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Hello and welcome to this webinar. My name is Commander Mark Freedman, and I am a U.S. public health service veterinary officer at the Centers for Disease Control and Prevention. Vaccines are critical tools that we have to protect populations, and in this webinar, we’re going to discuss the systems in place in the United States for monitoring and reporting vaccine safety.

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Vaccines are one of the greatest success stories in public health.

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Through use of vaccines, we have eradicated smallpox and nearly eliminated wild polio virus.

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Vaccines have also reduced the morbidity and mortality from many other diseases, including measles, diphtheria and pertussis. The number of people who experience the devastating effects these of preventable infectious diseases is at an all-time low.

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Additionally, we now have multiple vaccines authorized for emergency use by the Food and Drug Administration to combat SARS COV 2, the virus causing the ongoing COVID-19 pandemic.

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To ensure the continued success of all vaccines, it’s crucial to make sure that vaccines are safe [CLICK]. As a frontline healthcare provider, you should be aware of our nation’s long-standing multiple vaccine safety systems to ensure that vaccines are as safe as possible.

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By knowing these critical safety systems, you can build rapport with your patients, encourage vaccine uptake, and save lives.

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In this webinar, we will review the vaccine life cycle and understand how safety is monitored at every phase of the life cycle, [CLICK] learn how federal agencies like the Centers for Disease Control and Prevention and the Food and Drug Administration monitor vaccine safety through special programs, and [CLICK] know how adverse events are monitored and reported. With this knowledge, [Click] we hope that you as a frontline healthcare worker can educate your patients about vaccine safety.

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Although no vaccine is actually 100% safe or effective for everyone because each person’s body reacts to vaccines differently, vaccines are the best defense we have against infectious diseases, and knowing how vaccines are monitored for safety will help you answer your patient’s questions. Let’s get started!

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Let’s first begin with an overview of vaccine life cycle.

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Before vaccines are approved, scientists test them extensively to ensure they are effective and safe. The vaccine life cycle describes the process by which every vaccine must go through before it hits the market and follows the same general pathway as for drugs and other biologics.

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Safety is a priority during each phase of this life cycle.

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Let’s start with the first phases of this life cycle, when scientists conduct basic research, develop new vaccines, and conduct pre-clinical studies.

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When novel vaccines are developed, they are tested extensively in laboratory settings to ensure their safety.

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First, researchers use computer models to predict how the vaccine will interact with the human immune system.

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Then, researchers test the vaccine on animals such as mice, monkeys, rabbits, and guinea pigs. An IND or investigational new drug application is submitted to the FDA after this initial phase.

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Once the vaccine has passed pre-clinical studies, the next step is performing clinical trials.

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All vaccines must undergo three phases of clinical trials.

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**Phase 1** trials are small, involving only 20 to 100 volunteers, and last only a few months. The purpose of phase one trials is to evaluate basic safety and identify very common reactions.

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**Phase 2** trials are larger and involve several hundred participants. These studies last anywhere from several months to two years and collect additional information on safety and efficacy. Data gained from phase two trials can be used to determine the composition of the vaccine, how many doses are necessary, and a profile of common reactions.

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**Phase 3** trials are the next step, unless the vaccine is ineffective or causes health problems, and are expanded to involve several hundred to several thousand volunteers. Typically, these trials last several years. Because the vaccinated group can be compared to those who have not received the vaccine, researchers are able to identify true reactions. A BLA or biologics license application is then submitted to FDA.

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The next step in the life cycle is the

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FDA review process, where vaccine manufacturers must provide the FDA with their test results for vaccine safety, potency, and purity. The FDA must make a determination of whether to approve the new vaccine, or in emergency situations, to authorize the use of the vaccine under emergency use.

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The Advisory Committee on Immunization Practices (ACIP) then reviews vaccine safety and effectiveness data and develops recommendations for target audiences based on that data. ACIP comprises medical and public health experts who develop recommendations on the use of vaccines in the civilian population of the United States.

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Finally, Phase 4 safety monitoring and research begins after a vaccine is licensed or authorized and recommended for public use.

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During this phase, the FDA requires that all manufacturers submit samples from each vaccine lot prior to its release.  [CLICK] Each lot must be tested because vaccines are sensitive to environmental factors like temperature, and can be contaminated during production. [CLICK] Although rare, the FDA rarely has recalled vaccine lots, for concerns such as mislabeling, contamination during production, and potential manufacturing problems at a production plant.

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We have now covered the vaccine life cycle, and as you can see vaccine safety is incorporated into each phase of this robust process. This life cycle can often be a lengthy process, typically lasting at least 6 years.

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For the development of the COVID-19 vaccines, an accelerated vaccine development process was used, formerly known as Operation Warp Speed.  During public health emergencies, such as the COVID-19 pandemic, the vaccine life cycle may be accelerated to authorize a vaccine for emergency use. Vaccines must still meet FDA's rigorous scientific standards for safety, effectiveness, and manufacturing quality.

The traditional vaccine timeline was accelerated in stages by:

* Creating vaccine candidates immediately after the viral genome sequence was available
* Using vaccine platforms developed for other diseases
* Conducting large scale phase 3 clinical trials which allowed for rapid collection and earlier analysis of safety and efficacy data
* Funding large-scale manufacturing of the vaccine candidates during phase 3 trials to ensure any vaccine proven safe and effective was immediately available upon FDA EUA approval or authorization
* Recommended allocation methodology based on pandemic flu planning
* Planning for infrastructure and distribution before any vaccines were authorized

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Next, let’s first discuss how CDC monitors vaccine safety.

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The Centers for Disease Control and Prevention or CDC and the Food and Drug Administration or FDA are the primary national agencies that [monitor the safety of vaccines](https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/index.html) after they are approved or authorized for use.

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If a problem is found with a vaccine, CDC and FDA will inform health officials, health care providers, and the public.

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CDC and FDA have many systems in place to monitor vaccine safety.

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One system that is co-managed by both agencies is the [CLICK] [Vaccine Adverse Event Reporting System or VAERS](https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/index.html)

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While clinical trials provide important information on vaccine safety, the data are somewhat limited because of the relatively small number of study participants.

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Rare side effects and delayed reactions might not be evident until the vaccine is administered to millions of people.

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Therefore, CDC and FDA established the VAERS system.

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VAERs serves as a nationwide vaccine safety surveillance program to monitor adverse events following vaccination.

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The system can provide an early warning to detect possible safety issues with U.S. vaccines by collecting information about adverse events such as possible side effects or health problems that occur after vaccination.

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Specifically, VAERS is meant to detect any new, unusual or rare adverse events, especially those that are unexpected. VAERS also monitors any increases in known side effects, like arm soreness where a shot was given. Additionally, VAERS identifies potential patient risk factors for particular types of health problems related to vaccines. All in all, [CLICK] the system is meant to assess the safety of licensed vaccines once they have been approved or authorized by the FDA and they have entered Phase 4 monitoring.

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The VAERS form can be accessed online at vaers.hhs.gov, and collects information about the type of vaccine received, the timing of the vaccination, the onset of the adverse event, current illnesses or medications, past history of adverse events following vaccination, and demographic information

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The number of VAERS reports submitted varies each year. In 2019, VAERS received over 48,000 reports.

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About 85-90% of the reports describe mild side effects such as fever, arm soreness, and crying or mild irritability.

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The remaining reports are classified as serious, which means that the adverse event resulted in permanent disability, hospitalization, life-threatening illness, or death.  While these problems happen after vaccination, they are rarely caused by the vaccine.

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It is important to keep in mind that anyone who gives a licensed vaccine, such as a healthcare provider

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Anyone who receives a licensed vaccine

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can report any significant health problem that occurs after vaccination. VAERS is open to healthcare providers and the lay public alike.

Slide 47

An adverse event can be reported even if it is uncertain or unlikely that the vaccine caused it.

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Reporting to VAERS helps scientists at CDC and FDA better understand the safety of vaccines. CDC recommends that providers report all vaccine administration errors to VAERS.

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A full discussion on VAERS isn’t complete without considering the strengths and limitations of this surveillance system, as listed here.

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Apart from VAERS, CDC maintains three other systems to monitor vaccine safety.

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Let’s start with the Vaccine Safety Datalink or VSD

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The VSD started in 1990 and continues today in order to monitor safety of vaccines and conduct studies about rare and serious adverse events following immunization. The VSD is a collaborative project between CDC’s Immunization Safety Office and nine health care organizations. It monitors vaccine safety, investigates rare and serious adverse events that occur after vaccinations, and provides recommendations to federal agencies.

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Here’s a map showcasing the 9 healthcare organizations that are involved in VSD.

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The VSD uses electronic health data from each participating site. This includes information on vaccines: the type of vaccine given to each patient, date of vaccination, and other vaccinations given on the same day. The VSD also uses information on medical illnesses that have been diagnosed at doctors’ offices, urgent care visits, emergency department visits, and hospital stays.

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The VSD then conducts vaccine safety studies based on this information from electronic health records. The VSD also conducts vaccine safety studies that come from questions or concerns in the medical literature or from other vaccine safety systems, like VAERS. Whenever there are new vaccines that have been recommended for use in the United States or if there are changes in how a vaccine is recommended, the VSD will monitor the safety of these vaccines.

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VSD uses Rapid Cycle Analysis to detect adverse events following vaccination in near real time so the public can be informed quickly of possible risks. Using VSD data that are updated each week, the rates of adverse events that occur in people who have received a particular vaccine are compared to the rate of adverse events that occurs in a similar group of people who have not received that vaccine. If the rate of adverse events among vaccinated people is higher than among the comparison group, the vaccine may be associated with an adverse event.

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Vaccination protects pregnant women and unborn babies from several preventable diseases. Because it is so important to protect pregnant women, evaluating the safety of vaccines given to women during pregnancy is a high priority for the VSD. VSD has developed algorithms to identify pregnant women and determine the start and end dates of the pregnancy. VSD is also able to use data to study the health of children born to women who were vaccinated during pregnancy.

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Let us now move on to the next program that CDC manages, which is the Clinical Immunization Safety Assessment or CISA.

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CDC’s Clinical Immunization Safety Assessment (CISA) Project was established in 2001 to address the unmet vaccine safety clinical research needs of the United States. CISA is a national network of vaccine safety experts from CDC’s Immunization Safety Office, seven medical research centers, and other partners. The network provides a comprehensive vaccine safety public health service to the nation.

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Here’s a map showcasing the current CISA project sites.

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CISA aims to accomplish many goals. The network serves as a vaccine safety resource for consultation on clinical vaccine safety issues, including individual case reviews, and to assist with immunization decision-making. CISA also assists CDC / Health and Human Services (HHS) and partners in developing strategies to assess individuals who may be at increased risk for adverse events. CISA also conducts studies to identify risk factors and preventive strategies for adverse events, particularly in special populations. Finally, the CISA Project provides consultation to US clinicians who have vaccine safety questions about a specific patient residing in the US. In addition, CISA provides consultation to US healthcare providers and public health partners on vaccine safety issues, and reviews clinical adverse events following immunization involving the US-licensed vaccines.

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Let us finally turn to the last program that CDC manages, the V-Safe program.

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**V-safe** is the newest of the programs we have discussed so far. It was established during the ongoing COVID-19 pandemic and is a voluntary, smartphone-based tool that uses text messaging and web surveys to provide personalized health check-ins after a patient receives a COVID-19 vaccine. Through **v-safe**, patients can quickly tell CDC if they experience any side effects after getting a COVID-19 vaccine. Depending on a patient’s answers, someone from CDC may call the patient to check and get more information. The program allows CDC to evaluate any side effects that may result after individuals receive a COVID-19 vaccine.

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Now that we have discussed the many vaccine safety systems that are managed by federal agencies, let us present a few success stories where policies and guidance changed because of the robust surveillance systems we have in place to monitor vaccine safety.

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In the last decades, numerous changes in vaccine production and administration have reduced the number of side effects and resulted in safer vaccines.

* + VAERS and CISA helped confirm that Tdap was safe to administer during pregnancy.
	+ VAERS picked up on febrile seizures in toddlers receiving both the flu and pneumococcal vaccines concomitantly, thus leading to educating parents of the potential that could happen.
	+ VAERS identified the risk of intussusception with RotaShield, the first rotavirus vaccine licensed in the United States, leading to its withdrawal from the market.

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We hope that this webinar provides you with an understanding of the systems that we have in place to ensure vaccine safety. Thank you for being a frontline healthcare provider, and for your commitment to vaccinating your patients!

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Additional resources on the topics we presented in this webinar are listed on the following slides.

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[No voiceover]

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[No voiceover]

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I would like to thank the CDC COVID-19 Vaccine Task Force Clinical Education Team for their contributions to this webinar

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This concludes this webinar, and thank you so much for your attention.