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1.0 Purpose

The purpose of this document is to provide health workers and public health practitioners with some general principles and guidelines to follow in order to effectively manage concerns about vaccination safety in their countries. This is not meant to be a comprehensive guide to immunization—issues such as vaccine licensing, cold chain adequacy, proper storage and handling, syringe quality, injection techniques, and disease surveillance are not addressed here—but rather a focus on the public health management of vaccination safety issues.

The proper implementation of these guidelines will provide further information on immunization safety. These data will complement the information collected through other analytical studies including pre-licensure clinical trials, therefore maintaining confidence in the national immunization programs.

The benefits of immunizing against the vaccine-preventable diseases far outweigh the minimal risks of vaccination. In order to maintain or improve the strength of every national immunization program, workers at each level of the public health community (from local health workers to health department officers) should be educated about the issues surrounding vaccination and they should be prepared to respond to any public concerns. The quick response to a public concern regarding vaccines and the rapid, honest communication of explanations and actions will ensure the integrity of immunization programs throughout the Americas.

2.0 Introduction

One of the greatest public health success stories has been the prevention of infectious diseases by immunization. Few other public health interventions have averted more deaths and illness than vaccines used in planned out immunization programs. Although vaccine development and introduction began at the end of the 18th century, the amazing potential of vaccines had not been truly recognized until 1977, when smallpox eradication was achieved. Case fatality rates of smallpox prior to vaccine introduction was often around 10%, with a majority of the deaths occurring in children <5 years of age. Since 1796, when the first smallpox vaccine was introduced, illness and death has been prevented in millions of people worldwide because of this vaccine. Approximately 170 years after Edward Jenner began vaccinating people with his smallpox vaccine; the disease was completely eradicated. There are currently around 30 vaccine-preventable diseases, but sadly enough, children and adults are still suffering illness and death due to these diseases. Worldwide efforts to control these diseases are currently underway and substantial progress has been made, by implementing, strengthening and maintaining immunization programs in all regions of the world.

In the Americas, using the lessons learned from the smallpox eradication efforts; other eradication campaigns have been conducted for poliomyelitis and measles. Before the polio vaccine was available, annual epidemics of polio often left tens of thousands of mostly children in wheelchairs, braces, and iron lungs. As a result of the strong commitment of public health practitioners and parents to immunization, the last case of polio due to wild-type poliovirus in the Americas was in August 1991. Worldwide, the campaigning continues and the case numbers reflect the success of these efforts—in 1988, there were 35,000 polio cases throughout the world and after a decade the cases dropped to 5,298. Measles transmission is slowing after a few years of disease resurgence in Latin America and campaigns are currently underway to eradicate measles by the year 2000. In other parts of the world, the main focus is on eradicating polio, but there is also a strong commitment to controlling measles. As we move closer to eradicating two more diseases in the world, thousands of children will not have
to suffer the paralysis from polio, the encephalitis and brain damage from measles and death which occurs with both diseases.

Although immunization has been an important public health accomplishment over the past 200 years, it is not without controversy. Vaccine safety issues have been undergoing visible public debate most noticeably over the past 20 years. At times, immunization programs worldwide have been jeopardized by public reaction to the debate. Although vaccines are not completely effective at all times, they are one of the safest interventions in the medical armamentarium. Although there are known side effects from certain vaccines, the benefits of vaccination far outweigh the risks of the disease (See Appendix 1).

The world has already witnessed the dangers and effects of stopping vaccination. In the United Kingdom during the 1970's, public concern regarding the safety of pertussis vaccines led to a rapid decline in immunization coverage rates. Prior to this time, coverage was over 80% with an average of 2,000-8,000 cases reported annually. After the coverage rates decreased to 30%, the number of pertussis cases soared to over 100,000—resulting in deaths and hospitalizations which could have been prevented. After two large epidemics and some education about the disease and the vaccine, the public slowly regained trust in the vaccine and the immunization programs. As a result, vaccination coverage reached 95% in the mid 1990's with the lowest recorded number of pertussis cases in UK history.

Every immunization program should ensure the safety of vaccines and be prepared to deal with any public concerns about vaccination safety. Some of the events may be known effects observed during pre-licensing clinical trials or during experimental stages of vaccine development. In addition, many medical events that are reported as allegedly vaccine-related are background illnesses that are transmitted through the community regardless of vaccination. The first few years of a child's life are the most vulnerable years with regard to illness and it is also the time period when other diseases begin to manifest themselves (i.e. developmental disorders, hearing difficulties, etc). These early years are also when vaccines are administered. It is not difficult for the "coincidental" vaccination to be misinterpreted as causal and for many of these events; it is nearly impossible to find out the true cause, even with the most detailed investigation. Any medical event perceived by the public, by the parents, by the recipient or by health workers to be allegedly vaccine-related should be examined on the local level. If deemed appropriate (i.e. the time period and symptoms support a suspicion of being vaccine-related), a more formal standardized investigation (see Section 4.0) should be initiated.

Upon completion of the investigation, these events should be classified into one of the following categories: program-related, vaccine-related, not related, or unknown (inconclusive investigation). The purpose of detecting, investigating and analyzing these events is to take action based on the conclusions reached by this process. These actions may include: reassurance of parents/caregivers/adults, communication with the public and other health care workers, treatment, correction of program errors (vaccine handling, storage, administration and syringe issues), discussions with manufacturers (regarding vaccine quality and effectiveness), recall of the vaccine or further research. Ultimately, by taking action, confidence in the immunization program is reinforced, but only if there is open and honest communication with the public.

Communication with the public and other health workers during critical periods of wavering public confidence is vital to the success of any immunization program. When rumors or allegations are circulating in the community, they should be addressed immediately. Immunization program personnel should be trained to prepare media statements— these explanations for the public about circulating stories or known ongoing investigations are a great way to be proactive in managing the issue. Also, once an investigation has been initiated, and public awareness has been heightened, all
attempts at two-way open communication should occur. This could include getting community leaders involved, establishing lines of communication with the media and identifying key people within the health department who could respond to any questions about the issue. In the future, all countries in the Americas should work to improve their communication systems—within the country, with other countries and with the Pan American Health Organization.

One of public health’s greatest tools is education. The field of vaccines and immunization needs to use this resource more today than ever before. Parents and adults need to be fully informed about what to expect after vaccination (possible side effects) and they also need to learn about what may happen if they refuse vaccination (disease effects)—that way they are prepared and have made the decision knowing potential outcomes of either decision. However, educating the general community about weighing the risks and benefits of vaccination does require the health worker to be properly trained to effectively communicate the facts, and to appropriately deal with questions regarding vaccine safety. The summary tables at the end of this document comparing the effects of vaccines versus the effects of disease the vaccine protects against will help to prepare health workers for this communication (See Appendix 1).

As technology improves with time, so does the quality and effectiveness of the vaccines used. Although vaccines today are much safer than they were 40 years ago, with new vaccines arriving on the market every year and an increase in information dissemination via the Internet, public concerns of safety and benefits of vaccines continue to grow. Consequently, immunization programs have a duty to address these concerns. Hopefully, this document should help every immunization program in the Americas develop mechanisms to:

- report, investigate and analyze alleged vaccine-related events;
- take action to correct any problems identified from the investigation;
- communicate efficiently and effectively with the community, other public health practitioners, health workers and the media;
- educate health workers to recognize potential vaccine-related events;
- educate parents about the known side effects of vaccines and of the diseases they protect against.

3.0 Vaccine Quality and Safety

All vaccines procured through the World Health Organization (WHO) for national immunization programs must meet WHO requirements. The suppliers for the vaccines must go through the WHO pre-qualifying process which involves an examination of the vaccine characteristics, adherence to Good Manufacturing Practice standards during vaccine production and the activities of the National Control Authority (NCA). WHO considers a vaccine to be of known good quality provided: the NCA controls the quality of the vaccine according to the six critical functions defined by WHO and there are no unresolved confirmed reports of problems related to quality. These six critical functions are:

- a published set of licensing requirements
- review of clinical data collected during surveillance of vaccine field performance
- a system of lot release
- laboratory testing
- regular inspections for compliance with Good Manufacturing Practice standards
- evaluation of clinical performance.
The safety and efficacy of vaccines are demonstrated during the clinical trials conducted before licensing. These trials undergo different phases under controlled conditions evaluating the efficacy and safety of the vaccine, to fulfill conditions required to registration. Follow-up studies of vaccines after licensing occur when the vaccine is applied to the population. This follow-up provides information about the effectiveness of the vaccine and if communicated properly can add valuable knowledge to the vaccine profile.

Many reported events that have been allegedly related to vaccines indicate a problem with vaccine administration: contamination, improper injections, cold chain problems and dosage/dilutant mistakes. These problems can be easily fixed with proper training, handling and storage techniques. It is imperative that every local level health worker is aware of these potential problems and recognizes them when they occur, so rapid correction can be instituted.

Medical events thought to be related to vaccination are listed in the tables in Appendix 1. These events vary in severity and frequency for each vaccine. This list is not completely comprehensive and there are many debates about these events and establishing a true causal link for some is difficult.

4.0 Investigation of Events Attributed to Vaccination

Assessing whether or not the occurrence of an alleged reaction to vaccination truly resulted from vaccine administration and subsequent immunization is difficult, especially in young children. Many alleged side effects of vaccines occur with some frequency in this age group to begin with, and separating the temporality of vaccine administration from the natural occurrence of the event is nearly impossible. Also, the number of side effects seen is directly related to the number of doses administered— if a vaccination campaign is occurring where many doses of vaccine have been given, it is expected that the number of side effects will also increase, but the frequency (# side effects/ #doses) should remain the same. So, it is important to remember that the occurrence of an event post-vaccination does not in any way prove that the vaccine caused any signs or symptoms of the event and it is expected that the number of side effects seen will increase in proportion to the number of vaccinations given.

For currently used vaccines, any alleged reaction to a vaccine should be examined on the local level, and if it meets the criteria set below, an investigation into the event should begin.

The purpose of the investigation is to: confirm or rule out the reported event, identify other possible causes, determine whether the event is isolated and inform the parties involved as appropriate.

4.1 Steps of Investigation

Initial assessment:
As soon as any event is alleged to be vaccine-related, the health care worker should inform parents/guardians about the safety of immunization, reassure them, and explain that coincidental events can occur.

Any serious event, rumors or events occurring in clusters require(s) an investigation.
Until the investigation is complete, it will be impossible to determine the cause(s) of the event. These could be program-related, vaccine-related, not related to vaccination or unknown. In some situations, outside evidence will be necessary to identify the cause.

Program-related:
- Dosage level.
- Method of administration.
- Sterilization of needle and syringe.
- Improper handling of used needles.
- Vaccines reconstituted with wrong dilutant.
- Improper amount of dilutant.
- Improper preparation of vaccines.
- Drugs substituted for vaccines or dilutants.
- Contaminated vaccine or dilutant.
- Improperly stored vaccines.
- Failure to discard vaccines after their expiration date and subsequent use.
- If there are several cases, observe whether the same health worker administered the vaccine.
- Unimmunized population in the same age group and same geographical area showing the same symptoms.
- Other people immunized with the same lot of vaccine in the same geographical area showing the same symptoms.
- Other people immunized with the same vaccine lot at the same facilities on the same day without the same symptoms.

Vaccine-related
This is a personal and highly unusual incident (see Appendix 1). It is very important to investigate each case, and it is expected that a low incidence of vaccine-related events will be confirmed.

Not related to vaccination
When clinical events coincide with vaccination, it means that the event could have occurred even if the person had not been immunized. The best evidence to support the argument that this may have been a coincidental event, is for the same event to have been occurred in a population that was not immunized.

4.2 Information Required for the Investigation
The investigation report should include:

- Reasons for the diagnosis and possible causes.
- Person or number of persons found to have the same problem.
- Suspected antigen.
- Symptoms and signs common to all patients.
- Population vaccinated with the same vaccine lot.
- Names of the health workers who vaccinated the population in question.
- Whether health workers involved used the same vaccine lot.
- How many of the unimmunized population in the same age group and same community or health center in the area in question presented the same symptoms.
- Time between vaccination and onset of symptoms.
• Immunization practices of health workers involved, including handling, storage, transportation, and administration of vaccines.
• Laboratory findings, if necessary.
• Investigation form used to collect the information (if one was used).

4.3 Investigation
1. Investigation should be conducted within the first 24 hours.
2. General guidelines for the investigation:
   • Basic variables to be collected:
     ✓ Demographic data.
     ✓ Age, sex, place of residence.
     ✓ Recent case history (symptoms and signs, when they appeared, duration, clinical examination, treatment, outcome, diagnosis).
     ✓ Type, date of appearance, duration, and treatment of the clinical event.
     ✓ History of pathology and clinical history of the patient, (previous reactions to vaccines, drug allergies, preexisting neurological disorders, current medications, etc.).
     ✓ Vaccination history: type of vaccine used and date of last dose.
   • Identification of the vaccine used:
     ✓ Lot number.
     ✓ Manufacturing and expiration dates.
     ✓ Manufacturing laboratory.
     ✓ Origin of the vaccine, as well as shipment and transportation data.
     ✓ Physical appearance of the vaccine.
     ✓ Results of quality control procedures of the vaccine.
   • Review of operational aspects of the program:
     ✓ Storage of the vaccine.
     ✓ Handling and transportation of the vaccine.
     ✓ Use of dilutants, reconstitution of the vaccines, and forms of administration.
     ✓ Proper dosage.
     ✓ Availability of needles and syringes and appropriate practices.
   • Determination of whether the event reported is an isolated incident or whether there are other associated cases.
     ✓ Population vaccinated with the same lot of vaccine in the same period and showing the same symptoms.
     ✓ Unvaccinated population or population vaccinated with a different lot of vaccines (from the same or a different manufacturer) showing similar symptoms, to determine whether a similar incident has occurred, either in the unvaccinated population or with another lot.

After the investigation, the information should be analyzed to determine the cause, confirm the diagnosis or suggest other possible diagnoses.

Important at this stage will be the data collected on the case’s clinical diagnosis, based on the patient’s signs and symptoms, his/her clinical history and history of pathology, the event that may have precipitated the investigation, data leading to suspect the vaccine, and any laboratory results.

4.4 Actions to be taken
The actions to be taken should be based on the conclusions of the investigation, which will have one of the following outcomes:

1) The event is definitely not related to vaccination.
2) The event is related to vaccination.
• Program-related
• Vaccine-related

3) The investigation is inconclusive.

4.4.1 The event is definitely not related to vaccination.
Inform concerned parties of the results of the investigation. This may entail clear communication and information that may go to the parents, town, state, regulatory authorities, health authorities, professional associations, or the entire country, involving the mass media when appropriate.

Although the event was not related to vaccination, it may require appropriate medical follow up, in which case a referral should be made.

4.4.2 The event is related to vaccination.

Program-related
Inform concerned parties of the results of the investigation. This may entail clear communication and information that may go to the parents, town, state, regulatory authorities, health authorities, professional associations, or the entire country, involving the mass media when appropriate.

Corrective actions should be implemented immediately, and these should include logistical, training and supervisory aspects.

Vaccine-related
a) The event occurred within an expected frequency (see Appendix 1).
Inform concerned parties of the results of the investigation. This may entail clear communication and information that may go to the parents, town, state, regulatory authorities, health authorities, professional associations, or the entire country, involving the mass media when appropriate.

b) The event was unexpected or occurred at an unexpected frequency.
Inform concerned parties of the results of the investigation. This may entail clear communication and information that may go to the parents, town, state, regulatory authorities, health authorities, professional associations, or the entire country, involving the mass media when appropriate.

The following actions should immediately occur:
✓ Stop vaccinating with the vaccine implicated.
✓ Coordinate with the NCA to reassess the quality of the vaccine and contact manufacturer as appropriate.
✓ Recall the vaccine when is appropriate.
✓ Report investigation results to the Pan American Health Organization for international information dissemination.

4.4.3 The investigation is inconclusive.
Inform concerned parties of the results of the investigation. This may entail clear communication and information that may go to the parents, town, state, regulatory authorities, health authorities, professional associations, or the entire country, involving the mass media when appropriate.
In any case Pan American Health Organization is available for consultation to help the National Immunization Program (NIP) investigate and analyze the results.

5.0 Communication About Immunization Safety Concerns

Countries should work to improve the communication paths to the community and to health care workers. Messages should be disseminated quickly and they should address the concern(s) of the public. Educational materials promoting vaccination and expressing the risks and benefits of vaccination should be available. Key information about any investigation into a vaccine concern should be relayed to the public and other health care workers with honesty, completeness and accuracy.

A dedicated spokesperson within the health department should have special training for preparing media releases and developing public statements for rumor control. This person should also be a contact for the local health workers to provide assistance formulating plans regarding any alleged vaccine-related issues that may arise.

6.0 Education About Immunization Safety

Education materials should be available for health care workers to use during their encounters with children and their parents/guardians. These materials should provide information regarding known side effects and frequency at which they occur.

Also, health care workers need to know about events caused by program-related errors. Every health care worker should undergo training to learn how to avoid making program-related errors, which could lead, to an increase in side effects attributable to vaccination. During critical time periods (i.e. vaccination campaigns, ongoing investigations, etc.) health care workers should have information readily available to learn the facts about immunization, and disseminate accurate and truthful information to parents/guardians/adults.
## APPENDIX

**Summary Table for Vaccines and Vaccine-Preventable Diseases**

<table>
<thead>
<tr>
<th>Side Effects of Vaccine</th>
<th>Disease</th>
<th>Effects of the Disease</th>
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<tbody>
<tr>
<td><strong>OPV</strong>&lt;sup&gt;a&lt;/sup&gt; (oral polio-Sabin)</td>
<td><em>Poliomyelitis</em>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4-8% of infections have mild symptoms (fever, nausea, vomiting). 1-2% of infections result in aseptic meningitis; &lt;1% result in paralysis. Case fatality rate for paralytic cases ranges from 2-10%.</td>
</tr>
<tr>
<td>&lt;1% vaccine recipients develop fever, diarrhea, headache, myalgias Vaccine-associated paralytic poliomyelitis: 1 case/2.4 million doses distributed (overall rate); 1 case/750,000 initial doses; and 1 case/6.9 million subsequent doses.</td>
<td>Organism: <em>Poliovirus</em></td>
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<tr>
<td><strong>DTP</strong>&lt;sup&gt;a&lt;/sup&gt; (diphtheria, tetanus, pertussis)</td>
<td><em>Diphtheria</em></td>
<td>Effects are related to the toxin. Case fatality rate is 5-10% (higher death rates in the young and elderly). Cardiomyopathy and neuritis/neuropathy. Cutaneous and nasal forms of the disease exist also.</td>
</tr>
<tr>
<td>Mostly due to the pertussis component of the vaccine. Local reactions such as pain, erythema and edema are very common, and incidence increases with subsequent doses. Fever occurs 1, 2 doses, high fever (≥40.5°C) 1/330 doses, collapse 1/1,750 doses, convulsions 1/1,750 doses. Sterile abscesses are rare (6-10/million doses).&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Organism: <em>Corynebacterium diphtheriae</em></td>
<td></td>
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<tr>
<td><strong>Pertussis</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td><em>Bordetella pertussis</em></td>
<td>Highly communicable disease (&gt;90% attack rates in unvaccinated contacts) of the respiratory tract. Characteristic paroxysmal cough with inspiratory whoop is the origin of the term “whooping cough” used to describe this disease. Can also cause pneumonia, seizures and encephalopathy. About 1/200 cases &lt;6 months of age dies. Worldwide, approximately 200-300,000 deaths are attributed to pertussis infection.</td>
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<tr>
<td><strong>Tetanus</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td><em>Clostridium tetani</em></td>
<td>Infection causes painful muscle contractions, starting in the muscles of the neck and jaw (“lockjaw”) and then progressing to trunk muscles. For neonatal tetanus, the case fatality rates are high (for those cases with short incubation periods, &gt;80%). Case fatality rates for tetanus are country dependent and range from &lt;1-90%.</td>
</tr>
<tr>
<td>Local reactions- erythema, tenderness and induration are common. Fever, chills and headaches are less common. Rarely, cases of Guillain-Barré Syndrome (GBS) have occurred after vaccine administration. Hypersensitivity reactions may occur with frequent vaccination.</td>
<td></td>
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<tr>
<td><strong>TT</strong>&lt;sup&gt;a&lt;/sup&gt; (tetanus toxoid)</td>
<td>See tetanus above.</td>
<td>See tetanus above.</td>
</tr>
</tbody>
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<sup>a</sup>There is currently no scientifically sound evidence to establish a causal relationship between autism, SIDS, infantile spasms or Reye syndrome and the DTP vaccine.
<table>
<thead>
<tr>
<th>Side Effects of Vaccine</th>
<th>Disease</th>
<th>Effects of the Disease</th>
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<tbody>
<tr>
<td>MMR (measles, mumps, rubella)</td>
<td>Measles</td>
<td>Acute highly communicable disease with fever, conjunctivitis, coryza, cough and Koplik spots in the mouth. Characteristic red rash appears 3-7 days later. Complications may arise from bacterial superinfection in 10% of cases. The case fatality rate in developed countries is approximately 0.2%, and in developing countries it is 3-5%. Acute encephalitis occurs in 1/1,000 cases and subacute sclerosing panencephalitis (SSPE) occurs as a late complication (years after infection) in 1/100,000 cases.</td>
</tr>
<tr>
<td>Mumps</td>
<td>Measles Organism: Measles virus</td>
<td></td>
</tr>
<tr>
<td>Rubella</td>
<td>Organism: Rubella virus</td>
<td></td>
</tr>
<tr>
<td>Rubella</td>
<td>Organism: Rubella virus</td>
<td>About 50% of the cases are sub-clinical. Infection causes a mild febrile illness with a rash and lymphadentopathy. Arthritis and arthralgias occasionally occur. Encephalitis and thrombocytopenia are rare complications. <strong>Congenital rubella syndrome</strong>-This syndrome occurs in approximately 90% of all infants infected during the first trimester of pregnancy. These infants have congenital malformations- deafness, cataracts, microcephaly, mental retardation, heart defects, bone disease, etc. and they are at risk for spontaneous abortion.</td>
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<tr>
<td>Mumps</td>
<td>Organism: Mumps virus</td>
<td>About 1 in every 200 children develops encephalitis. About 2/3 of those infected develop swelling of the salivary (parotid) glands. Orchitis (inflammation of the testicles) occurs in 1 out of every 5 post-pubertal males. Sterility is a rare complication. Deafness may occur, but is uncommon.</td>
</tr>
</tbody>
</table>

\[b\] There is currently no scientifically sound evidence to establish a causal relationship between neuropathy or residual seizure disorder and the mumps vaccine.
<table>
<thead>
<tr>
<th>Side Effects of Vaccine</th>
<th>Disease</th>
<th>Effects of the Disease</th>
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</table>
| **Hib** *Haemophilus influenzae* type b. | **Haemophilus influenzae** infections  
Organism: *Haemophilus influenzae* type b | Before the introduction of the vaccine, *H. flu* was the most common bacterial cause of meningitis. Case fatality rate of meningitis is about 5%. About 10-15% has serious neurological sequelae and deafness in 15-20%. Also major cause of epiglottitis before vaccine was available. Case fatality rate of epiglottitis is 1%. Responsible for cellulitis and pneumonia. |
| Side effects are transient and minor—pain at the injection site (5-15%), fever (2-3% - usually low grade), nausea, dizziness, malaise, myalgia and arthralgia. Anaphylaxis is uncommon and occurs at an estimated rate of 1/600,000. Although various events (demyelinating diseases, Guillain-Barré syndrome, arthritis, and sudden infant death syndrome) have been reported, there is inadequate evidence to either accepts or rejects the possibility that they are caused by hepatitis B vaccination. | **Hepatitis B** infections  
Organism: Hepatitis B virus | Causes a wide range of disease manifestations: fulminant fatal hepatitis, clinical hepatitis with jaundice, subacute illness with non-specific symptoms and asymptomatic seroconversion. Chronic hepatitis B infection occurs in up to 30% of children infected after birth and in 5-10% of older children/adolescents. Acute illness has a case fatality rate of 1-2%. Chronic infection may lead to hepatic cirrhosis or hepatocellular carcinoma. |
| Mild symptoms (headache, myalgia, etc) occur in 2-5% vaccine recipients. Allergic reactions occur at a rate of 1/1 million. Encephalitis temporally associated with vaccine administration has occurred in 18 reported cases (one was fatal) in the past 55 years, with an estimated 300 million doses delivered. | **Yellow fever**  
Organism: Yellow fever virus  
Vector: Mosquito | About 15% of those infected develop a serious illness with several phases: acute, remission and toxic. Once the toxic phase is reached, the case fatality rate is about 50%. Immunized (naturally or vaccinated) individuals seem to have a milder clinical illness, case fatality rates in unimmunized populations can exceed 50%. |
| Reactions at the injection site are expected and indicate successful vaccination: erythema, papule/pustule formation and ulceration. Suppurative adenitis is rare, occurring in 0.2-4.0 vaccine recipients per 1,000. Disseminated BCG infection occurs in 1/1 million doses and usually in immunocompromised individuals. Keloid formation may occur if injection given in improper site. | **Tuberculosis**  
Organism: *Mycobacterium tuberculosis* | Causes pulmonary disease, meningitis and disseminated infection. Infection is usually latent for long periods of time, only to be re-activated later in life. |

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There is currently no scientifically sound evidence to establish a causal relationship between multiple sclerosis, chronic fatigue syndrome, rheumatoid arthritis, autoimmune disorders or inflammatory bowel disease and the hepatitis B vaccine.
<table>
<thead>
<tr>
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<th>Side Effects of Vaccine</th>
<th>Disease</th>
<th>Effects of the Disease</th>
</tr>
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<tbody>
<tr>
<td><strong>Pneumococcal</strong></td>
<td>Local reactions are common. Serious events are uncommon. Low-grade fever is common. Anaphylaxis and other allergic reactions are extremely rare.</td>
<td>Pneumococcal infections (Organism: <em>Streptococcus pneumoniae</em>)</td>
<td>Since the introduction of Hib vaccine, pneumococci are one of the most common bacterial causes of meningitis. Case fatality rates for pneumococcal meningitis range from 10-30%. This organism also causes acute otitis media, pneumonia and other invasive diseases. Mortality from invasive disease is high in populations with chronic illnesses and with compromised immune systems.</td>
</tr>
<tr>
<td><strong>Meningococcal</strong></td>
<td>Most common localized reaction is erythema. Usually localized reactions are mild and infrequent. Low-grade fever may occur in 2% of recipients.</td>
<td>Meningococcal disease (Organism: <em>Neisseria meningitidis</em>)</td>
<td>Since the introduction of Hib vaccine, this organism is one of the most common causes of meningitis (along with pneumococci). Also, meningococcemia is another invasive disease caused by this bacterium. Fulminant cases may have purpura, disseminated intravascular coagulation, shock, coma and death.</td>
</tr>
</tbody>
</table>
References


