

Vaccination Strategies to Contain an Outbreak



When deciding how to focus your smallpox response efforts, there are several factors to be considered.

First is your vaccine supply. The number of available doses could make the difference between focusing only on the ring of contacts and the contacts of contacts and focusing on an entire community.

The second item to consider is the extent of the outbreak. Is the outbreak confined to one small area? Or are there multiple areas in various places around the country? Localized cases could mean choosing a smaller number of people to vaccinate. Cases around the country could indicate a multi-pronged attack and lead to the decision to immunize the entire population.

Eradication Strategy of the 1970s

- Vaccination of close contacts of cases.
- Occasionally supplemented with broader campaigns.
- Vaccine was readily available.



During the eradication program conducted in the 1970s, vaccination campaigns focused primarily on the vaccination of close contacts of smallpox cases. Occasionally, depending on the makeup of the area, broader campaigns were undertaken in order to help break a chain of transmission. But this was also a time in which vaccine was readily available; giving options to public health planners that we might not have today.

Smallpox Realities Today

- No cases of smallpox.
- Threat unknown.
- Susceptible population.
- Many people at risk for adverse events from vaccination.
- Limited vaccine supplies.

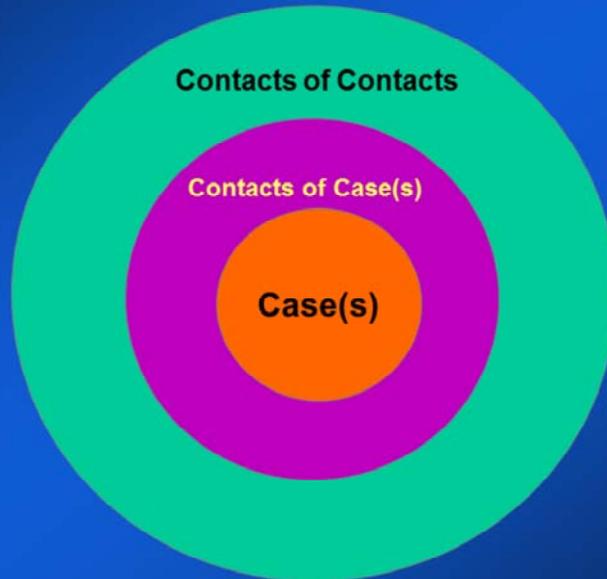


So how do we go about defining a vaccination strategy? Today, we have no cases of smallpox. Whether or not a group has smallpox for use as a weapon remains unclear. And since regular vaccination with smallpox was stopped over thirty years ago, we have an entire population who is vulnerable.

In addition, we have many more people at risk from adverse events from vaccination than we did thirty years ago. Now people with immune system disorders, transplants and chemotherapy are commonplace. Can we be sure that it will be possible to screen them out? What possible complications could arise from the way we live now that could add to that risk?

And most importantly of all, we have limited vaccine supplies. If we wanted to immunize everyone today, we probably couldn't do it with the supplies of vaccine we have.

Ring Vaccination Strategy



As we have discussed elsewhere, the Ring Vaccination strategy has been used successfully in the past. This involves vaccinating not only contacts of the case, but the contacts of contacts in order to interrupt the chain of transmission. This has been so useful because we know that most transmission occurs from close contact.

Ring Vaccination Strategy

- Primary strategy to stop transmission.
- Depends upon prompt identification of contacts.
- Judicious use of vaccine supply.
- Minimizes risks of adverse events.



While the ring vaccination strategy is our primary means of stopping the chain of transmission, we know that it depends on the prompt identification of contacts, which will mean having trained staff who can do this.

However, this strategy allows us to conserve a limited vaccine supply and it minimizes the risks of adverse events by covering only those who are at highest risk.

Contact Vaccination

- Face-to-face contact (≤ 6 feet) and household members at greatest risk.
- May prevent or lessen severity of disease (3-day window).
- Followed by monitoring for fever.



So let's review the ring vaccination strategy.

Contacts are defined as those having face-to-face contact with a smallpox case, usually within 6 and a half feet, and/or those who are household members of a smallpox case. If we can immunize them within 4 days of exposure, we might be able to prevent a case completely, or at least lessen the severity of the disease if they're already infected.

These contacts should be monitored for fever, the first indication of possible smallpox infection, for 18 days from their last exposure to the smallpox case.

Contraindications for Vaccination Contacts

NONE

In general, the risk of developing smallpox for face-to face contacts **outweighs** the risk of developing vaccine complications for those contacts with contraindications to vaccination.



For the contacts of a smallpox case, there are no contraindications for the use of vaccine. Because of the infectiousness of smallpox, we know their risk of vaccine adverse events is far outweighed by their risk of getting the disease.

Vaccination of Contacts of Contacts

- Household members of a contact without contraindications.
- Household members of a contact with contraindications, who are not vaccinated, must avoid the contact (18 days).



The contacts of contacts are those who are household members of contacts to a smallpox case. Those without contraindications should be vaccinated.

Unlike in the instance of direct contacts, the contact's household members who have a contraindication to the vaccine are not as at high risk. They should not be vaccinated and should avoid the contact for 18 days.

Contraindications for Vaccination of Contacts of Contacts

1. Immunodeficiency *.
2. Allergies to polymyxin B, streptomycin, tetracycline, or neomycin.
3. Eczema; including past history *.
4. Pregnancy.
5. Acute or chronic skin conditions (until resolved).

* Risk of accidental inoculation from household vaccinee's site



What are the contraindications to the smallpox vaccine?

1. Immunodeficiency;
2. Allergies to polymyxin B, streptomycin, tetracycline, or neomycin;
3. Eczema – including those who do not currently have symptoms;
4. Pregnancy;
5. And, any acute or chronic skin condition. Once those with acute symptoms are resolved, they can then be vaccinated.

It's important to note that those with immunodeficiency and eczema also have a risk of accidental inoculation from those who've been immunized. These contacts of contacts should consider removing themselves from the household until all the scabs have fallen off of all those who have been vaccinated.

High-Risk Priority Groups for Vaccination

- Exposure to initial virus release.
- Close contacts.
- Public health, medical, and transportation personnel.
- Laboratory personnel.
- Laundry, housekeeping, and waste management staff.
- Support of response: law, military, emergency workers.
- Others at hospitals.



Other high-risk groups to consider are:

-Anyone else who may have had exposure to the initial virus release, if they are not already displaying symptoms.

-Anyone who transported the patient to the hospital and took care of him medically; including the public health workers who are investigating the case.

-Laboratory personnel who handled the patient's lab work.

-Support staff in the hospital who have exposure to the linens, clothes, and waste from the patient's medical care.

-Other groups to now consider would include the response personnel who would manage additional cases, and others at hospitals who may have to assist in the event of a large outbreak.

Vaccine Administration Support

- Establish vaccination sites for contacts.
- Establish vaccination sites for personnel.
- Establish adverse events reporting and tracking system.



In order to immunize these contacts, you will need to establish vaccination sites. Clinics will need to be established for contacts and healthcare personnel. Establishing central clinic sites will minimize vaccine wastage. However, it will be important to evaluate whether or not vaccine supplies and personnel available can make it possible for vaccine to be taken directly to the homes of the contacts.

No matter what method of vaccination you choose, establishing an adverse events reporting system will be key; as will creating some way to ensure all those exposed are either vaccinated or managed appropriately.

Vaccination Clinics Why do them?

- Minimizes vaccine wastage.
- Security issues.
- Regulatory issues.



Because of the limited vaccine supply, planning in the United States has centered around vaccination clinics, rather than having workers carry vaccine directly to immunize contacts. This setup allows us to minimize vaccine wastage. With 100 doses in a vial, fewer vials can be opened and then used up. In addition, there is reason to suspect that in an outbreak situation, demand for the vaccine could mean that there would be those who would demand the vaccine, which may be limited, or who would try to obtain the vaccine to sell it. Public health officials might also be in the situation where drug control regulations require extensive counseling and paperwork that can be more easily managed in the clinic setting.

Supplemental Strategies Mass Vaccination

- Number of cases or locations too large for effective contact tracing.
- No decline in number of new cases after 2 generations.
- No decline after 30% of vaccine has been used.
- Not a first-line strategy.
- If used, would supplement ring vaccination process of search and containment.



While the United States will be relying primarily on ring vaccination if an outbreak of smallpox were to occur, broader vaccination might be considered if the number of cases grows too large for effective contact tracing, if the number of new cases after two generations fails to decline, and if the vaccine stores used under the ring vaccination process declines by 30% without a decline in cases; indicating that contact tracing is not working.

Supplemental Strategies Dilution of Vaccine

- Dilution of vaccine:
 - May stretch vaccine supply.
 - Evaluation of 1:5, 1:10 dilution
- May provide valuable alternative for personnel with time to verify vaccine take.



Because of the limited supply of vaccine available, the United States undertook studies to see if existing vaccine could be diluted to stretch the vaccine supply. Evaluation of the efficacy of the vaccine at both a 1:5 and 1:10 dilution indicated similar rates of takes at around 95% of those vaccinated. Therefore, diluting the vaccine supply might be a way to stretch limited stores when the vaccinee has not been directly exposed to a case, such as in the case of mass vaccination.

Vaccination Strategies Conclusions

- Ring vaccination most effective.
- Groups for vaccination must be prioritized.
- Strategy may change as the situation develops.

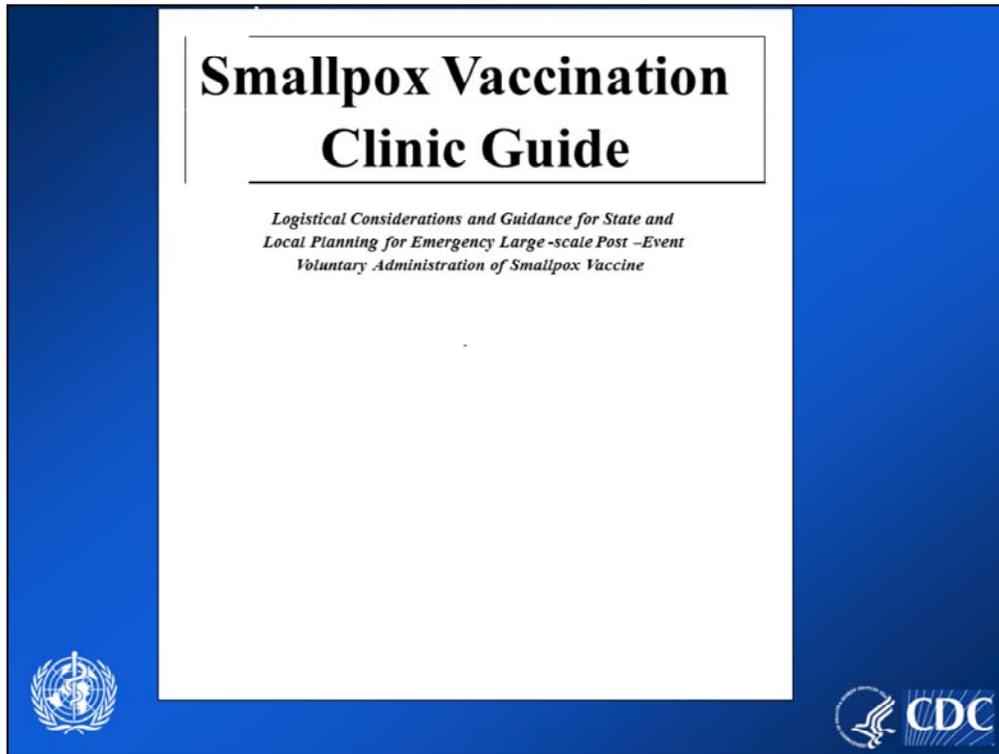


In the current climate of limited smallpox vaccine, and even when there is sufficient vaccine supply, ring vaccination is the most effective strategy for the control of smallpox. Public health officials will need to prioritize, ahead of time, those groups for whom vaccination will be the priority. They must also be prepared to change their strategy as the outbreak unfolds.

Organizing Vaccination Operations



If you decide to conduct smallpox vaccinations in the clinic setting, proper organization will be important.



The Smallpox Vaccination Clinic Guide was released in the United States as part of the national Smallpox Response Plan. Its purpose is to prepare state and local public health for the logistics involved in conducting mass vaccination clinics after a case of smallpox has occurred.

Given the complicated setup for mass immunizations, it's important for public health officials to start planning before the event occurs. This guide discusses the logistics surrounding the facility, the personnel, and the supplies needed for such a large undertaking.

Timeline of Vaccination in US

- 1971 – Routine vaccination ended, only laboratory/researchers vaccinated.
- December, 2002 – Military.
- January, 2003 – Response and Healthcare Teams.



In the United States, routine vaccination ended in 1971. Since that time, only laboratorians and researchers working with orthopoxviruses have been receiving the vaccine. However, in December of 2002, President Bush announced that vaccinations would resume. Members of the military would begin vaccination immediately. Those in the civilian sector who volunteered for response teams — to help in contact management and tracing — and healthcare teams — to help in the care of cases — began vaccination in January of 2003.

Large-Scale Vaccination

- Establish “time-frame” to meet vaccination goals:
 - Set Goals - How many and how fast?
 - Balance PH and Socio-political “goals.”
 - Trade-off allowances.
- Centrally run system impractical:
 - Scope of program (nationwide?).
 - Resource limitations.
- Prepare existing national vaccination infrastructure.



The window to prevent smallpox through vaccination is limited. Strategies have to be determined to get the maximum protection in the smallest time possible.

While the ring vaccination strategy must continue in order to prevent the spread from known cases, the community will most likely demand vaccination to feel secure. Conducting mass vaccination clinics may take valuable resources and time away from other public health interventions, it is important to consider the disruption that could be caused by the demand and worries of the public.

The federal government running these clinics would be impractical. It lacks the direct care personnel to make it happen. Local communities know best how to work within their own infrastructure.

Vaccine Deployment Goals

- Initial vaccine to site(s) with suspected case(s):
 - Can be delivered by deployed CDC Smallpox Response Team(s):
 - High suspicion rash.
 - On-site to begin vaccination as soon as confirmed.
 - Up to 150,000 doses can be deployed with team.
 - Arrive within hours of notification.
 - Additional vaccine can arrive within 12 hours.



The federal government maintains a supply of smallpox vaccine that can be deployed very quickly.

In the event of a highly suspect case, CDC Smallpox Response Teams can be deployed and can bring an initial supply of vaccine with them. Most teams can be onsite within hours. Additional doses of vaccine can begin arriving within 12 hours.

Vaccine Deployment Goals The First 75 Million Doses

- Packaged in “Vaxicool” systems for rapid deployment:
 - Self contained shipping/storage unit.
 - 150,000 doses per Vaxicool (300 vials).
- Goal to move 500 “Vaxicools” throughout US within 24-36h:
 - Vaccine stored at multiple locations throughout US.
- Ancillary supplies to arrive with Vaxicools:
 - Diluent.
 - Transfer needles for vaccine reconstitution.
 - Bifurcated needles for single use administration.
 - CD-Rom: IND and information materials.



The Vaxicool system is a refrigerated shipping and storage unit that can maintain cool temperatures for hours without needing recharging.

Using the National Pharmaceutical Stockpile, or NPS, large amounts of vaccine can be delivered throughout the US in less than two days.

Clinics will receive other ancillary supplies necessary to conduct vaccination, including the needles and diluent needed for administration, as well as the forms necessary for IND vaccines.

Vaccine Deployment Goals Remainder of Stockpile

- Requires local plan and equipment for refrigeration/storage.
- Shipping containers to accommodate 10,000; 15,000; or 150,000 doses/container.
- NPS goal capability once vaccine available:
 - Deployment of total 280 million doses within 5 days.
 - Deployment to multiple locations that include cities of $\geq 10,000$ population.



Since the Vaxicool containers will need recharging, public health planners should consider the logistics involved with having electrical outlets ready for the units.

Logistics for Mass Vaccination

- Rapid vaccine delivery to multiple sites (NPS).
- Vaccination clinics:
 - Facilities that meet needs for size/access/security.
 - Training and staffing resources.
 - Supplies (non-vaccine related).
- Public communication:
 - Who and why.
 - Which clinic to go to.
 - When to go and how to get there.
 - What to do before going and what to expect.
 - Information hotlines.



Public health planners should pre-identify community sites based on their geography and the distribution of the population in the area. Those sites will need to have large floor space and be accessible. Sites to consider include schools, auditoriums and large churches or temples.

Staff and supply sources will need to be identified beforehand.

Planners should also consider developing their communication materials as part of the planning process to save time during a response.

Logistics for Mass Vaccination

- Medical Screening:
 - High-risk conditions (contraindications).
 - More extensive than for any other vaccine:
 - More questions to answer.
 - Greater medical counseling requirement.
 - What to do with high-risk/low benefit individuals who want vaccine?



Because the smallpox vaccine is not licensed in the United States, it will have to be administered under Investigational New Drug, or IND, protocols. This requires more extensive paperwork and explanations than with most vaccines so that patients will be able to make an informed decision.

Since the last time smallpox vaccine was used, there are more patients with immune system issues that could indicate contraindications to the vaccine. More thorough medical screening will need to take place to minimize the possibility of severe adverse events.

Logistics for Mass Vaccination Tracking/Surveillance

- Adverse events:
 - Passive system.
 - VIG and medical care.
 - Unexpected rates or reactions?
- Vaccine response rates:
 - Expected % of “takes”?
 - Passive system/self-reporting.
- Daily number of vaccinations administered:
 - On-target for vaccine administration goal?
 - Need for additional clinics.



Part of your planning should also take into account data needs. Staff will be needed to keep records so that policy makers can monitor progress and further refine their response, as necessary.

Close monitoring for Adverse Events will be critical since the vaccine hasn't been used on a large scale for decades. This should be kept as up-to-date as possible so that unexpected risk factors can be quickly communicated to healthcare providers.

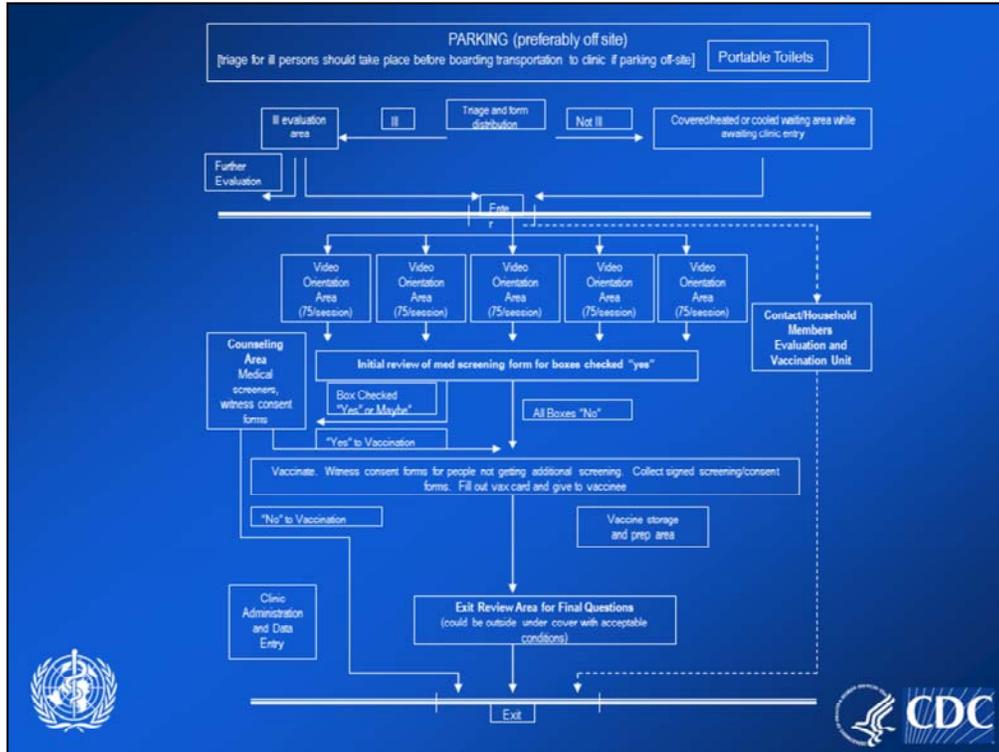
Additional Logistical “Factors”

- IND vaccine:
 - Regulatory requirement for informed consent.
 - PI (or multiple co-PIs) must assume oversight for vaccine administration sites.
 - FDA and IRB approval.
 - Formal safety monitoring mechanisms.
 - Paperwork:
 - Information materials/Screening and consent form.
- Liability:
 - Adverse events.



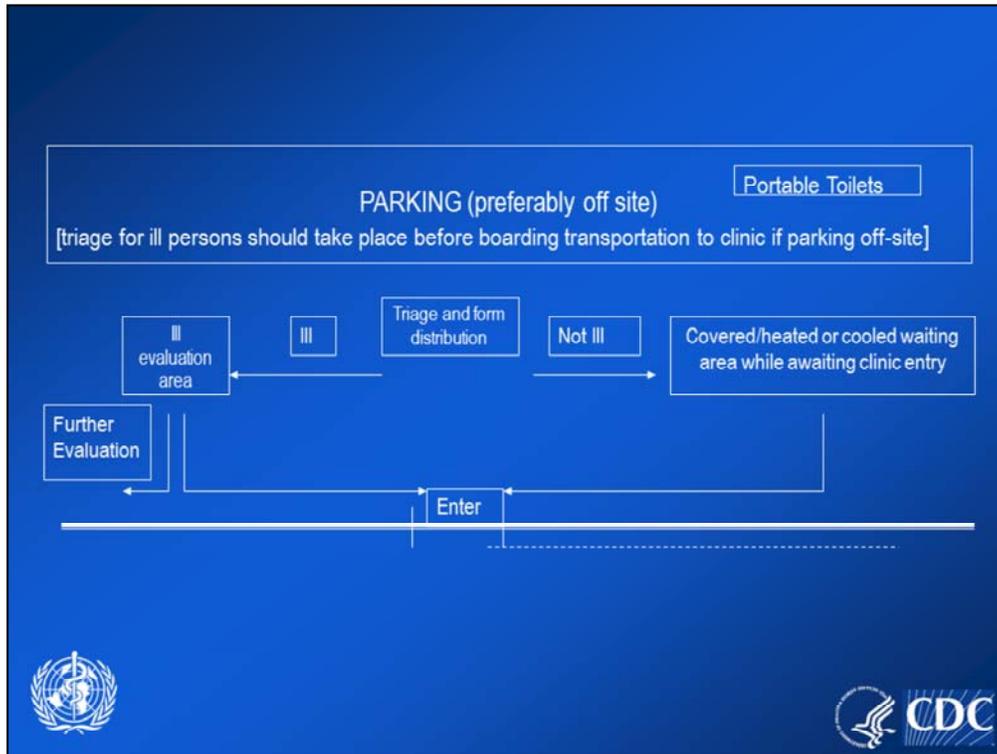
Because the vaccine is IND, there are strict regulatory requirements for informed consent that must be followed. The guide contains examples of the types of forms that must be completed by each patient to ensure they understand the risks and benefits of the vaccine. The most current forms will be supplied with the vaccine shipment.

The additional paperwork, however, will take up more clinic time. Staffing and clinic flow should be modified accordingly to handle this.



This is an example of the model clinic flow described in the Guide.

As you can see, it's a bit complicated, so let's take a close-up look at the various parts.

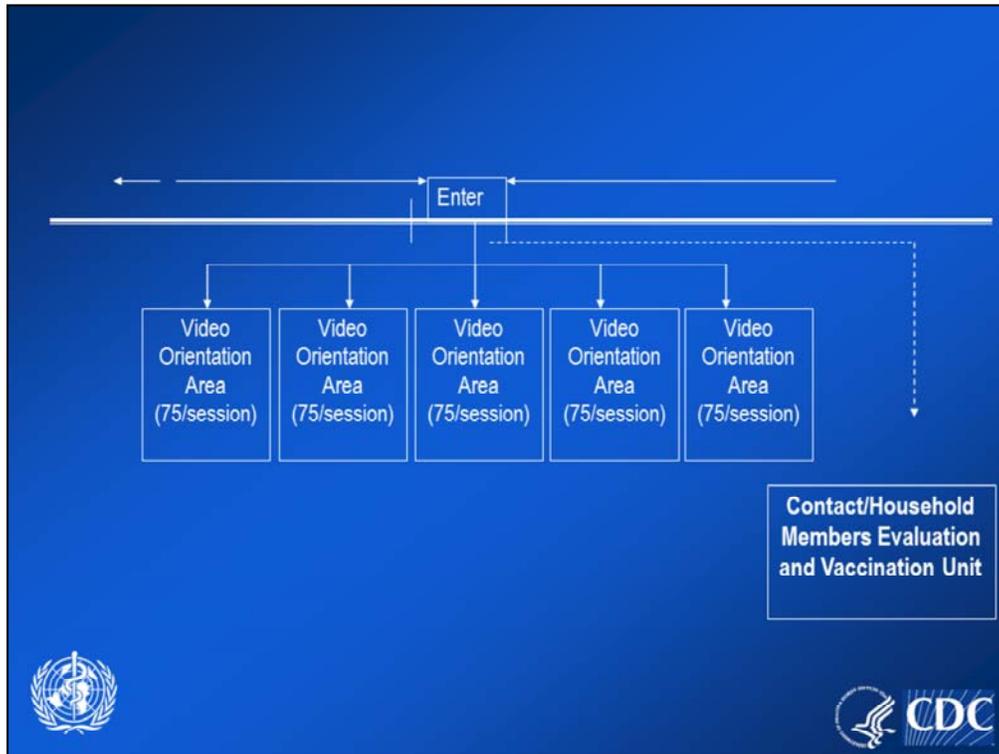


Given the demand for the vaccine we would expect, the parking around the clinic could quickly fill. Planners should consider identifying off-site parking and making arrangements for busing patients into the clinic site.

There should be some sort of triage system set up to deal with those patients who appear to be ill so that they can be further evaluated and monitored by public health.

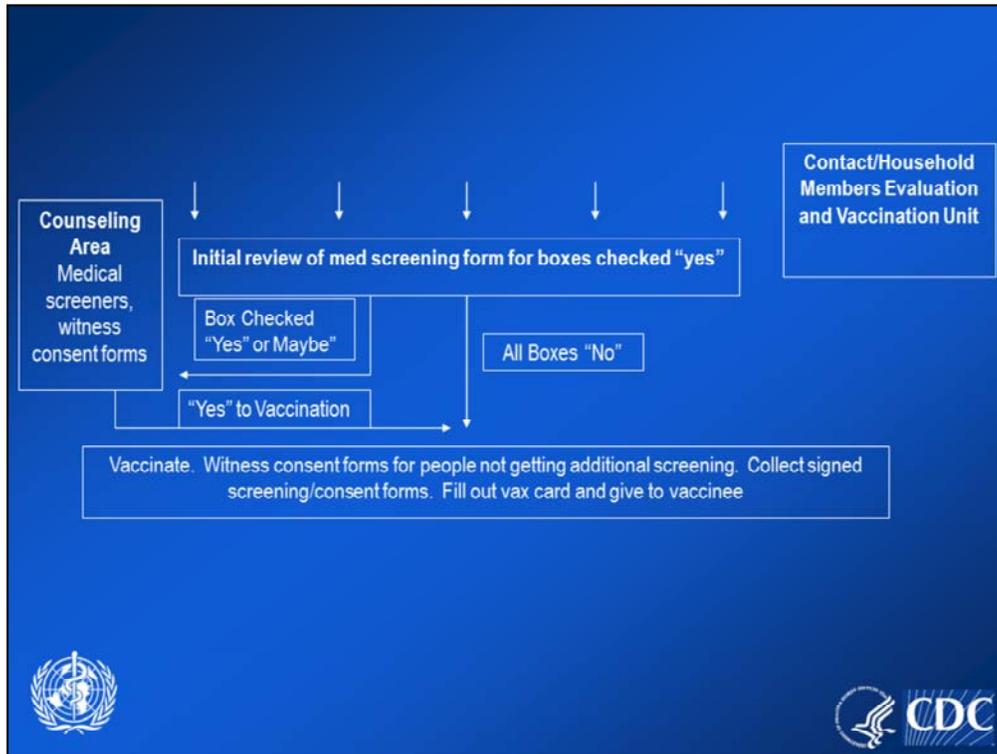
Since there could be a wait to get into the clinic, consideration should be given as to how to protect patients from the elements while they wait.

When they enter, patients should be handed a packet with all the printed information materials and volunteers should guide them to the next portion of the clinic.



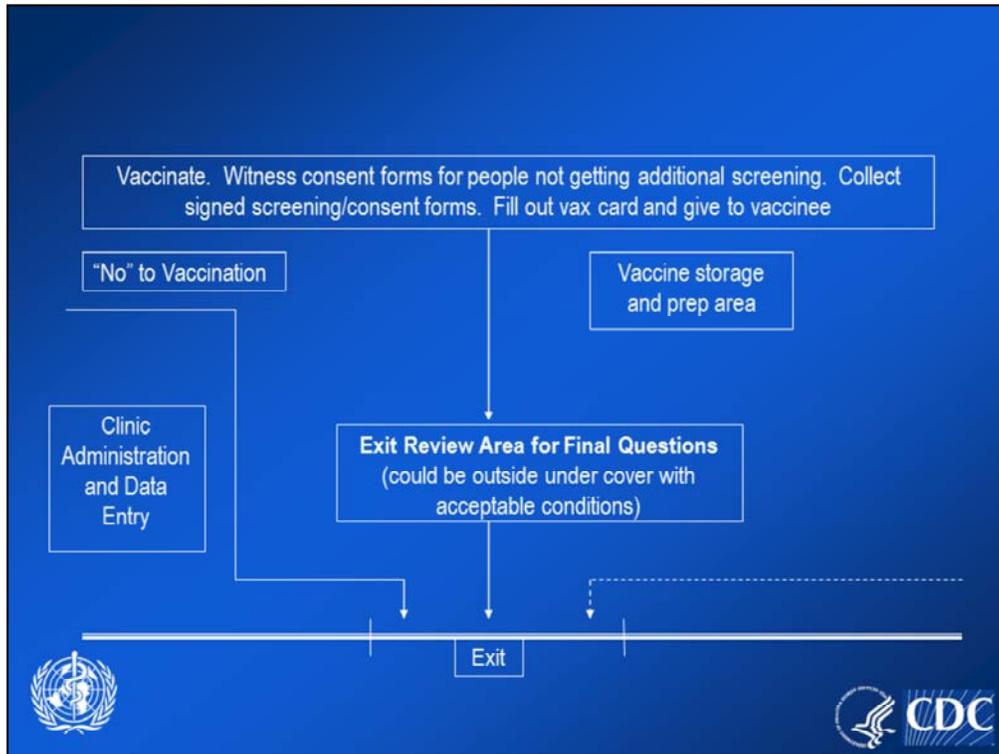
Those patients who have been identified as contacts or household members of contacts to a case should be moved out of the mass vaccination clinic flow and taken to a unit that will manage the intervention portion of the response.

Those who are not contacts should be entered into the mass vaccination clinic flow. A video will be provided that explains the IND process and the risks and benefits of vaccination. Multiple sites to view the video should allow more people to move through.



A quiet area with tables and chairs should be set up for patients to sit and review the paper forms.

Those who indicate they have contraindications or who have questions should be referred to medically-trained counselors who can help the patient decide whether or not it's prudent to take the vaccine. These screeners will also instruct those who choose not to get vaccinated on what to watch for and who to contact if they have problems.



The actual vaccination should be relatively fast, compared to the informed consent portion of the clinic.

Before exiting the clinic, patients should be given one more chance to ask questions. Forms should be brought directly over to the data entry staff from here.