ Toxic Appearance, Distant from Vaccination Site (or in Contact) and see Consultation and Reporting Information .**

**Differential diagnosis for localized smallpox vaccine adverse reactions**

Consider conditions not related to smallpox vaccine such as:

- Acute contact dermatitis
- Furuncle/ carbuncle
- Pyoderma/ ecthyma
- Herpes simplex virus (HSV)
- Anthrax
- Atypical mycobacteria
- Molluscum contagiosum and other pox viruses
- Pyoderma gangrenosum
- Brown recluse spider bite

**Consultation and Reporting Information**  
 Civilian health care providers who need clinical consultation with or without release of Vaccinia Immune Globulin (VIG) (first line agent) or Cidofovir (second line agent) for potential smallpox vaccine adverse reactions should contact their state/ local health department or the CDC Clinician Information Line at 877-554-4625. Military health care providers should call 888-USA-RIID or 301-619-2257. Health care providers should report smallpox vaccine adverse events to their state/ local health department and to the Vaccine Adverse Event Reporting System (VAERS) at <http://www.vaers.org> or 800-822-7967.

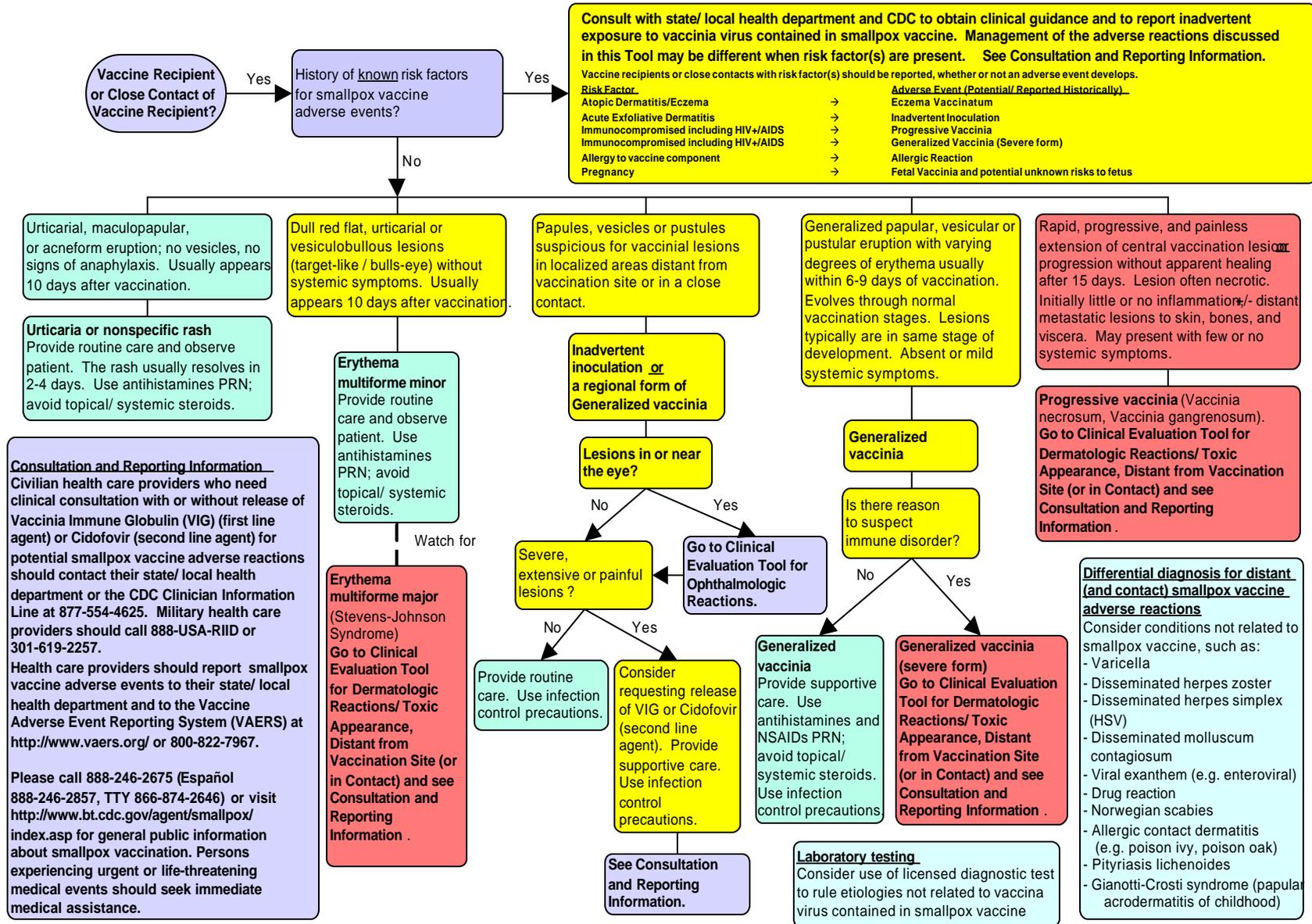
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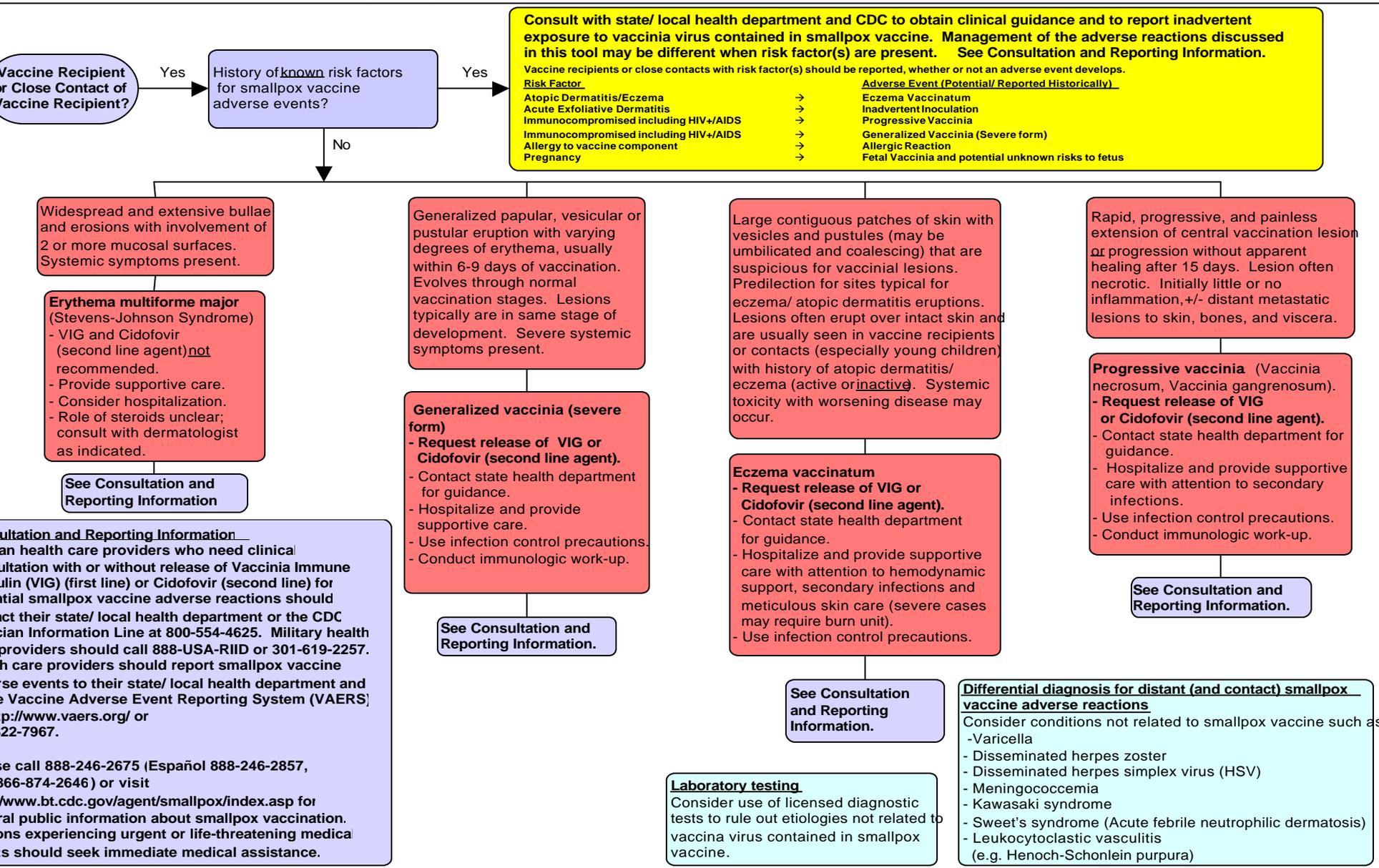
**Disclaimer** The CDC and its partners in the Clinical Immunization Safety Assessment (CISA) network have developed Clinical Evaluation Tools to help health care providers manage patients with potential adverse reactions from smallpox vaccination in the absence of circulating smallpox virus (pre-event setting). These Tools are based on studies conducted before routine childhood US smallpox vaccination was discontinued in 1972 and on expert opinion; they are not entirely evidence-based. The Tools may not apply to all patients with smallpox vaccine adverse events and are not intended to substitute for evaluation by a trained clinician. This Tool was last updated on 1-20-03. Please direct feedback on these Tools to [spoxtool@cdc.gov](mailto:spoxtool@cdc.gov).

# Clinical Evaluation Tool for Smallpox Vaccine Adverse Reactions

## Dermatologic Reactions/ Nontoxic Appearance, Distant from Vaccination Site (or in a Close Contact) (1-20-2003Version)

[www.bt.cdc.gov/agent/smallpox/vaccination/clineval](http://www.bt.cdc.gov/agent/smallpox/vaccination/clineval) **DRAFT DO NOT DISTRIBUTE**





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# Clinical Evaluation Tool for Smallpox Vaccine Adverse Reactions Ophthalmologic Reactions/Inadvertent Inoculation, Vaccinee (or in a Close Contact) (1-20-2003 Version)

[www.bt.cdc.gov/agent/smallpox](http://www.bt.cdc.gov/agent/smallpox)

Consult with state/local health department and CDC to obtain clinical guidance and to report inadvertent exposure to vaccinia virus contained in smallpox vaccine. Management of the adverse events discussed in this tool may differ when a risk factor is present. See Consultation and Reporting Information below. Vaccine recipients or close contacts with risk factor(s) should be reported, whether or not they develop an adverse event.

Risk Factor

Adverse Event

Atopic Dermatitis/Eczema (including severe ulcerative blepharitis) ? Eczema Vaccinatum

Vaccine recipient or close contact of vaccine recipient?

Yes

History of known risk factors for smallpox vaccine adverse events?

Yes

No

New onset red eye and/or lesions suspicious for vaccinia (papules, vesicles, pustules or ulcerations) in or near the eye.

**Patient history and physical exam of eye:** Use infection control precautions. Consider differential diagnosis (see separate box). Conduct ophthalmic evaluation to include:

- o Visual acuity testing
- o Presence or absence of lesions
- o Location of lesions
- o Presence and severity conjunctival inflammation ("red eye")
- o Presence and severity of corneal and lid involvement

Magnified exam of eye surface (slit lamp exam if available) and fluorescein exam for corneal epithelial

Probable **inadvertent inoculation** in or near eye

Possible **inadvertent inoculation** in or near eye

White non-inflamed eye associated with suspicious lid [2] or **periocular** [1] lesions only. No visible lesions in eye.

Red inflamed eye (**conjunctivitis** [3]) with suspicious lesions in or near the eye

Red eye (**conjunctivitis** [3]) only – no visible lesion in or near the eye.

No

Corneal [4] lesions?

Yes

Lesions on or near lid margin (**blepharitis** [2])

Conjunctival [3], lid [2] or periocular [1] lesions.

Associated conjunctival [3] or lid [2] lesions?

Evaluate using differential diagnosis for patient with new onset red eye but include vaccinia infection in differential. Close observation for development of suspicious lesions. Recommend ophthalmology consultation as indicated to evaluate for possible vaccinia versus other unrelated causes. Further treatment as indicated by ophthalmic exam.

No

Yes

**Isolated periocular lesions:** Close observation. Consider ophthalmology consultation to assist in

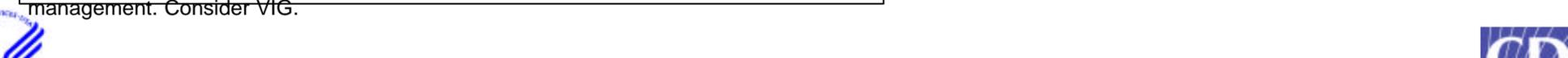
**Mild:** Begin **prophylaxis** [5] Urgent ophthalmology consultation. Consider VIG.  
**Severe:** Begin **prophylaxis** [5], Emergent ophthalmology consultation. Recommend VIG.

**Keratitis only:** Begin topical antiviral **treatment** [6]. Emergent ophthalmology consultation to evaluate and assist with management.

**Blepharitis and/or conjunctivitis associated with keratitis:** Emergent ophthalmology consultation  
**Mild:** Begin topical antiviral **treatment** [6]. Consider VIG  
**Severe:** Begin topical anti

**Mild Blepharitis:** Consider topical antiviral **prophylaxis** [5] especially if lesions are present on lid margin. Recommend ophthalmology consultation to assist in management  
**Moderate/Severe Blepharitis:** Begin topical antiviral **prophylaxis** [5]. Ophthalmology consultation in 12-24 hours (or sooner depending on severity) to evaluate and assist in management. Consider VIG.

VIG not indicated.



## **Clinical Evaluation Tool for Smallpox Vaccine Adverse Reactions Neurologic Reaction/Vaccine Recipient (or in a Contact)**

**I. Cognitive symptoms:  
encephalopathy defined  
as altered mental status  
or personality changes  
of > 24 hour duration**

**II. Sensory or motor  
symptoms with a  
temporal  
relationship to  
vaccination**

**III. Headaches are a  
common  
neurologic  
symptom after  
smallpox vaccination.  
The question of  
when to refer for  
severe headache  
for neurologic  
consultation will  
be addressed in  
separate algorithm  
currently under  
development.**

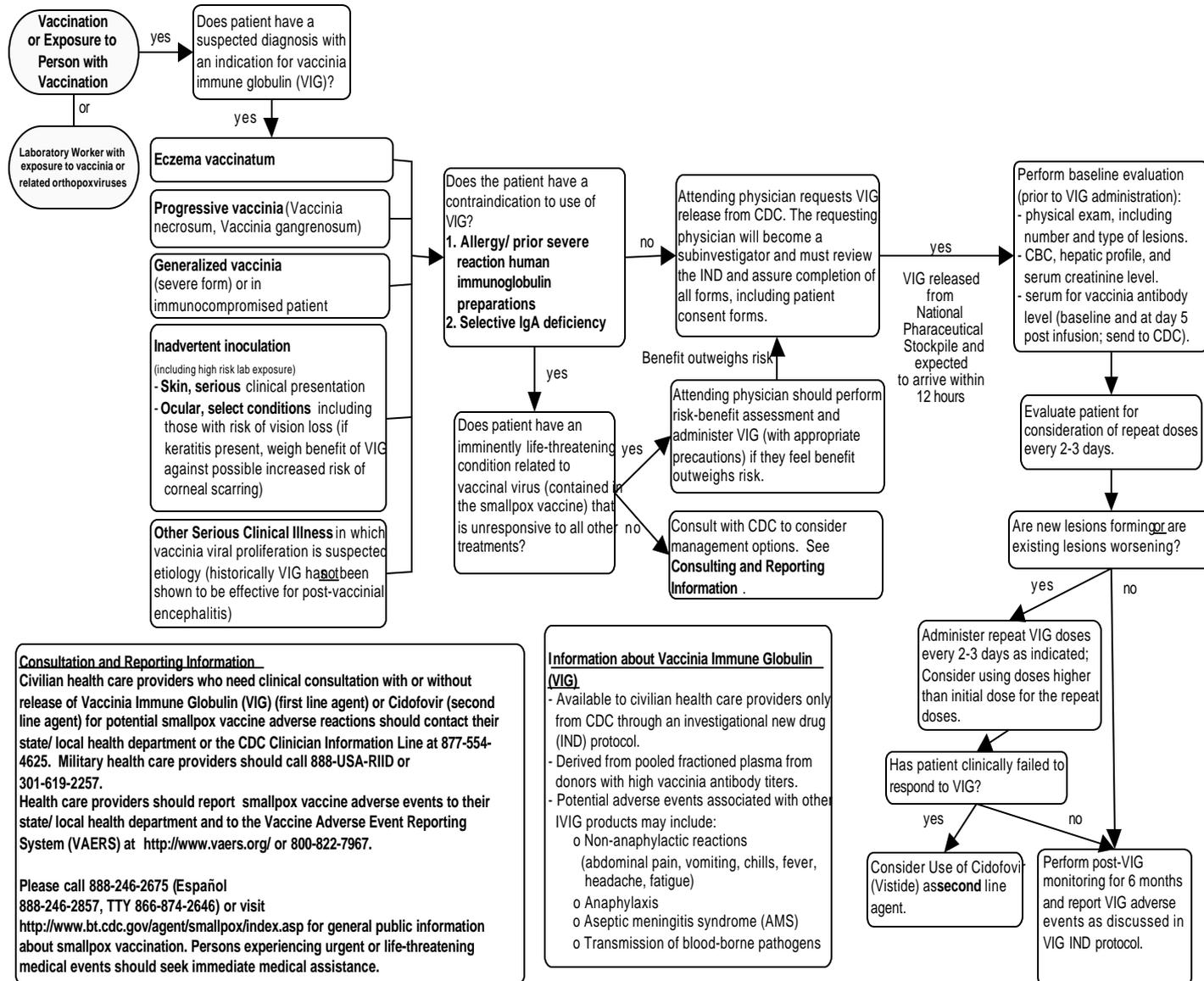


# Clinical Evaluation Tool for Smallpox Vaccine Adverse Reactions

## Use of Intravenous Vaccinia Immune Globulin (VIG) (first line agent), Vaccinee (or in a Close Contact) (1-21-2003 Version)

[www.bt.cdc.gov/agent/smallpox/vaccination/clineval](http://www.bt.cdc.gov/agent/smallpox/vaccination/clineval)

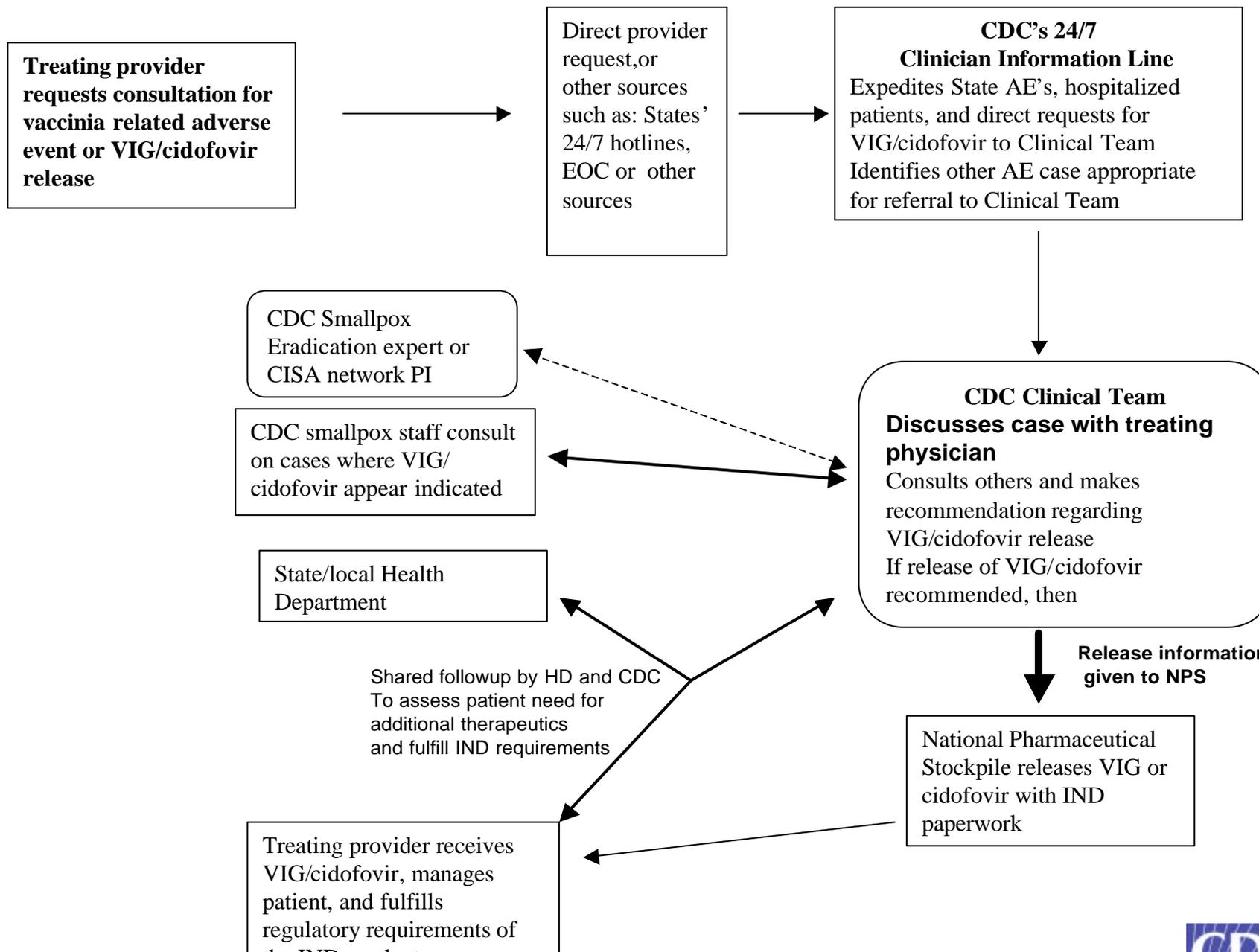
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 Please call 888-246-2675 (Español) 888-246-2857, TTY 866-874-2646) or visit <http://www.bt.cdc.gov/agent/smallpox/index.asp> for general public information about smallpox vaccination. Persons experiencing urgent or life-threatening medical events should seek immediate medical assistance.

**Information about Vaccinia Immune Globulin (VIG)**  
 - Available to civilian health care providers only from CDC through an investigational new drug (IND) protocol.  
 - Derived from pooled fractionated plasma from donors with high vaccinia antibody titers.  
 - Potential adverse events associated with other IVIG products may include:  
 o Non-anaphylactic reactions (abdominal pain, vomiting, chills, fever, headache, fatigue)  
 o Anaphylaxis  
 o Aseptic meningitis syndrome (AMS)  
 o Transmission of blood-borne pathogens

**SCHEMATIC FOR CDC RESPONSE TO REQUESTS FOR CLINICAL CONSULTATION  
or USE OF VACCINIA IMMUNOGLOBULIN AND CIDOFOVIR  
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**Suggested Clinical Case Definitions for Suspected  
'Clinically Significant' Adverse Events that should  
be referred through the Clinician Information Line  
to the CDC Clinical Team for evaluation and follow-  
up (jointly with State AE Coordinators)**

