

Clinical Researcher

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Clinical Researcher—May 2020 (Volume 34, Issue 5)

PEER REVIEWED

What is a Human Challenge Trial and How Does it Expedite Vaccine Development?

Seema Garg, MS, MBA, CQA, CSSGB



In light of the current COVID-19 crisis, we are seeing an intense focus on the question of how soon we can make a vaccine available to protect the public from the novel SARS-CoV-2 coronavirus. Typically, developing a vaccine against any illness can take years and millions of dollars, and in some cases we still may not have complete success. For example, we have a vaccine for influenza, but it is not a universal vaccine; there is no vaccine for HIV, even after decades of research.

The last global pandemic was the 2009 H1N1 influenza (flu) pandemic. The first H1N1 case detected in United States was in April 2009, and by June 11 the World Health Organization (WHO) signaled that a global pandemic of H1N1 influenza was under way. On July 23, the U.S. Food and Drug Administration's (FDA's) Vaccine and Related Biological Advisory Committee indicated agreement with the agency's proposal to license a H1N1 vaccine candidate via a "strain change" pathway, and this was only possible because already-approved influenza vaccines existed for other strains of influenza virus, which unfortunately is not the case with the current COVID-19 pandemic. On September 15, 2009, FDA approved four vaccine candidates for H1N1 influenza and on November 16, 2009, approval was granted for a fifth vaccine. {1}

So, what could expedite the development a vaccine against COVID-19? One tool in the research community’s toolbox is known as the human challenge trial (HCT). Open Orphan, a European clinical research organization, has launched a human coronavirus challenge study model aimed to guide and test the efficacy of new and existing vaccine candidates for COVID-19.{2}

Defining a Human Challenge Trial

According to the WHO, HCTs are “trials in which participants are intentionally challenged (whether or not they have been vaccinated) with an infectious disease organism. This challenge organism may be close to wild-type and pathogenic, adapted and/or attenuated from wild-type with less or no pathogenicity, or genetically modified in some manner.”{3}

Essentially, in a typical Phase I trial, new drugs or vaccines are tested in healthy volunteers to determine the safety of the investigational product; the subjects are only given the drug or the vaccine that is being studied—they are never intentionally administered the disease-causing agent. In the case of an HCT, the healthy volunteers are administered the disease-causing agent to study their reactions to it. Depending on the design of the HCT, the healthy volunteer may or may not be administered a protective drug or vaccine before or after administration of the disease-causing agent.

Why Conduct a Human Challenge Trial?

The purpose of an HCT is the same as that of animal challenge studies and models, with the added advantage of studying the potential drug/vaccine candidates directly in humans in a controlled environment. This allows the research community to screen potential drug/vaccine candidates and move the most promising candidates to larger trials.

The advantage of an HCT over an animal challenge study is the speed it offers for identifying a good drug/vaccine candidate. Typically, when drug/vaccine candidates are studied in several different species of animals, the results are extrapolated to how these drug/vaccine candidates can be effective in humans and then tested in volunteer participants.

Not all drug/vaccine candidates that show promise in animal studies produce successful results in Phase I studies. With an HCT, the effectiveness of a drug/vaccine candidates that shows promise can be determined much faster. The new drug/vaccine candidates still have to go through the routine Phase I, II, and III trials, but the speed of taking a drug/vaccine candidate from the lab to Phase I trials can be cut significantly with HCTs.

Are Human Challenge Trials Ethical?

Is it ethical to administer a healthy individual with disease-causing agent? After all, the Declaration of Helsinki states: “The health of my patient will be my first consideration”{4} and “While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.”{4}

By and large, the clinical research community has reached a consensus that, with proper oversight, it is ethical to conduct HCTs when they offer the greatest chance for rapid development of much-needed treatments. The argument is that HCTs can screen potentially effective drug/vaccine candidates in a much more controlled in-patient setting and with a much lower number of participants compared to routine testing in much larger populations. The early safety-determining advantages of this tactic extend into the somewhat less controlled environments of Phase II and III trials.{5}

So, one could argue that it is better to generate initial effectiveness data in small populations—and in a controlled setting—than to expose large populations to the potential drug/vaccine candidates in a less controlled environments. You might call this a “do less harm” kind of policy, and of course it can save time and money in critical healthcare situations.

What Do You Need to Conduct a Human Challenge Trial?

What you need to conduct an HCT depends on what kind of challenge agent is being studied. There are no special requirements as far as U.S. regulations are concerned, but there are many guidance documents on the topic issued by different agencies and regulatory bodies. The most prominent guidances are the ones issued by Centers of Disease Control (CDC) on the topic of infection control, since most challenge agents being studied will be infectious organisms.

Some of the guidance documents issued by the CDC are on general infection prevention and some are specific to the organisms/disease being handled. An important page to bookmark for these guidance documents is <https://www.cdc.gov/infectioncontrol/guidelines/index.html>. {6} You can find infection control guidelines on activities ranging from basic disinfection and handwashing to preventing the spread of influenza and Ebola.

It is important to keep in mind that guidances issued by the CDC are not specifically about the conduct of HCTs, but they are for infection control within healthcare settings when caring for confirmed cases, probable cases, and cases under investigation for infection. However, these guidances can be applied depending upon the exact nature of disease agent a Human Challenge Unit plans to study.

A Human Challenge Unit is essentially a healthcare facility that handles patients with diseases—the only difference is that the unit knows what challenge agent it is studying at any given time, whereas a hospital must be always prepared for all common infectious agents. The premise of having the processes and systems for infection control, however, will be the same for both facilities. Some of the systems and processes for infection control that both type of facilities need to include are:

- Procedures for using personal protective equipment (PPE): gowning, gloving, masking before entering the areas where the infected patients/participants are housed and for de-gowning, de-gloving, and de-masking before the staff and/or other personnel leave these areas. {7}
- Procedures to disinfect or sterilize medical waste before it leaves the facility, including used PPE. {8}
- Procedures for movement in the facility: To reduce the potential for contamination, the facility should be designed for uni-directional movement; staff or patients/participants should move from low infection areas to high infection areas and not vice versa. {6}
- Procedures for environmental infection control: The cleaning and disinfection of all items used in the Challenge Unit, including bed rails, tables, chairs, and other items that tend to stay in participants' rooms, and things that are more mobile, like laundry, service utensils, etc. Everything must be treated as a potential infection carrier. {9}

- Engineering controls: One of the most important infection control mechanism is the design of the facility and a facility's ventilation system. There are many recommendations for how this should be done covering air flow, air exchanges, filters to be used in the ventilation systems, and whether the air should be re-circulated. {6}

All of this should be done based on what challenge agent the Challenge Unit plans to work with, so it is important to have agile facilities that can adapt to the different requirements of different organisms being studied. It is also important for the operational team to know the limits of its facilities and resources, and to never agree to study an organism that is incompatible with the biosafety level of the facilities. Know your expertise, but also know your limitations.

Current Regulatory Framework

Challenge agents that have been or are being studied around the world include viruses, toxins, allergens, bacteria, and fungi. Some examples include studies on cholera {10} and influenza. {11} Many of these studies are listed on <https://www.clinicaltrials.gov/ct2/home>.

In the United States, challenge agents are considered to be drugs, and therefore the FDA has jurisdiction over the challenge studies. However, in the United Kingdom and European Union, the regulatory authorities do not consider challenge agents to be drugs. {12}

The FDA has included human challenge studies in its Guidance for Development of Vaccines to Protect Against Global Infectious Diseases, but has mostly said that study sponsors should discuss their development plan with the Center for Biologics Evaluation and Research prior to initiation of such studies. {13}

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SPECIAL FEATURE

Safety Precautions for Laboratory Research with SARS-CoV-2 Positive Specimens and COVID-19 Subjects

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The global pandemic caused by the coronavirus (SARS-CoV-2) and the disease it causes (COVID-19) have brought biosafety to the forefront of most everyone's minds. Things like hand hygiene, personal protective equipment (PPE), and respiratory protection are no longer niche topics.

In the research community, we're seeing a surge of interest in the requisite safety practices for research involving specimens from SARS-CoV-2 positive individuals and COVID-19 subjects. The Centers for Disease Control and Prevention (CDC), the Occupational Safety and Health Administration (OSHA), and the American Biological Safety Association International (ABSA International) have issued guidelines for implementation of well-established safety practices for such research. {1–4}

Start with a Risk Assessment

According to the CDC's *Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 (COVID-19)*, “[a]ll laboratories should perform a site-specific and activity-specific risk assessment to identify and mitigate risks.”{1}

The CDC's emphasis on “site-specific” and “activity-specific” assessments is telling—there is no single approach that ideally fits all laboratories and all research procedures. Each risk mitigation plan must be based on the potential biological hazards unique to the activity and the environment where the activity takes place. The CDC notes the assessment and accompanying risk mitigation measures depend on:

- The procedures performed
- The hazards involved in the process/procedures
- The competency level of personnel performing the procedures
- The facility and its laboratory equipment
- The resources available

Risk assessments begin with defining the risks associated with the hazard. SARS-CoV-2 is believed to be transmitted through exposure of the mucous membrane such as the eyes, nose, and mouth with:

- Infectious respiratory droplets, and/or
- Direct contact with infected body fluids, and/or
- Exposure to contaminated fomites (such as contaminated PPE or used tissue paper).{5}

The virus may also be transmitted by inhaling infectious aerosols.{6,7} The virus' genetic material (RNA) has been detected in various types of clinical specimens including blood, urine, feces, anal swabs and oropharyngeal swabs, as well as sputum and bronchoalveolar lavage fluid.{8,9} Respiratory secretions are associated with higher levels of viral RNA and viral transmission and are therefore considered to pose the highest risk of the specimens mentioned. The presence of SARS-CoV-2 RNA in patient blood implies infection via exposure to contaminated sharps is a possibility; however, the likelihood is unknown. With the hazards

identified, the next step is discerning the level of risks posed by different experimental procedures.

Developing the Risk Mitigation Plan

A comprehensive risk mitigation plan will address foreseeable risks associated with the research materials, starting with their origination and transport to the laboratory and ending with waste treatment and disposal. The risk mitigation plan should also address incident response and reporting. Comprehensive risk mitigation plans must also include procedures to follow in the event of spills or exposures to infectious agents. A thorough risk mitigation plan will address:

- Employee training regarding the hazards
- Necessary safety precautions for employees to safely conduct their duties
- Engineering controls and PPE necessary to safely conduct the research
- Treatment and disposal of infectious/regulated medical waste
- Occupational health and incident response
- Administrative controls such as inspections and competency drills

The OSHA general duty clause states employers must provide employees a work environment free from recognized hazards that are likely to cause serious physical harm or death.^{10} Work involving human blood and tissues is subject to the OSHA bloodborne pathogen (BBP) standard.^{11} The BBP standard requires employers to determine which employees are at risk of an occupational exposure to bloodborne pathogens and ensure they are properly trained, provided with PPE, enrolled in an occupational health program, and offered hepatitis B vaccinations.

OSHA also requires employers develop a bloodborne pathogen exposure control plan (ECP). Depending on the type of proposed research, the ECP may also serve as a risk mitigation plan. At the very least, the ECP or an existing biosafety manual may provide a starting point for drafting a risk mitigation plan for coronavirus research.

Here are some considerations for developing the risk mitigation plan:

Low-Risk Procedures

Low-risk procedures which are not anticipated to produce infectious droplets or aerosols may be performed in a Biosafety Level 2 (BSL-2) laboratory as long as standard precautions are taken when handling clinical specimens. This includes proper hand washing practices and the use of appropriate PPE, such as gloves, lab coats or gowns, and eye protection.

Procedures that are not anticipated to produce infectious droplets or aerosols include receiving potentially infectious specimens and performing microscope-based assessment of fixed slides. If working with unfixed samples, the use of surgical masks, N95 respirators, or biosafety cabinets may be recommended, based on a risk assessment.

Procedures with Potential to Generate Droplets or Aerosols

Procedures with mild to moderate potential to produce infectious droplets or aerosols can be performed in BSL-2 laboratories with enhanced safety practices. Such procedures should be performed in an adjoining room from the rest of the laboratory. The room should have a door which can be shut to restrict access, and occupancy should be limited to the fewest number of individuals necessary to perform the laboratory procedures. Inward airflow should be exhausted directly out of the lab without recirculation to the rest of the facility.

All procedures with potential to produce infectious droplets or aerosols should be performed within a certified biosafety cabinet (see Figure 1) or other HEPA filtered aerosol containment device. Respiratory protection such as N95 respirators or powered air purifying respirators should be considered, based on a risk assessment. Centrifugation should be performed within centrifuges equipped with safety cups or sealed rotors loaded and opened within a biosafety cabinet. If utilizing suction to aspirate infectious liquids, the procedures should be performed within a biosafety cabinet, and the vacuum line should be equipped with a HEPA filter.

Figure 1: Biosafety Cabinet

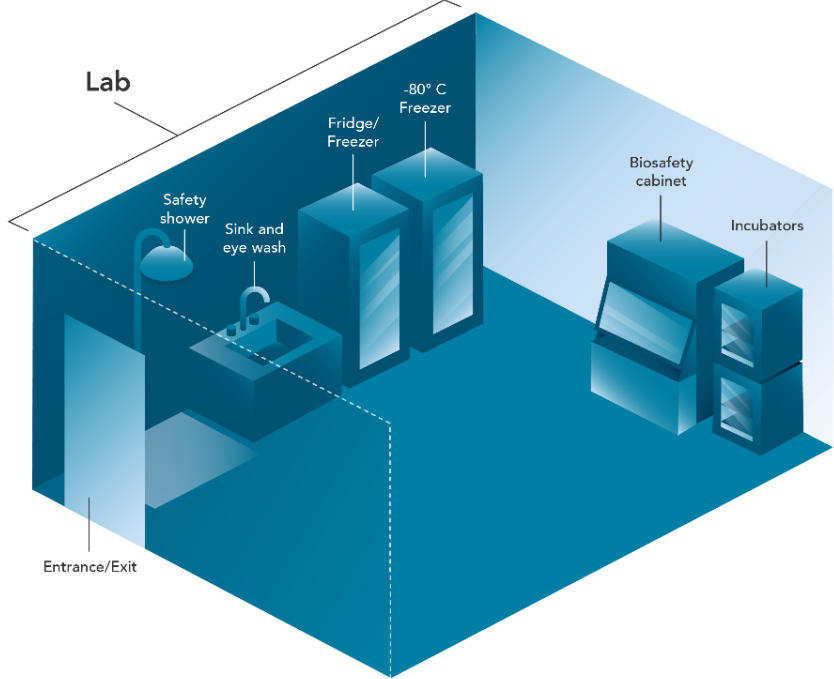
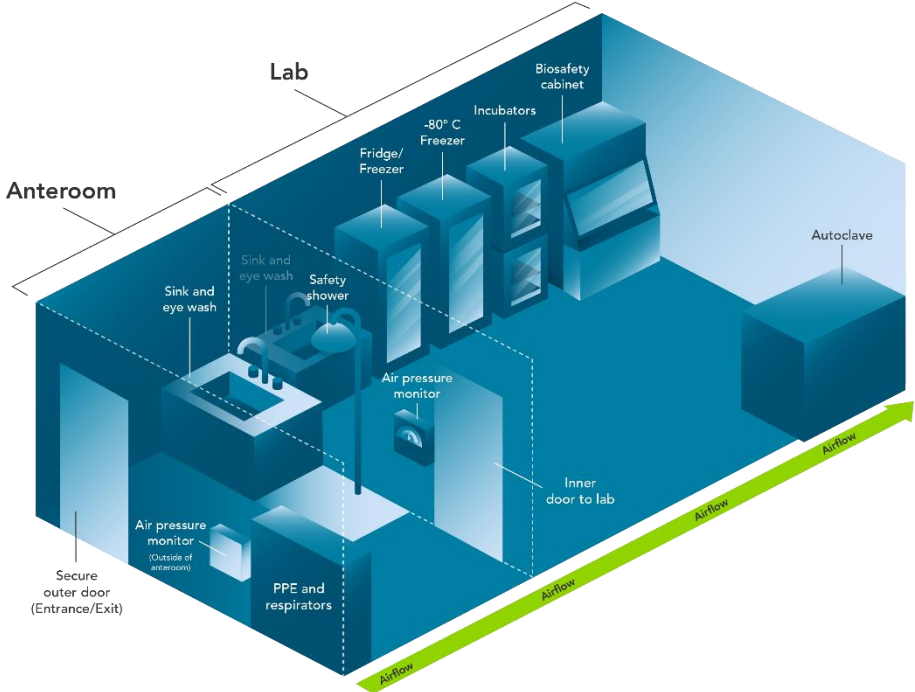


Biosafety cabinets provide an enclosure to contain droplets and operate under negative air pressure (i.e., suck inward) to protect users from exposure to aerosolized infectious agents. Any infectious aerosols are sucked in through the grills positioned at the front and back of the work surface and removed by HEPA filtration. The HEPA-filtered exhaust protects the community and environment from exposure to aerosolized research materials. The hood also blows sterile, HEPA-filtered air from the top toward the work surface to protect the research materials from contamination with non-sterile, ambient room air.

Virus Isolation, Characterization, and Vaccine Studies in Animal Models

While a typical BSL-2 laboratory provides adequate containment for diagnostic assays as well as quantification of viral and antibody titers, Biosafety Level 3 (BSL-3) containment is required for culturing and characterizing the virus or conducting vaccine challenge studies in animal models. BSL-3 laboratories are designed to contain aerosol transmissible pathogens (see Figure 2).

Figure 2: Key Features of BSL-2 and BSL-3 Laboratories

Key Features	Laboratory Design
<p>Biosafety Level 2 (BSL-2) laboratories are designed for work with clinical specimens and microorganisms that cause mild to moderate disease in healthy adults.</p> <p>Lockable doors restrict access and allow posting of hazard signage. A sink with an eye wash is available as well as a safety shower.</p>	
<p>BSL-3 laboratories are designed to contain aerosol-transmissible pathogens. Design criteria builds on requirements for BSL-2, including:</p> <p>An anteroom</p> <p>Visual airflow indicators</p> <p>Unidirectional, inward-flowing, single-pass air that should be exhausted through a HEPA filter</p> <p>Biosafety cabinet(s)</p> <p>Autoclave</p>	

BSL-3 lab design criteria include a two-door entry system to provide security and an anteroom for donning and doffing PPE (including respiratory protection). The laboratory must have unidirectional, inward-flowing, single-pass air that should be exhausted through a HEPA filter. Visual airflow indicators such as air pressure monitors must be available. All work must be performed within a negative-pressured and HEPA-filtered biosafety cabinet or another aerosol containment device. The facility must contain an autoclave for sterilizing infectious waste.

The Most Common Laboratory Procedures for COVID-19 Research

The two most common procedures conducted on COVID-19 specimens are the real-time polymerase chain reaction (real-time PCR or RT-PCR) and the enzyme-linked immunosorbent assay (ELISA).{12} RT-PCR is a genetic test used to confirm the presence of the viral genome. The technology can also be applied to measure viral load.{13,14} ELISAs are utilized to quantify the amount of a specific protein in a sample. That protein may be the viral spike protein used to confirm infection or the research participant's antibody proteins against the spike protein. The latter can be used to determine if an individual has been exposed to the virus and how well his or her immune system is mounting an adaptive immune response; this is an essential measure for vaccine efficacy studies.

Obtaining the final readout for these tests involves low-risk procedures. However, the following initial steps in setting up these assays run the risk of creating infectious droplets or aerosols, which creates an occupational exposure risk for lab staff:

- Extracting the viral RNA for RT-PCR
- Pipetting participant samples into an ELISA plate, as well as the aspiration and washing of these plates

Transporting Specimens from COVID-19 Patients

Potentially infectious materials are contained within a primary container, such as a blood collection tube, and should be transported within a facility in a durable, leak-proof, and biohazard-labelled secondary container, such as a sealed specimen bag. Shipping or transport of packages containing infectious materials requires a triple-packaging system.

Outside an individual facility, regulations for transport and shipment of infectious substances are provided by the U.S. Department of Transportation (DOT) for ground and International Air Transport Association (IATA) for air. {15–17} Both DOT and IATA require training for individuals who package hazardous materials as well as for those transporting or shipping hazardous materials.

The training requirement for individuals preparing the package means research participants cannot ship their own specimens without DOT/IATA-compliant training. Personnel transporting specimens must also have DOT/IATA-compliant training. It is worth noting the “Exempt Human Specimen” classification only applies to specimens for which there is a minimal likelihood that pathogens are present, based on professional judgement of the source’s known medical history, symptoms, and endemic local conditions. The exemption does not apply to specimens which contain or are suspected of containing infectious agents. {17} Specimens submitted to the CDC for SARS-CoV-2 testing must be shipped as Biological Substance Category B, rather than Exempt Human Specimens. {18}

Work Surface Disinfection, Waste Treatment, and Disposal

Equipment and work surfaces utilized in conjunction with infectious agents should be disinfected at each step in the experimental process and after any spills. Simply wiping down a surface with soap and water will not neutralize these agents. Instead, utilize an Environmental Protection Agency (EPA)-registered disinfectant that is labeled to be effective against SARS-CoV-2, and follow the manufacturer’s recommendations on dilution, contact time, and safe handling. The EPA provides a list of disinfectants with established efficacy against SARS-CoV-2. {19}

Treatment and disposal of infectious waste/regulated medical waste vary by state, so check your local regulations for specific guidance. This may involve contacting your organization’s environmental health and safety department, your institutional biosafety committee (IBC), or the state health department or EPA.

Decontamination of Spills

When spills of infectious materials occur, the focus must be on protecting research personnel as well as containing and disinfecting the spill. Personnel in the area must be instructed to leave and allow droplets to settle and aerosols to be removed by the ventilation system. Exposed personnel can utilize this time to treat any wounds or exposures as well as replace contaminated PPE.

Once an adequate period has lapsed, employees may re-enter the spill area and place disinfectant-soaked paper towels around the spill, moving from the periphery toward the center of the spill. The manufacturer's recommended contact time must be allowed for adequate disinfection before disposing of the waste as infectious waste.

Post-Exposure Procedures

The risk mitigation plan must address post-exposure procedures to be followed immediately after the exposure, such as washing the exposed site or use of an eye wash, as well as seeking medical evaluation. Exposed employees may be asked to remain in isolation at home and self-monitor for signs and symptoms of coronavirus infection for the duration of the 14-day incubation period. The occupational health provider may require daily reports in the form of calls or e-mails, which may include body temperature readings and listing any signs or symptoms of infection.

Incident Reporting

The principal investigator/supervisor must be notified of any incidents in the laboratory. Furthermore, various types of reporting may be required, based on the research oversight structure at a site as well as local health department requirements. Exposures must be reported as part of the organization's exposure control plan and documented in the OSHA 300 incident log.

Also, IBC-approved research must be reported to the Biosafety Officer/IBC. National Institutes of Health (NIH) Guidelines require immediate reporting to the NIH Office of Science Policy in the event of spills or accidents resulting in an overt exposure to engineered genetic materials in laboratories operating at Biosafety Levels 2 or greater. {20} Local requirements may also mandate reporting to the local health department.

Expert Review of Risk Mitigation Plan

It is good practice to have the risk mitigation plan reviewed by a panel of subject matter experts to ensure it comprehensively addresses the risks associated with the proposed research. A hospital's bloodborne pathogen committee may seem like the appropriate panel to review the plan, but such committees typically focus on standard of care and medical procedures involving sharps rather than review of laboratory-based research protocols. Assessing risks involving recombinant DNA and infectious agents may be outside the committee's scope or realm of expertise.

An IBC may be a better fit for reviewing the risk mitigation plan, as IBCs focus on risk assessment and risk mitigation for research involving engineered genetic materials and may cover microbiological safety. Institutions that have conducted NIH-funded research and conduct research involving engineered genetic materials are required to have IBCs. {20} Sites without IBCs may opt to have their risk mitigation plans reviewed by an independent commercial IBC or another third party. Having a documented plan reviewed and approved by an independent panel of subject matter experts provides the highest level of safety and legal protection to everyone involved.

Depending on local requirements, an organization's risk mitigation plan may need to be filed with the local health department.

Conclusion

The initial risk assessment is key to determining the appropriate risk mitigation measures for coronavirus research at your location. Biosafety practices must be customized to the proposed research as well as the existing facility and local regulatory requirements. Proper biosafety measures are critical to conducting safe, high quality research during this uncertain time.

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HOME STUDY

LESSONS LEARNED FOR RESEARCH ACCESS, SAFETY, AND HUMAN SUBJECT PROTECTIONS

Article 1: What is a Human Challenge Trial and How Does it Expedite Vaccine Development?

LEARNING OBJECTIVE

After reading this article, the participant should be able to compare and contrast human challenge trials (HCTs) to and with more traditional clinical trial designs and explain the utility of HCTs in the present coronavirus health crisis.

DISCLOSURE

Seema Garg, MS, MBA, CQA, CSSGB: *Nothing to disclose*

1. The article cites which of the following as a difference between vaccine development in the H1N1 and COVID-19 pandemics?

- A. An H1N1 vaccine was never studied in U.S. trials.
- B. COVID-19 is only half as lethal as H1N1 in most cases.
- C. An H1N1 treatment could be based on existing vaccines.
- D. A COVID-19 vaccine will be far less expensive.

2. What is the hallmark design feature of a human challenge trial (HCT)?

- A. Participants are divided into placebo and treatment groups based on age.
- B. Participants are never told whether they have the illness under study.
- C. Participants are allowed to spread the disease under study to others.
- D. Participants are intentionally exposed to an infectious disease organism.

3. How does a typical Phase I study differ from an HCT?

- A. Subjects are seriously ill with the disease under study.
- B. Subjects are not administered a disease-causing agent.
- C. Subjects do not have to sign an informed consent.
- D. Subjects cannot be paid for their participation.

- 4. What is the main advantage for vaccine development of an HCT versus an animal challenge study?**
- A. Speed
 - B. Expense
 - C. Regulations
 - D. Efficacy
- 5. What happens after a potential vaccine shows promise in an HCT?**
- A. It proceeds directly to use in regular patient populations.
 - B. An independent study sponsor must duplicate the results.
 - C. It is next tested at higher doses in animal models.
 - D. It goes as far through Phase I, II, and III trials as possible.
- 6. HCTs are conducted in which of the following settings?**
- A. Random, community
 - B. Controlled, in-patient
 - C. Isolated, emergency
 - D. Private, commercial
- 7. What are the regulatory expectations for HCTs in the United States?**
- A. There are no special requirements for HCTs in the U.S.
 - B. Requirements are spelled out in the Declaration of Helsinki.
 - C. The same as in Canada but less stringent than in the European Union.
 - D. That they can only be conducted by the National Institutes of Health.
- 8. What is a healthcare facility that would run an HCT called?**
- A. Infectious Disease Ward
 - B. Human Challenge Unit
 - C. Vaccine Screening Lab
 - D. Emergency Medicine Department
- 9. Infection control systems and processes that should be included in both facilities for HCTs and hospitals include which of the following?**
- A. Hyperbaric treatment chamber procedures
 - B. Legal indemnification from infection/transmission procedures
 - C. Medical waste disinfection/sterilization procedures
 - D. Companion animal screening procedures
- 10. What is a difference between challenge studies in the U.S. versus in the United Kingdom (UK) and European Union (EU)?**
- A. In the UK/EU, challenge studies are not considered to be ethical.
 - B. In the UK/EU, challenge agents are not considered to be drugs.
 - C. In the UK/EU, challenge studies must be monitored by lawyers.
 - D. In the UK/EU, challenge agents cannot be derived from toxins.

Article 2: Safety Precautions for Laboratory Research with SARS-CoV-2 Positive Specimens and COVID-19 Subjects

LEARNING OBJECTIVE

After reading this article, the participant should be able to describe how to conduct a risk assessment and develop a risk mitigation plan related to laboratory safety practices, facilities, and equipment for research involving specimens from SARS-CoV-2 positive individuals and COVID-19 subjects.

DISCLOSURE

Daniel Eisenman, PhD, RBP, SM(NRCM), CBSP: *Nothing to disclose*

11. CDC guidelines recommend that laboratory biosafety risk assessment related to COVID-19 be focused on which of the following areas?

- A. Virus-specific and equipment-specific
- B. Sponsor-specific and coordinator-specific
- C. Site-specific and activity-specific
- D. SOP-specific and data-specific

12. Which of the following is noted as something that should be assessed as a risk for SARS-CoV-2 transmission in a laboratory?

- A. Personal protective equipment
- B. Animals being used for study procedures
- C. The electronic data capture system
- D. Vehicles used by research staff

13. What activities are considered to be the final steps of a risk mitigation plan?

- A. Assignment of blame and financial penalties
- B. Reports to the IRB and sponsor(s)
- C. Local and federal certifications of site decontamination
- D. Waste treatment and disposal

14. Work involving human blood and tissues is subject to a standard issued by which of the following entities?

- A. CDC
- B. OSHA
- C. FDA
- D. OHRP

15. Which of the following is a setting in which laboratory procedures with potential to produce infectious droplets or aerosols would be performed?

- A. Licensed containment facility
- B. Certified biosafety cabinet
- C. Cold chain warehouse
- D. Accredited biorepository room

16. Which of the following are the most common procedures conducted on COVID-19 specimens?

- A. CBC and lipid panel
- B. BMP and CMP
- C. RT-PCR and ELISA
- D. Cultures and ABG

17. DOT/IATA-compliant training is required for which of the following activities?

- A. Packaging, transporting, or shipping hazardous materials
- B. Obtaining, culturing, and disposing of biospecimens
- C. Remote monitoring, data collection, and reporting on study sites
- D. Transporting, screening, and entering subjects into trials

18. Procedures to be followed after an employee has been exposed to a contaminant should be addressed in which of the following?

- A. DOT/IATA inspection
- B. Clinical trial agreement
- C. Risk mitigation plan
- D. CLIA certification manual

19. Laboratory incidents must be reported to various entities, including which of the following?

- A. Good clinical practice oversight committee
- B. State-based scientific review board
- C. Study principal investigator/supervisor
- D. National Institute of Allergy and Infectious Diseases

20. Risk mitigation plans should be reviewed by which of the following?

- A. Principal investigators
- B. Data and safety monitoring board
- C. Human subject volunteers
- D. Subject matter experts