

# Smallpox

## 1. DISEASE REPORTING

### 1.1. Purpose of Reporting and Surveillance

Rapid detection of orthopox-related illness to allow prompt identification of the source of infection, implementation of control measures and prompt treatment of those who are ill.

### 1.2 Laboratory and Physician Reporting Requirements

Laboratories and physicians are required to report suspect or confirmed cases immediately upon diagnosis or identification of the variola virus.

### 1.3 Local County Health Department Reporting and Follow up Responsibilities

Notify ACDP immediately of any suspect smallpox infections; ACDP notifies CDC immediately.

Coordinate with ACDP and other state and federal agencies to determine source of infection, conduct contact investigation, and administer post-exposure prophylaxis

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

### 2.1 Etiological Agent

Smallpox is caused by the variola (və-ri' - ə-lə) virus, a double-stranded DNA virus of the genus *Orthopoxvirus*. Smallpox has been eradicated worldwide due to a successful vaccination program. The last case of smallpox in the United States was in 1949; and, the last naturally occurring case in the world was in Somalia in 1977. The likelihood of reintroduction of smallpox is extremely low, except in the event of an intentional release.

There are two clinical forms of variola — variola major and variola minor. Variola major is the severe and predominant form of smallpox. Variola major has an overall fatality rate of about 30 percent. Flat and hemorrhagic manifestations of smallpox are usually fatal. Variola minor is less common and a much less severe form of smallpox, with death rates of 1 percent or less.

Variola replicates in the cytoplasm of host cells, forming inclusion bodies, rather than replicating in the nucleus as do other viruses. Environmental survival of variola virus is shortened by increased temperature and humidity.

### 2.2 Description of Illness

There are four presentations of variola major: (1) ordinary (the most frequent type, accounting for 90 percent or more of cases); (2) modified (mild and occurring in previously vaccinated persons); (3) flat; and (4) hemorrhagic (both rare and very severe). Variola major is characterized by a prodrome with fever, firm, deep-seated vesicles or pustules rash in the same stage of development, and a slow progression of the rash. Smallpox progresses through three phases: incubation, prodrome and pox.

Exposure to the virus is followed by the incubation period and then prodrome stage. The prodrome stage lasts 2–4 days and is characterized by a fever >101°F (100%), headache (90%), backache (90%), chills (60%) and vomiting (50%). Following the prodrome, a rash emerges, often first as a small red spot in the

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mouth or on the face ("herald spots"). Subsequently, the rash spreads in a centrifugal pattern on the skin starting on the face, spreading to the arms and legs and then to the palms and soles of the hands and feet. Usually the rash spreads to all parts of the body within 24 hours.

Lesions are initially maculopapular: raised, red bumps (days 1–2); followed by firm, deep-seated, well-circumscribed vesicles filled with a thick opaque fluid, often with a depression in the center (days 3–5); afterwards, the vesicles turn into firm pustules (days 7–14); pustules gradually flatten and scab over by the end of the second or third week, leaving marks on the skin that eventually become pitted scars. Lesions may be discrete (relatively few in number), semiconfluent, or confluent. In contrast to the succession of crops of vesicles seen with chickenpox, the lesions of smallpox appear and progress synchronously. In partially immune persons, the clinical course may be much less severe, and the rash may be atypical with fewer lesions and more rapid healing (i.e., "modified smallpox").

### 2.3 Reservoirs

Humans are the only natural hosts of variola.

### 2.4 Modes of Transmission

Transmission typically occurs during direct and fairly prolonged close face-to-face contact with an infected person(s). Smallpox can also be spread through direct contact with infected bodily fluids or contaminated objects such as bedding or clothing. Rarely, smallpox has been spread by virus carried in the air in enclosed settings such as buildings, buses and trains.

### 2.5 Incubation Period

Typically 12–14 days (range 7–17 days).

### 2.6 Period of Communicability

Smallpox may be contagious during the *prodrome* phase, but is most infectious during the first 7–10 days following rash onset. The person is contagious until all pox lesions have crusted over (about 2–3 weeks after rash onset).

### 2.7 Treatment

There is no specific treatment for smallpox disease, and the only prevention is vaccination. Supportive and symptomatic treatment includes hydration and medication management for fever, pain and secondary respiratory or skin infections.

## 3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

In the absence of smallpox disease in the world, the suggested approach to surveillance relies on a highly specific clinical case definition, which is focused on identifying the ordinary type of smallpox.

### 3.1 Clinical Case Definition

An illness with acute onset of fever  $\geq 101^{\circ}\text{F}$  ( $\geq 38.3^{\circ}\text{C}$ ) followed by a rash characterized by firm, deep-seated vesicles or pustules in the same stage of development without other apparent cause.

Clinically consistent cases are those presentations of smallpox that do not meet the classical clinical case definition: (a) hemorrhagic type, (b) flat type, and (c) *variola sine eruptione*.

(Detailed clinical descriptions are available on the CDC web site: [www.bt.cdc.gov/agent/smallpox/index.asp](http://www.bt.cdc.gov/agent/smallpox/index.asp)).

### 3.2 Laboratory Criteria

Polymerase chain reaction (PCR) identification of variola DNA in a clinical specimen, OR

Isolation of smallpox (variola) virus from a clinical specimen (National Reference Laboratory only; confirmed by variola PCR).

### 3.3 Confirmed Case

A case of smallpox that is laboratory-confirmed, OR

A case that meets the clinical case definition and is epidemiologically linked to a laboratory-confirmed case.

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### 3.4 Probable/Presumptive Case

A case that meets the clinical case definition, OR

A case that does not meet the clinical case definition but is clinically consistent and has an epidemiological link to a confirmed case of smallpox.

### 3.5 Suspect Case

A case with a generalized, acute vesicular or pustular rash illness, with fever preceding development of rash by 1–4 days, OR

A case that has an atypical presentation and is not laboratory-confirmed but has an epidemiological link to a confirmed or probable case of smallpox.

### 3.6 Diagnostic Criteria

CDC has developed protocols outlining laboratory testing to be undertaken in different smallpox risk scenarios according to diagnostic criteria. For more information, see "Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States," available at:

<http://emergency.cdc.gov/agent/smallpox/diagnosis/pdf/poxalgorithm5-2-14.pdf>.

#### 1. Major Diagnostic Criteria for Smallpox

- Febrile prodrome: occurring 1–4 days before rash onset: fever  $\geq 101^{\circ}\text{F}$  and at least one of the following: prostration, headache, backache, chills, vomiting or severe abdominal pain;
- Classic smallpox lesions: deep-seated, firm or hard, round, well-circumscribed vesicles or pustules; as they evolve, lesions may become umbilicated or confluent;
- Lesions in the same stage of development: on any ONE part of the body (i.e., the face, or the arm) all the lesions are all in the same stage of development (i.e. all are vesicles or all are pustules).

#### 2. Minor Diagnostic Criteria for Smallpox

- Centrifugal distribution: greatest concentration of lesions on face and distal extremities;
- First lesions on the oral mucosa or palate, face, or forearms;
- Severity: patient appears toxic or moribund;
- Slow rash evolution: lesions evolved from macules to papules to pustules over days (each stage lasts 1–2 days);
- Lesions on the palms or soles.

### 3.7 Services Available at Oregon State Public Health Laboratory (OSPHL)

Laboratory confirmation of smallpox is performed only at CDC. Initial testing and presumptive detection is conducted at OSPHL only after assessment and approval from ACDP. OSPHL can perform two PCR assays; the *Detection of Non-variola Orthopox DNA*, and the *Detection of Orthopoxvirus DNA*. OSPHL can also provide supplies to LHDs and other providers for collection of specimens; advice regarding packaging and handling of specimens; receive and facilitate shipment of specimens to CDC; and report results.

**NOTE: Local laboratories must not attempt to undertake isolation or identification of variola virus.**

## 4. ROUTINE CASE INVESTIGATION

### 4.1 Identifying Source of Infection

Discovery of a single, lab-confirmed case should be treated as a bioterrorism incident until proved otherwise. Any resulting investigation is therefore both a public health and a criminal investigation; indeed a key component of the response would be to identify and stop the perpetrator.

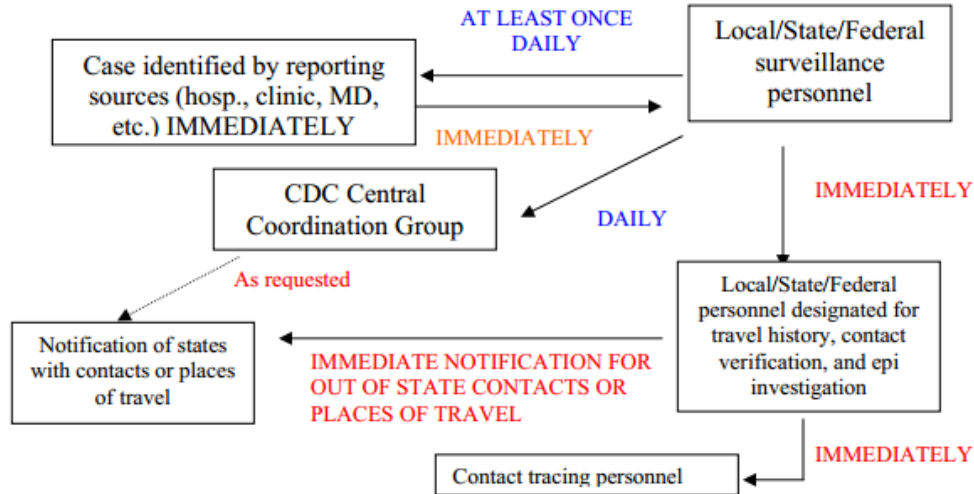
All suspect, presumptive and confirmed cases of smallpox should be interviewed immediately. Other criteria for immediate investigation include: (1) an outbreak of a clinically compatible illness, pending etiologic confirmation; (2) reports of suspected or probable cases after an outbreak has been identified elsewhere in the country; and (3) confirmation of smallpox virus in an environmental sample, package, or device associated with human exposure.

The highest priority of smallpox investigation and surveillance is to interrupt transmission by immediate identification and vaccination of high-risk contacts and isolating cases while still infectious. All personnel involved should be vaccinated prior to first contact with cases or exposed contacts.

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Active surveillance in hospitals caring for persons with smallpox is required during a smallpox outbreak. Even if there are no suspected smallpox patients, each hospital under surveillance should still send a report to notify the health department indicating that surveillance was conducted and has not yielded suspect patients (“zero reporting”). See Figure 1 for a diagram of surveillance reporting and information flow.

**Figure 1. Surveillance Reporting and Information Flow**



Resources to help clinicians identify smallpox cases are available at:

- Evaluating Patients for Smallpox: Acute, Generalized Vesicular or Pustular Rash Illness Protocol poster <http://emergency.cdc.gov/agent/smallpox/diagnosis/pdf/spox-poster-full.pdf>
- Worksheet for evaluating a rash illness suspected of smallpox: <http://emergency.cdc.gov/agent/smallpox/diagnosis/riskalgorithm/>
- Acute, Generalized Vesicular or Pustular Rash Illness Testing Protocol in the United States: <http://emergency.cdc.gov/agent/smallpox/diagnosis/pdf/poxalgorithm5-2-14.pdf>

### 4.2 Identify potentially exposed persons

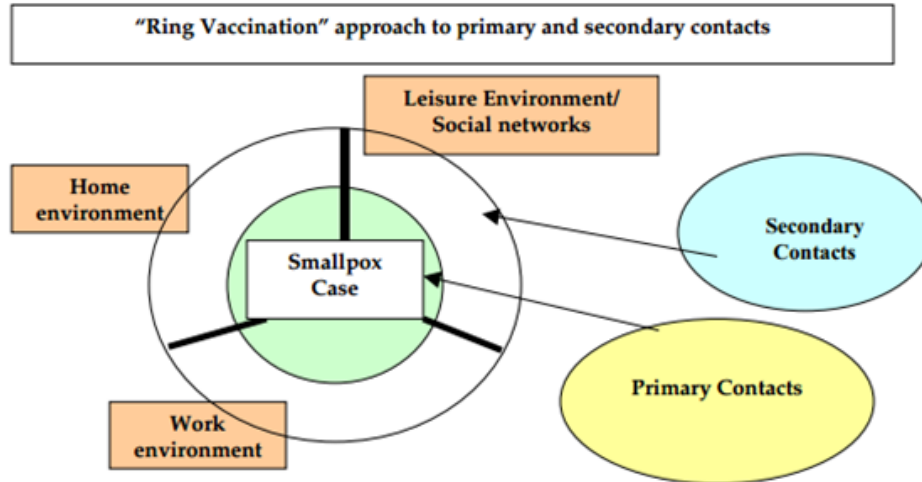
Begin contact investigation immediately upon hearing of suspected or probable, as well as confirmed cases: do not wait for lab confirmation. Vaccination of contacts and their contacts (search and containment, also known as ring vaccination) is the primary strategy for outbreak control (see figure 2). If contact becomes a smallpox case, expand the investigation by interviewing that new “contact-case” for his/her contacts, and provide appropriate care for the expanded group of potentially exposed persons.

- **Primary contact:** Person who had face-to-face, household, or close-proximity contact (usually within a distance of 2 meters), with a confirmed, probable, or suspected case of smallpox during the infectious period. Investigation priority should be given to primary contacts.
- **Secondary contacts:** Household members of all primary, non-household contacts and persons who work in the household of a primary contact.
- **Priorities for investigation of contacts, from highest to lowest are as follows:**
  - Case household members and others spending  $\geq 3$  hours in the household since the case’s onset of fever.
  - Non-household members with contact within 2 meters of a case with rash for  $\geq 3$  hours.
  - Non-household members with contact within 2 meters of a case with rash for  $< 3$  hours.
  - Non-household members with other contact (not necessarily within 2 meters) with a case with rash for  $\geq 3$  hours.
  - Non-household members with other contact (not necessarily within 2 meters) with a case with rash for  $< 3$  hours.

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Continue effort to identify contacts and evaluate them for infection as long as you are finding evidence of smallpox transmission (e.g. symptoms developing among contacts under surveillance) or for 3 weeks (21 days) after last exposure to a case. A decision may be made to stop contact investigation for one transmission environment (for example, a school or worksite), while simultaneously expanding the investigation in another environment based on evidence found among exposed contacts.

**Figure 2. Ring vaccination approach**



## 5. CONTROLLING FURTHER SPREAD

### 5.1 Education

Disseminating public information about smallpox is important. Educate potentially exposed persons about symptoms of smallpox. Fever, prodrome or development of smallpox lesions should prompt immediate medical evaluation. Detailed descriptions of expected and adverse reactions of the smallpox vaccine must be explained to recipients.

### 5.2 Isolation

Encourage strict airborne isolation of hospitalized cases from 24 hours prior to rash (if admitted during prodrome) until all pox scabs have fallen off. If case is at home, the case should stay in isolation in a room alone with the door closed. If it is necessary for the case to leave isolation, the case should wear a surgical mask. Isolation can be stopped after all smallpox scabs have dried and fallen off. Quarantine laws may need to be used to detain individuals who are suspected or known to be infectious to others.

### 5.3 Decontamination

Variola virus is sensitive to physical or chemical disinfection. There are no disinfectant products registered by the U.S. Environmental Protection Agency (EPA) specifically for the inactivation of variola virus on surfaces. It has been established, however, that viruses with biophysical and biochemical properties similar to those of variola virus (e.g., vaccinia virus) are readily inactivated by a variety of active ingredients found in EPA-registered chemical germicides that provide low- or intermediate-level disinfection during general use. All sterilization methods currently cleared by Federal Drug Administration (FDA) for medical instruments and devices will inactivate variola viruses. Textiles and fabrics (e.g., protective clothing, bed linens and clothing) from cases should be handled with minimum agitation to avoid contamination of air, surfaces and persons. Most, if not all forms of containment used for routine healthcare laundry are acceptable for decontaminating fabrics soiled with smallpox virus.

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### 5.4 Prophylaxis

Vaccination of close contacts to smallpox cases is key to stopping transmission, and targeted vaccination of close contacts should be the mainstay of smallpox outbreak control efforts. Public health authorities may supplement this strategy with broader vaccination campaigns to increase the level of community immunity to smallpox. Although smallpox vaccine is generally safe and effective, vaccine adverse events can occur, and prioritizing vaccination based on risk of exposure can help minimize vaccination of those at risk for serious adverse events.

In the event of an intentional release of variola virus, vaccination would be recommended for persons exposed, including:

- Persons exposed to the initial release of the virus;
- Persons who had face-to-face, household, or close-proximity contact (within 2 meters) with a confirmed or suspected smallpox patient after the patient developed fever.
- Medical providers involved in assessment or treatment of cases;
- Public health investigators who may have contact with cases;
- Persons transporting or handling cases;
- Laboratory personnel who collect or process clinical specimens from cases;
- Persons with risk of contact with infectious materials from cases (e.g., persons handling medical waste, linen and room waste);
- Others whose job puts them at increased risk of exposure to smallpox;
- Persons present at the hospital during the time that a case presented and was not yet placed in isolation; and,
- Others as identified by public health investigation.

Vaccination within 3 days of exposure will significantly modify risk of disease. Vaccination 4–7 days after exposure will likely offer some protection from disease or modify the severity of the disease. See Oregon Model Standing Orders for post-exposure prophylaxis for smallpox for more information on smallpox vaccination:

<https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Pages/stdgordr.aspx>.

## 6. OTHER SPECIAL CONSIDERATIONS

### 6.1 Smallpox Virus as a Bioterrorist Weapon

Bioterrorist release could occur through introduction of aerosol droplets into the air or by infected person(s) intentionally exposing the public. If the virus is aerosolized, it would likely be inactivated within 24 hours and therefore not be present by time cases developed symptoms, 7–17 days later. In the case of an infected person intentionally exposing the public, the index case and extent of the outbreak could potentially be tracked using standard epidemiologic and laboratory methods. In the event of a bioterrorist spread of smallpox, public health will work closely with law enforcement to conduct the investigation.

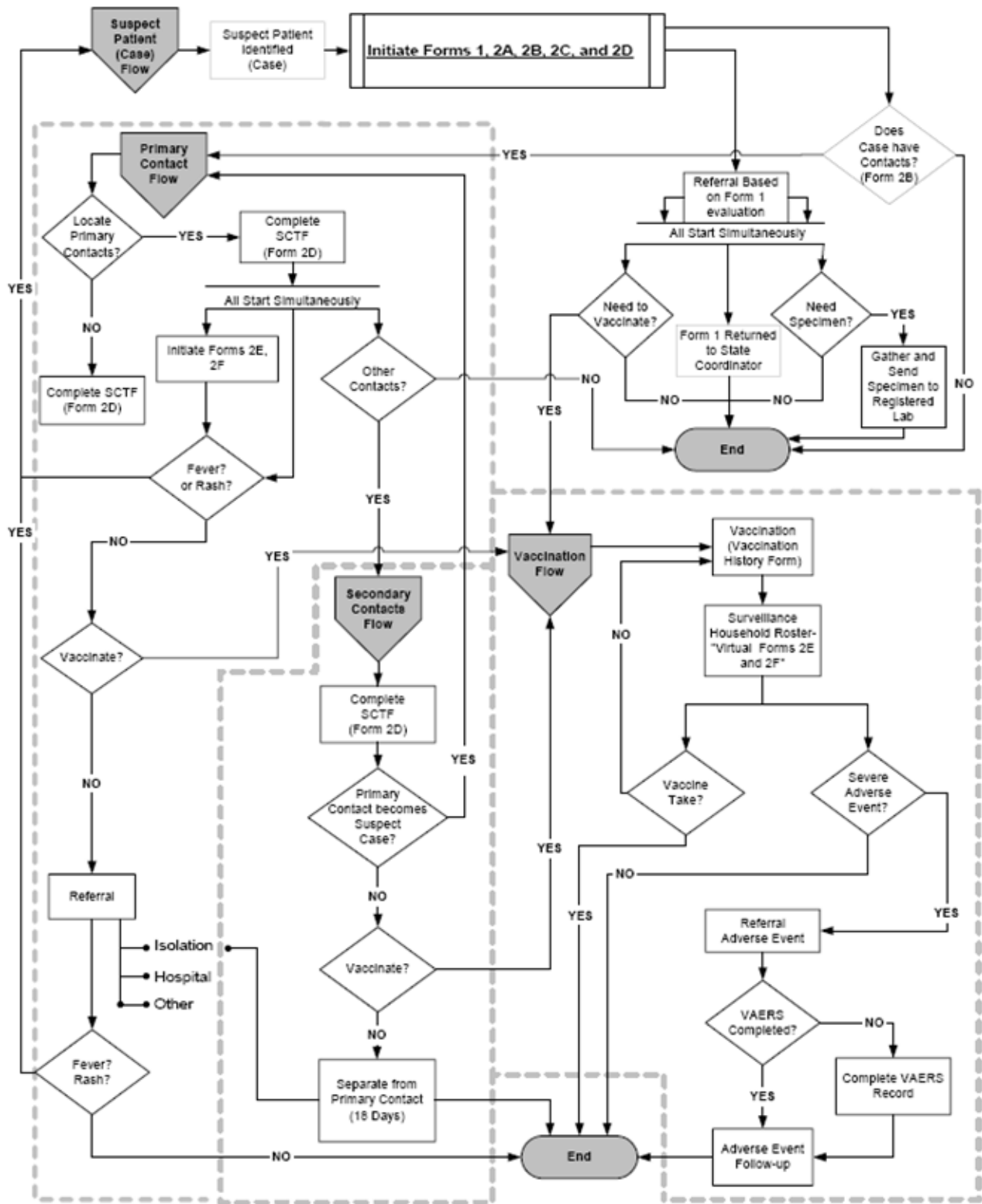
## UPDATE LOG

January 2004. IG created

July 2014. Reviewed and updated content. (T. Watts)

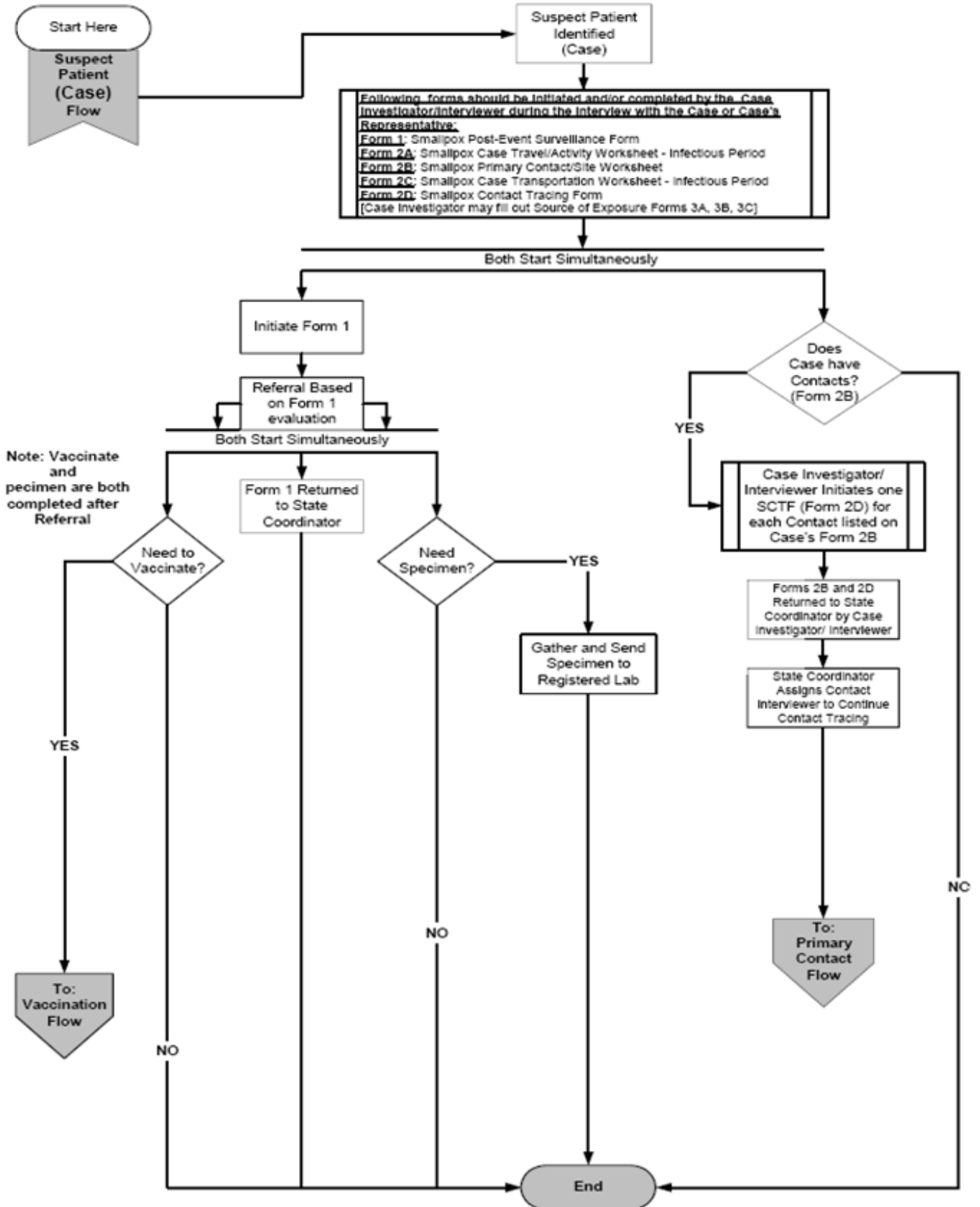
Appendix A: CDC Workflow Algorithms

High Level Process Flow



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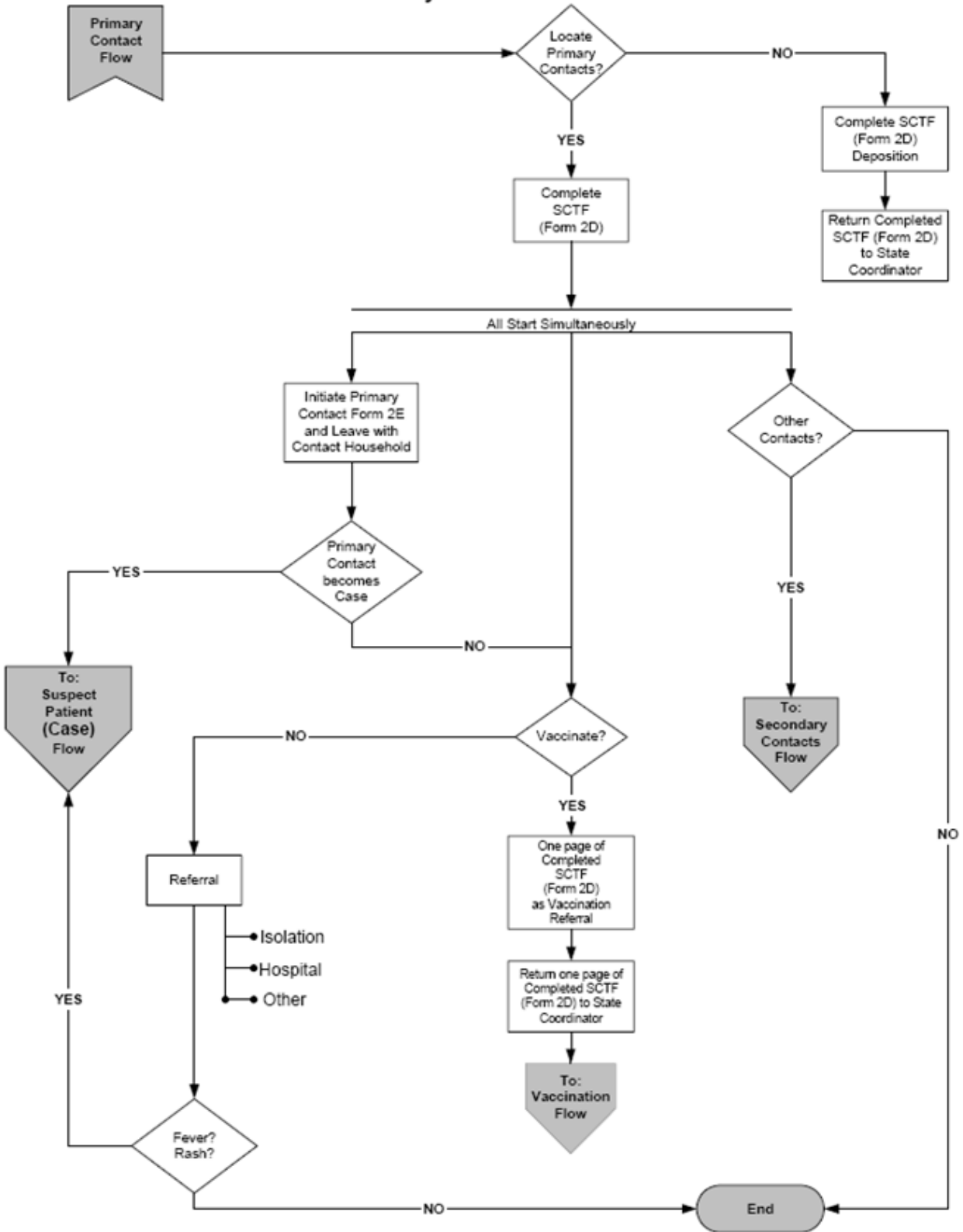
## Case Process Flow





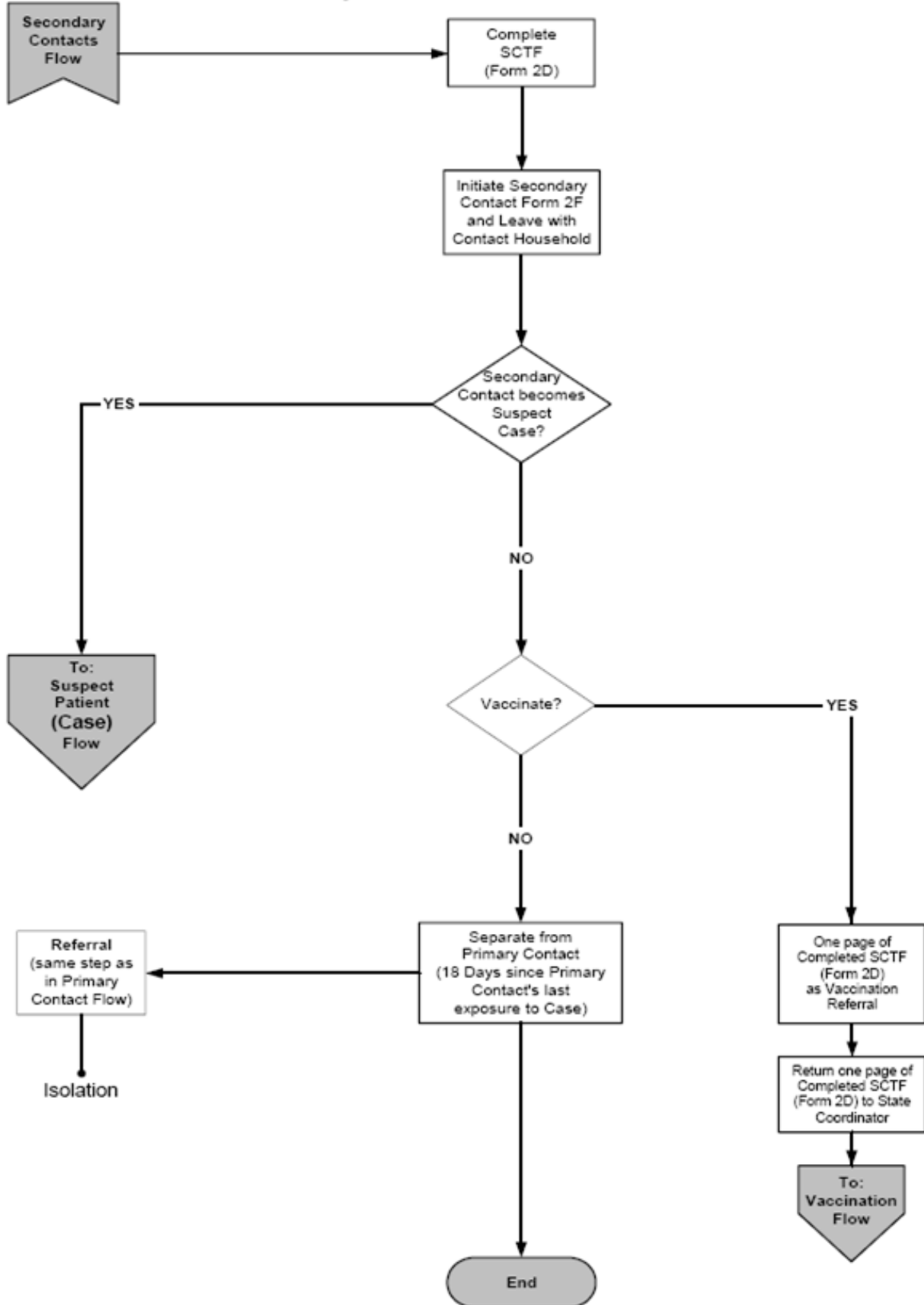
# Smallpox

## Primary Contact Process Flow



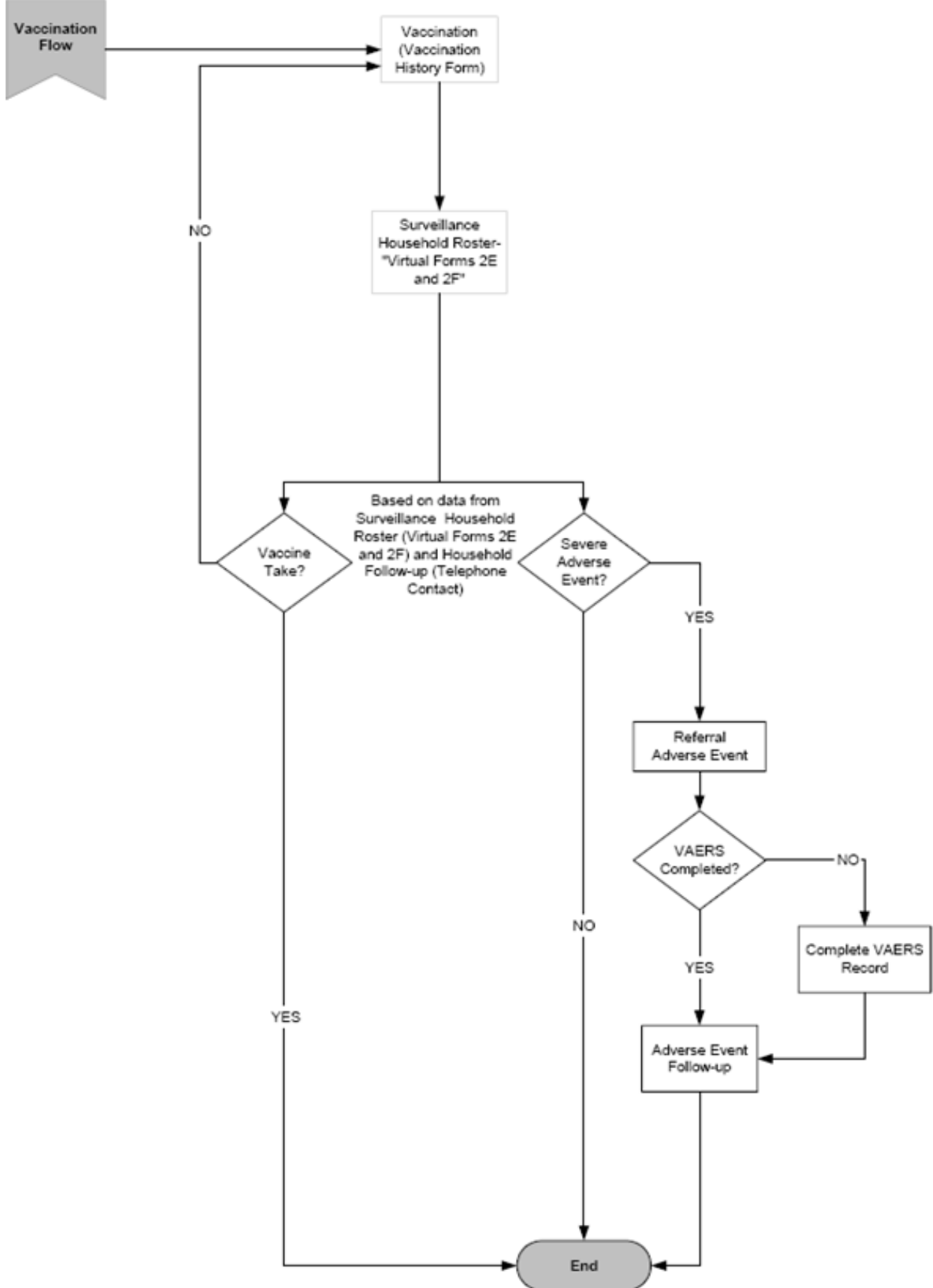
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## Secondary Contact Process Flow



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## Vaccine/Severe Adverse Event Process Flow



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### Appendix B: CDC Smallpox Forms

<b>CDC SMALLPOX FORMS</b> Forms for use by LHD public health staff in smallpox surveillance and contact investigation have been developed by CDC. (available online at <a href="http://www.bt.cdc.gov/agent/smallpox/response-plan/index.asp">http://www.bt.cdc.gov/agent/smallpox/response-plan/index.asp</a> ). These forms are not to be adapted or changed.	
Form Number and Name	Purpose
<b>Form 1: Smallpox (Case) Post-Event Surveillance Form</b>	Summarizes clinical and epi information about smallpox case patient. Report form for smallpox suspect, probable, and confirmed cases .
<b>Form 2A: Smallpox Case Travel/Activity Worksheet</b>	Records case activities during infectious period, to help with identifying exposed contacts.
<b>Form 2B: Smallpox Primary Contact/Site Form</b>	Lists contacts to case patient and prioritizes by risk.
<b>Form 2C: Smallpox Case Transportation Form</b>	Documents case patient travel history and modes of transportation, to identify possible exposed contacts.
<b>Form 2D: Smallpox Contact Tracing Form</b>	Documents referral for vaccination or clinical evaluation for each identified primary and secondary contact.
<b>Form 2E: Smallpox Case Household and Primary Contact Surveillance Form</b>	Documents surveillance of primary contacts for vaccine "take," as well as fever and symptoms.
<b>Form 2F: Smallpox Case Primary Contact Household Member Surveillance Form</b>	Documents vaccine "take," as well as fever and symptoms for all secondary contacts (household members and other close contacts of primary contact).
<b>Form 3A: Smallpox Case Exposure Investigation Form</b>	Assists in determining a common source of exposure. Records information on possible individuals and places as sources of infection. This form is not intended for use in every investigation.
<b>Form 3B: Smallpox Case Travel/Activity Form</b>	Helps identify possible sources of exposure (travel or movement during exposure period)
<b>Form 3C: Smallpox Case Transportation Worksheet</b>	Used to record the travel history of the case for up to 19 days before his/her date of onset of fever.