Master of Public Health

Integrative Learning Experience Report

Preparing Rabies Vaccination Data of Veterinary Health Professionals for Analysis and Best Practices for Rabies Vaccination for Animal Handling Personnel

by

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MASTER OF PUBLIC HEALTH

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Summary

Rabies is a fatal zoonotic viral disease which occurs in over 150 countries. Rabies is a significant concern in public health, especially for people who are at risk such as rabies laboratory workers, animal health care workers, people who work with animals such as farmers and slaughterhouse workers, and people who live in rabies-endemic countries. However, rabies can be prevented by vaccination before and/or after suspected or proven exposure to the virus. Therefore, it is important to understand rabies vaccination recommendations in people who are at risk. The primary focus of this project was rabies vaccination for animal handling personnel. The first part was to prepare human laboratory data for statistical evaluation and send to the evaluators at University of Washington School of Public Health to use, then summarize the process of preparing data. Next, I created a summary of the best practices for rabies vaccination and booster timing for personnel handling animals, and a poster for educating animal handling staff on rabies control and prevention. These products could be useful for animal handling personnel for rabies prevention.

Subject Keywords: rabies, vaccination, recommendation

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Chapter 1 - Literature Review

Rabies is a zoonotic viral infectious disease. It is caused by viruses in *Lyssavirus* genus, most often by rabies virus (RABV). Rabies occurs in more than 150 countries and territories around the world. According to the World Health Organization (WHO), there are more than 59,000 deaths caused by rabies per year globally, and over 95% of the cases occurred in Asia and Africa. Rabies is transmitted by the bite or scratch of rabid animal, but may also result from non-bite exposures, in which saliva or other potentially infectious material from a rabid animal is exposed to broken skin such as scratches, abrasions, or open wounds. The symptoms of rabies at the first stage may be nonspecific including lethargy, fever, vomiting, and anorexia. Next, clinical signs will progress within days to cerebral dysfunction, cranial nerve dysfunction, ataxia, weakness, paralysis, seizures, difficulty breathing, difficulty swallowing, excessive salivation, abnormal behavior, aggression, and/or self-mutilation. (*What Are the Signs and Symptoms of Rabies? | Symptoms | CDC*, n.d.) Once clinical signs appear, there is no effective treatment for rabies. This is a significant global public health concern, particularly for people who are at risk such as rabies laboratory workers, people who work with animals like veterinarians, farmers and slaughterhouse workers, and people who live in rabies-endemic countries. However, rabies can be prevented by vaccination and proper wound management in both humans and animals. Wound cleansing is especially important in rabies prevention since, in animal studies, thorough wound cleansing alone without other postexposure prophylaxis has been shown to markedly reduce the likelihood of rabies. (*Rabies Postexposure Prophylaxis (PEP) | Medical Care | Rabies | CDC*, n.d.) Pre-Exposure Prophylaxis (PrEP) is also recommended for people who are at risk of occupational exposure such as animal health care workers, medical professionals who routinely take care of people with rabies. Therefore, vaccination and knowledge about rabies prevention is very important for people who are at a high risk for rabies.

The Rabies Laboratory of Kansas State University is the primary diagnostic lab for the states of Kansas and Nebraska. This lab handles over 80,000 samples each year and is one of the highest volume rabies serology centers in the world for both humans and animals. The tests measuring rabies antibodies that this lab utilizes, includes the Fluorescent Antibody Virus Neutralization (FAVN) test, Rapid Fluorescent Focus Inhibition Test (RFFIT) and Enzyme-linked immunosorbent assay (ELISA). Both the Advisory Committee on Immunization Practices

(ACIP) and the WHO recommend the RFFIT to be the current gold standard serological assay for rabies. According to the WHO Expert Consultation on Rabies, the RFFIT test is recommended for measuring post-vaccination immune responses and for determining whether booster vaccination is necessary, because it has been correlated with protection in animal studies. (World Health Organization, 2018) The RFFIT is performed by mixing different dilutions of animal or human serum with rabies virus in a multi-chambered slide, then incubated to allow antibodies in the serum to neutralize rabies virus. Next, the mixture is added to Baby Hamster Kidney fibroblasts (BHK cells) and incubated for 20 hours, so the non-neutralized virus can replicate. The last step is fixing and staining the samples to detect rabies virus production, by reading the slide using a fluorescent microscope for each serum dilution which involves a fivefold dilution series and compared against a control slide containing reference serum and virus dilutions. The rabies virus neutralizing titer can be determined by the number of infected fields for each serum dilution, and this can be used for deciding whether to give boost vaccination when the neutralizing antibody level is lower than 0.5 IU/mL. Titer levels or IU/mL values equal to or above 0.5 IU/mL (1:50), provide evidence of a robust immune response after rabies vaccination. If the virus is not neutralized, infected fields can be found by using a fluorescent microscope; however, if the virus is neutralized, infected fields cannot be found. (See Figure 1.1 A and Figure 1.1 B)

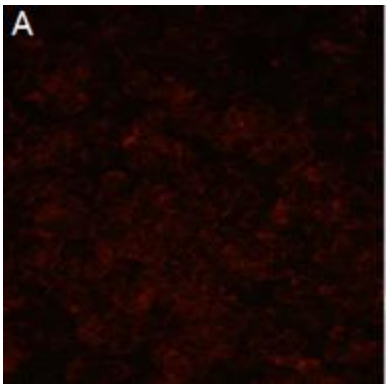

Figure 1.1 A. An example of a microscopic field where virus has been neutralized

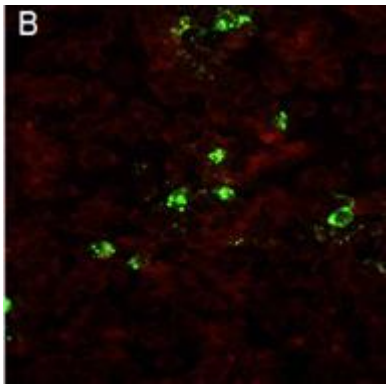

Figure 1.2 B. An example of a microscopic field where virus <u>was not neutralized</u>

PrEP is recommended for people who are at high risk of exposure to rabies because of their occupation or activities. Although neutralizing antibodies titers decrease or cannot be measured, vaccination produces immunological memory which assumed to persist for lifelong. However, those who are at risk after vaccination should be monitored for antibody titer as

recommendations depends on their risk, and booster vaccination would be recommended only if rabies neutralizing antibody titer fall to < 0.5 IU/mL.

This project primarily focused on rabies vaccination in animal handling personnel. The first part was preparing human laboratory data for statistical evaluation and sending the data to the evaluators from University of Washington School of Public Health. This data could be useful for determining rabies antibody titers for veterinarians to develop recommendation or use for further study in the future. The second part was to create a summary of the best practices for rabies vaccination and booster timing for personnel handling animals, and a poster for educating animal handling staff on rabies control and prevention. My preceptor and mentor for this project was Dr. Susan Moore who has a Doctor of Philosophy (Ph.D.) focused in Pathobiology from Kansas State University. She also has experience from being a clinical laboratory director with a demonstrated history of working in the global rabies serology industry, other pathogen serology methods, and immunohematology. She has skill in laboratory management, immunology, epidemiology, vaccines, biotechnology, laboratory medicine, and virology. Now, she is one of the work group who is working on the latest vaccination recommendation from the ACIP recommendations which are currently under review and will be published at the end of 2021. Dr. Moore is currently no longer a faculty member; she currently is the president at Compass Rabies Consulting, LLC.

Chapter 2 - Learning Objectives and Project Description

My Applied Practice Experience (APE) consists of two parts including the following: (1) preparing human laboratory data for statistical evaluation, and (2) creating a summary of the best practices for rabies vaccination and booster timing for personnel handling animals, and a poster for educating animal handling staff on rabies control and prevention.

Kansas State University Rabies Laboratory collected blood samples from veterinarians who attended veterinary conferences which were tested using the RFFIT. RFFIT measures the ability of rabies specific antibodies that may be present in a sample to neutralize and block rabies virus from infecting cells. VetView, the laboratory information management system (LIMS) which is a software-based system with features that support a modern laboratory's operations, is used for data entry, data collection, and data reporting intuitive for veterinarians, clinicians, and diagnosticians. In addition, other information about the sample were also collected at the veterinary conferences by using rabies titer submission forms called “Rabies Serology for Vaccine Titer Response by RFFIT Screen Method for Human Specimen Only”. The forms were electronically completed by each participant per rabies titer event and printed at the event for signature and sample processing. Then the forms were scanned and kept as electronic records. Before the first part of this project started, Dr. Moore, colleagues from University of Washington School of Public Health, and I had a meeting via zoom to discuss about the project and how they would like the prepared data to be. My role in this project was to prepare the data, including participants’ rabies titer, participants’ general information, and rabies vaccination history into a table for each veterinary conference using Microsoft Excel Spreadsheet Software. The prepared data includes ID, a number that assigned by VetView, gender of participants, year of birth of participants, region where participants live, conference number that assigned to each sample in each conference, date which each sample was drawn, rabies titer of participants, and vaccination history. The vaccination history section in the form is a blank section, for when participants were vaccinated and the reasons why they were vaccinated. The IRB number of Serology Assays Development, Optimization and Validation for Rabies Immunoglobulins Evaluation and Rabies Serology Analysis for Rabies Vaccine Response was 10151. All the data was anonymized to protect participants’ personal information. Then, the data was sent to the evaluators from the University of Washington School of Public Health for a project assessing rabies vaccine

response among this occupational group. During the process of preparing the dataset, Dr. Moore, colleagues from University of Washington School of Public Health, and I updated the process of our work and solved problems that occurred through email. In addition, I also created a Microsoft Word file to summarize the process of preparing human laboratory data for statistical evaluation. This summary consists of source of data, methods, difficulties, and the template for the final file. It describes source of data, and the methods to prepare the data step by step, so it can be understood easily. Besides source of data and methods, this summary also stated the difficulties during data preparation. This will be useful for improving data collection and management data in the future.

Next, I created a summary of the best practices for rabies vaccination and booster timing for personnel handling animals in a Microsoft Word file. This provides general information of rabies such as causative agent, transmission and clinical signs, and the recommendation for rabies vaccination in people who are at risk. The information used in this summary is based on research journals, the WHO, Centers for Disease Control and Prevention (CDC), and the ACIP. In this summary, Dr. Moore helped me understand the latest vaccination recommendations, since she was in the work group for the ACIP recommendations which are currently under review and new recommendations will be published at the end of 2021. This summary will help specific groups of people, such as animal handling personnel who are at risk for rabies, to understand and be aware more about rabies, and practice the right way for rabies prevention.

Finally, I created a poster for educating animal handling staff on rabies control and prevention. From my personal experience in veterinary medicine when I worked as a veterinarian with people who work with animals such as in animal hospitals and a zoo in Bangkok and Chiang Mai, Thailand, when they got bitten or scratched from animals, they sometimes ignore to have a proper wound management and rabies vaccination booster and are not aware about rabies. Additionally, most human deaths from rabies occurred in Asia and Africa, caused by bites from rabid dogs; however, according to the CDC, around 70% of human rabies cases in the United States were attributed to bat exposures. Bats were the most frequently reported rabid wildlife species (33% of all animal cases during 2018), followed by raccoons (30.3%), skunks (20.3%), and foxes (7.2%) in the United States. (Ma et al., 2020) In addition to rabies general information and vaccination recommendation, I included information about the website about rabies

information by state. This will provide information such as rabies reservoirs in each state and contact information for local health department.

2.1 Learning Objectives:

1. To design data preparation workflow that is ready to use for statistical evaluation from Rabies Laboratory Kansas State University and to create the protocol of data preparation
2. To develop interprofessional teamwork communication skill virtually during to the COVID-19 pandemic situation
3. To communicate risk of rabies and vaccination to animal handling personnel by creating a summary and a poster

Chapter 3 - Methodology and Results

Before the project started, I had an opportunity to meet with Dr. Moore to discuss the project and the datasets that Kansas State University Rabies Laboratory had already collected. The data were collected by using submission forms from veterinarians who attended veterinary conferences and their blood samples were sent to Kansas State University Rabies Laboratory for RFFIT. The sources of data that were used to prepare human laboratory data for statistical evaluation included VetView, rabies titer submission forms called "Rabies Serology for Vaccine Titer Response by RFFIT Screen Method for Human Specimen Only" (Appendix B.), and Excel spreadsheet files which were compiled from data entered into the electronic submission forms. After the first meeting, Dr. Moore and I also had a meeting with Julianne Meisner and Joni Anderson, the evaluators from University of Washington School of Public Health. We discussed the template of the table (Table 3.1) for the prepared data that they designed, and adjusted the table to make it consistent with the data that we have. The prepared data was next presented in a table in Microsoft Excel, it included ID, a number that is assigned by VetView, gender of participants, year of birth of participants, region where participants come from, conference number that is assigned to each sample in each conference, date for when each sample was drawn, titer of participants, and vaccination history. VetView was used as data source for ID, conference number, date which each sample was drawn, and titer of participants; while the rabies titer submission forms and Excel spreadsheet files compiled from the data entered into the electronic submission form were used for gender of participants, year of birth of participants, region where participants came from, and vaccination history. For gender, female was coded as 0 and male was coded as 1. Regions were labelled as a number according to United States Department of Health and Human Services. (*Regional Offices | HHS.Gov*, n.d.) (Figure 3.1) Finally, the vaccination history section in the submission form is a blank section, so the participants normally filled in the year that they were vaccinated and boostered, there were 3,711 samples which had either or both vaccinated and boostered. In addition, sometimes they filled in the reason why that vaccinated, there were 74 samples filled out for vaccination reasons. Therefore, vaccination history in the template was designed to have a time when they were vaccinated and the reason for vaccination along with a note column which can be filled in with all data that participants filled in the form in vaccination history section. However, there were

some participants who did not fill in the vaccination history which was equivalent to 488 samples. All samples were anonymized to protect participants' privacy and each table represented only one veterinary conference. Next, all prepared data was sent to the evaluators. After sending the prepared data to the evaluators, I summarized all the process of preparing data step-by-step. The summary also included the details of the sources of data and explained each column in the final prepared data table. (Appendix C.) The final product included 4,297 samples from 15 veterinary conferences.

A summary of the best practices for rabies vaccination and booster timing for personnel handling animals was created. It provides general information about rabies and recommendation for rabies vaccination (Appendix D.). I used the Flesch-Kincaid model which is an automated tool that can be used to determine reading level on https://readabilityformulas.com/flesch-grade-level-readability-formula.php. A poster for educating animal handling staff on rabies control and prevention (Appendix E.) was also created for the purpose of posting at worksites. This poster's reading level is 8th grade which readers' ages are 13-14 years old. The summary and poster information were based on WHO and ACIP guidelines.

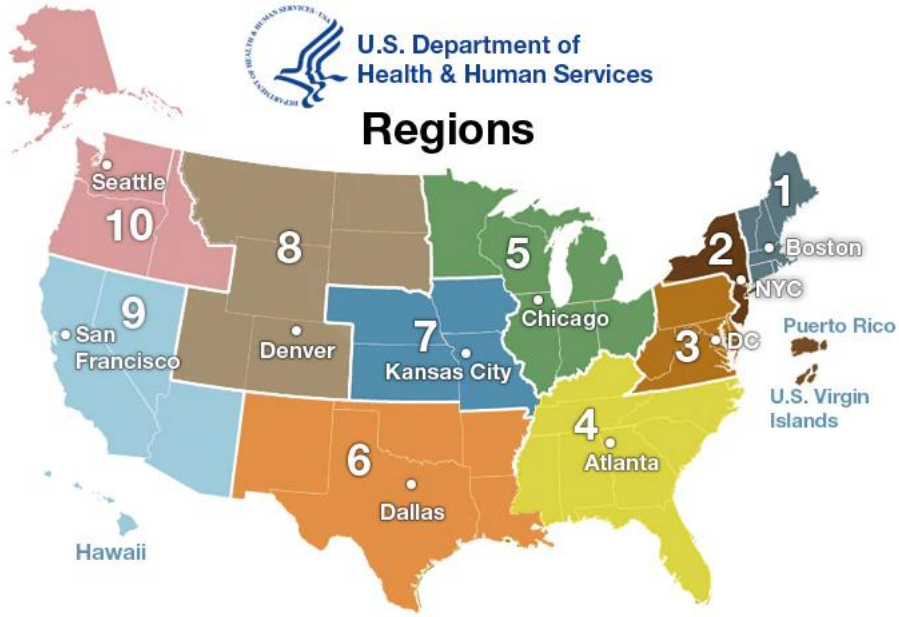

Figure 3.0. Regions in the United States classified by United States Department of Health and Human Services

Table 3.1 Template for Human Laboratory Data for Statistical Evaluation

ID	male	yob	region	conf	date	titer	Initial_vx	initial_vx_reason	booster1	booster1_reason	booster2	boster2_reason	booster3	booster3_reason	Last_booster	Last_booster_reason	Note

Chapter 4 - Discussion

The main goal of the part of this project was to prepare the data and send to the evaluators to evaluate this data and use it for further study. Dr. Moore and our colleagues were very helpful with the project since there were some problems that I experienced during data processing. First, the template that the evaluators designed needed to be adjusted to make it consistent with the data collected. There was a variety of answers in the vaccination history section since the vaccination history section in the submission form was a blank section. As participants could fill this section in many ways, we discussed this issue, and decided to divide the vaccination history to have the time that participants were vaccinated, and reasons why they vaccinated for the first, second, and third time. Time was collected as year. We added the latest booster column since there were some people that only remembered the last time they boostered. In addition, we also added a note column to fill in everything that participants filled in the blank section for vaccination history section.

Next, the submission forms were electronically completed by each participant per rabies titer event and printed at the event for signature and sample processing. Then, these forms were saved as scanned pdfs in batches. However, the submission forms did not scan in order, so it was difficult to find each sample and fill in the gender, year of birth, region, and vaccination history. This could be solved by scanning the submission form in order. Yet, considering for long term use, if we use available technology to help with this step, such as using electronic signature, it will make this step less complicated. By using electronic signatures, it would not be necessary to print the form and scan it. This also would help in putting data in order, and make it easier and less time consuming to find data. Another limitation is some of the participants could not remember when they were vaccinated and sometimes, they left the vaccination history section blank. We needed to input N/A which means not applicable or not available in the table, and this made it more complicate for the evaluators that need to evaluate the data. In the future, if vaccination can be recorded and the participants can access the information online, this could be another way to solve this problem. Using available technology would be one way to improve the data collection and management; however, there are also some limitations for using new technology such as high cost which are associated with acquisition of new technology and training of personnel, and health information privacy concerns. This prepared data can be very

useful in many ways such as consider immunological status of rabies for veterinarians in the U.S., used as an evidence-based decision making for health policy, and improving rabies vaccination recommendations in the future.

Besides a set of prepared human laboratory data for statistical evaluation, my project also included preparation of a summary of the best practices for rabies vaccination and booster timing for personnel handling animals, and a poster for educating animal handling staff on rabies control and prevention. The reading level is important because it affects general audiences' understanding. If the reading level is too high, the audiences might not understand what we want to communicate to them. I used the WHO and ACIP guidelines for rabies vaccination recommendations; however, ACIP for rabies vaccination recommendation is currently under review and new recommendations will be published at the end of 2021. Fortunately, Dr. Moore is a part of ACIP work group who are reviewing this. Both the summary and the poster included general information that can be understood easily. For the poster, it can be posted at worksites, so animal handling staff can read while they are working. In conclusion, I hope that the prepared data can be used to improve rabies vaccination recommendations and further studies, and the summary and poster would be useful to use as a guideline and raise awareness for rabies in animal handling personnel.

Chapter 5 - Competencies

Student Attainment of MPH Emphasis Area Competencies

Table 5.2 Summary of MPH Emphasis Area Competencies

MPH Emphasis Area:		
Number and Competency		**Description**
1	Pathogens and pathogenic mechanisms	Evaluate modes of disease causation of infectious agents.
2	Host response to pathogens/immunology	Investigate the response to infection.
3	Environmental/ecological influences	Examine the influence of environmental and ecological forces on infectious diseases
4	Disease surveillance	Analyze disease risk factors and select appropriate surveillance.
5	Disease vectors	Investigate the role of vectors, toxic plants, and other toxins in infectious diseases.

Competency #1: Pathogens and pathogenic mechanisms

The Fundamentals of Emerging Infectious Diseases (DMP 770) class explained the significance of recently identified emerging diseases and re-emerging diseases, and the conditions that enable their emergence, and the human health implications of each disease. The Introduction to Global Health (DMP 844) class provided principles of the spread of infectious diseases and key concepts concerning the prevention, transmission, and treatment of diseases. In addition, during the field experience, I also had an opportunity to research on rabies about the causative agent, and transmission of the disease.

Competency #2: Host response to pathogens/immunology

The Principles of Veterinary Immunology class (DMP 705) class provided insight into the immune response to pathogens and explained fundamental knowledge of vaccination, autoimmunity, immunodeficiency, and immunomodulation. Microbial Ecology (BIOL 687) class reflected the ecology of aquatic, terrestrial, animal and plant host-associated microorganisms in their natural environments. I also learned about immune response for rabies vaccination while working on my project.

Competency #3: Environmental/ecological influences

During the Environmental Health (MPH 802) class, I learned about pathogens, assessing risks and causality, determining health impact, environmental inspections, food and product safety, and environmental policy which help me have a better understand in the influence of environmental forces on infectious diseases. The Introduction to Global Health (DMP 844) class also provided how global health problems and various strategies to manage international health concerns. The problems also include environmental and nutritional issues threats to health.

Competency #4: Disease surveillance

The Introduction to Epidemiology (MPH 754) addressed the basic principles and methods of epidemiology in order to recognize and understand how disease affects populations. Additionally, this class also provided basic strategies for infectious diseases and disease surveillance methods.

Competency #5: Disease vectors

The Introduction to One Health course (DMP 710) explained the complex interrelationships among humans, animals, and the environment. For example, vectors in zoonotic diseases and environmental issues that impact human, animal, and ecosystem health.

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Appendices

Appendix A. Example of Prepared Human Laboratory Data for Statistical Evaluation

ID	male	yob	region	conf	date	titer	initial_vx	initial_vx	booster1	booster1 _reason	booster2	booster2 _reason	booster3	booster3 _reason	Last booster	Last booster_ reason	Note
R20-000192	1	1961	3	AAEP-6748	12/8/2019	>/= 0.5 IU/mL	1998	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1998?
R20-000168	1	1959	5	AAEP-6749	12/8/2019	>/= 0.5 IU/mL	1981	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1981
R20-000162	0	N/A	9	AAEP-6750	12/8/2019	>/= 0.1 IU/mL	1996	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1 of the series in 1996
R20-000156	0	1957	9	AAEP-6751	12/8/2019	LESS THAN 0.1	1990	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1990
R20-000180	0	1977	4	AAEP-6752	12/8/2019	>/= 0.5 IU/mL	2003	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2003
R20-000186	1	1959	5	AAEP-6753	12/8/2019	>/= 0.5 IU/mL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1989	N/A	Last booster 1989
R20-000174	0	1979	8	AAEP-6754	12/8/2019	>/= 0.1 IU/mL	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	~2009
R20-000150	0	1967	2	AAEP-6755	12/8/2019	>/= 0.5 IU/mL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	yes
R20-000144	0	1966	8	AAEP-6756	12/8/2019	>/= 0.5 IU/mL	1999	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1999
R20-000191	0	1949	4	AAEP-6757	12/8/2019	>/= 0.5 IU/mL	1999	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	20 years ago rabies series
R20-000179	0	1964	4	AAEP-6758	12/8/2019	>/= 0.1 IU/mL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
R20-000173	0	1960	4	AAEP-6759	12/8/2019	>/= 0.5 IU/mL	2004	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	15 years ago
R20-000185	0	1992	8	AAEP-6760	12/8/2019	>/= 0.5 IU/mL	2015	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vaccinated in 2015
R20-000161	0	1981	5	AAEP-6761	12/8/2019	>/= 0.5 IU/mL	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2009
R20-000167	0	1982	1	AAEP-6762	12/8/2019	>/= 0.5 IU/mL	2009	pre exposure	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	given pre exposure 2009 titer in 2010 was adequate
R20-000155	0	1991	4	AAEP-6763	12/8/2019	>/= 0.5 IU/mL	2013	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Vaccinated in 2013
R20-000149	0	1984	1	AAEP-6764	12/8/2019	>/= 0.5 IU/mL	2008	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1/1/2008
R20-000190	0	1978	8	AAEP-6767	12/8/2019	>/= 0.1 IU/mL	2009 or 2010	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2009 or 2010, completed series
R20-000135	0	1982	4	AAEP-6793	12/8/2019	>/= 0.5 IU/mL	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2009
R20-000076	1	1954	9	AAEP-6795	12/9/2019	>/= 0.1 IU/mL	2010	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2010
R20-000125	0	1983	6	AAEP-6798	12/9/2019	>/= 0.5 IU/mL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2018	N/A	last vaccine in 2018
R20-000088	0	1957	4	AAEP-6800	12/9/2019	>/= 0.1 IU/mL	1982	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1982
R20-000107	0	1992	9	AAEP-6801	12/9/2019	>/= 0.5 IU/mL	2014	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2014
R20-000120	0	1977	3	AAEP-6802	12/9/2019	>/= 0.5 IU/mL	2000	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	loading series 2000
R20-000100	1	1980	9	AAEP-6803	12/9/2019	>/= 0.5 IU/mL	2004	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2004
R20-000124	0	1986	5	AAEP-6804	12/9/2019	>/= 0.5 IU/mL	2011	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vaccinated in vet school 2011
R20-000126	0	1980	4	AAEP-6805	12/9/2019	>/= 0.5 IU/mL	1993	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1993
R20-000112	0	1975	8	AAEP-6806	12/9/2019	>/= 0.5 IU/mL	1998	1998	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1998
R20-000121	1	1958	4	AAEP-6807	12/9/2019	>/= 0.1 IU/mL	1985	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1985
R20-000089	0	1961	8	AAEP-6808	12/9/2019	LESS THAN 0.1	1999	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1999
R20-000095	0	1989	2	AAEP-6809	12/9/2019	>/= 0.5 IU/mL	2012	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2012
R20-000114	0	1984	5	AAEP-6810	12/9/2019	>/= 0.5 IU/mL	2008	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	series in 2008
R20-000077	0	1975	4	AAEP-6811	12/9/2019	>/= 0.5 IU/mL	2001-2002	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2001-2002
R20-000113	0	1982	9	AAEP-6812	12/9/2019	>/= 0.5 IU/mL	2004	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Spring2004
R20-000101	0	1955	6	AAEP-6813	12/9/2019	>/= 0.5 IU/mL	1979	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	human diploid 1979
R20-000082	0	1986	3	AAEP-6815	12/9/2019	>/= 0.5 IU/mL	2015	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2015
R20-000102	0	1988	3	AAEP-6816	12/9/2019	>/= 0.5 IU/mL	2010-2011	N/A	2016	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Booster 3 years ago, Initila series was in 2010-2011
R20-000108	0	1979	5	AAEP-6817	12/9/2019	>/= 0.5 IU/mL	1990	post exposure	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	post exposure series in 1990
R20-000090	0	1987	9	AAEP-6818	12/9/2019	>/= 0.5 IU/mL	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Series of 2 vaccines in 2009
R20-000096	0	1963	2	AAEP-6819	12/9/2019	>/= 0.5 IU/mL	1985	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1985
R20-000122	0	1992	2	AAEP-6820	12/9/2019	>/= 0.5 IU/mL	2014	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Vaccinated in 2014
R20-000078	1	1966	10	AAEP-6821	12/9/2019	>/= 0.5 IU/mL	1992	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1992
R20-000084	1	1968	4	AAEP-6822	12/9/2019	>/= 0.5 IU/mL	1994	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1994
R20-000115	1	1953	4	AAEP-6823	12/9/2019	>/= 0.5 IU/mL	1995	post exposure	2005	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Approx 1995 post exposure Approx 2005 vaccination
R20-000128	0	1980	10	AAEP-6824	12/9/2019	>/= 0.5 IU/mL	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vaccinated in 2009
R20-000123	0	1981	4	AAEP-6825	12/9/2019	>/= 0.5 IU/mL	2011	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2011
R20-000109	0	1975	7	AAEP-6826	12/9/2019	>/= 0.5 IU/mL	2003	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	3/2003
R20-000103	0	1982	5	AAEP-6827	12/9/2019	>/= 0.5 IU/mL	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2009
R20-000079	1	1946	8	AAEP-6828	12/9/2019	LESS THAN 0.1	1976	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1976
R20-000097	0	1972	5	AAEP-6829	12/9/2019	>/= 0.5 IU/mL	1999	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1999
R20-000098	0	1987	8	AAEP-6830	12/9/2019	>/= 0.1 IU/mL	2008	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Vacc. Approx 2008? No titer drawn
R20-000085	0	1968	3	AAEP-6831	12/9/2019	>/= 0.5 IU/mL	1989	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1989
R20-000104	1	1984	8	AAEP-6832	12/9/2019	>/= 0.5 IU/mL	2012	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2012
R20-000093	0	1982	10	AAEP-6837	12/9/2019	>/= 0.5 IU/mL	2006	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2006
R20-000099	0	1989	1	AAEP-6838	12/9/2019	>/= 0.5 IU/mL	2008	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Yes 3 shot series 2008
R20-000129	1	1992	Ash Shariqah	AAEP-6840	12/9/2019	>/= 0.5 IU/mL	2018	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	one year ago, five doses
R20-000119	1	1953	7	AAEP-6846	12/9/2019	>/= 0.5 IU/mL	1998	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	five shot series 1998?
R20-000130	0	1989	7	AAEP-6847	12/9/2019	>/= 0.5 IU/mL	2011	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2011
R20-000060	0	1987	4	AAEP-6853	12/9/2019	>/= 0.5 IU/mL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2012	N/A	Last vaccinated 2012
R20-000057	0	1978	5	AAEP-6857	12/9/2019	>/= 0.5 IU/mL	2004	N/A	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	initial vaccines in 2004, 1 booster in May 2009
R20-000061	0	1962	9	AAEP-6858	12/9/2019	>/= 0.5 IU/mL	1985	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1985
R20-000062	0	1987	9	AAEP-6859	12/9/2019	>/= 0.5 IU/mL	2014	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2014
R20-000070	0	1987	3	AAEP-6860	12/9/2019	>/= 0.5 IU/mL	2015	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vaccine 2015
R20-000063	0	1991	9	AAEP-6861	12/9/2019	>/= 0.5 IU/mL	2014	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vax 2014
R20-000064	0	1988	9	AAEP-6862	12/9/2019	>/= 0.5 IU/mL	2012	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vaccinated in 2012
R20-000068	0	1982	1	AAEP-6863	12/9/2019	>/= 0.5 IU/mL	2005	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2005
R20-000053	0	1960	4	AAEP-6864	12/9/2019	>/= 0.5 IU/mL	1984	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1984
R20-000069	0	1982	3	AAEP-6865	12/9/2019	>/= 0.5 IU/mL	2006	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vaccinated in 2006
R20-000055	0	1970	4	AAEP-6866	12/9/2019	>/= 0.5 IU/mL	1993	N/A	1993	N/A	1999	N/A	N/A	N/A	N/A	N/A	N/A
R20-000058	1	1981	10	AAEP-6867	12/9/2019	>/= 0.1 IU/mL	2010	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2010
R20-000071	0	1965	4	AAEP-6868	12/9/2019	>/= 0.5 IU/mL	1988	N/A	1997	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1988 initial, 1997 booster
R20-000065	0	1956	9	AAEP-6869	12/9/2019	>/= 0.5 IU/mL	had several y	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	had several years ago
R20-000066	0	1975	9	AAEP-6870	12/9/2019	>/= 0.5 IU/mL	1997	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1997 (in vet school)
R20-000059	0	1967	7	AAEP-6871	12/9/2019	>/= 0.5 IU/mL	2009	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2009 (Approximately)
R20-000067	0	1984	1	AAEP-6872	12/9/2019	>/= 0.1 IU/mL	2008	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2008
R20-000056	0	1985	3	AAEP-6873	12/9/2019	>/= 0.5 IU/mL	2008	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2008
R20-000054	0	1968	1	AAEP-6874	12/9/2019	>/= 0.5 IU/mL	2000	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	vaccinated 2000
R20-000072	0	1958	9	AAEP-6875	12/9/2019	>/= 0.5 IU/mL	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
R20-000016	0	1989	5	AAEP-6896	12/10/2019	>/= 0.5 IU/mL	2005	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	Vaccinated~2005
R20-000011	0	1963	6	AAEP-6898	12/10/2019	>/= 0.5 IU/mL	1989	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1989
R20-000012	1	1951	5	AAEP-6899	12/10/2019	>/= 0.5 IU/mL	2004	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	15 years
R20-000031	1	1958	5	AAEP-6915	12/10/2019	>/= 0.5 IU/mL	1982	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1982
R20-000030	1	1963	7	AAEP-6918	12/10/2019	>/= 0.5 IU/mL	>10 years	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	>10 years
R20-000027	0	1980	5	AAEP-6919	12/10/2019	>/= 0.5 IU/mL	2005	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	initial 3 dose series in 2005
R20-000021	1	1974	5	AAEP-6920	12/10/2019	>/= 0.5 IU/mL	2019	post exposure	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	series of 4 vaccines post exposure in July 2019
R20-000017	1	1981	9	AAEP-6921	12/10/2019	>/= 0.5 IU/mL	2008	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2008

Appendix B. Rabies Serology for Vaccine Titer Response by RFFIT Screen Method for Human Specimen Only submission form

Kansas State Veterinary DIAGNOSTIC LABORATORY

Rabies Serology for Vaccine Titer Response by RFFIT Screen Method for Human Specimen Only

The Rabies Laboratory
Kansas State University
2005 Research Park Circle
Manhattan, KS 66502

Phone: 785-532-4483
Fax : 785-532-4474
Email: rabies@vet.k-state.edu
http://www.ksvdl.org/rabies-laboratory/

All fields need to be printed legibly. Handwritten information is subject to interpretation by laboratory personnel.

For Lab Use only
Draw Date:

First Name: _____ DOB: _____

Last Name: _____ Sex: ___

Address: _____

City: _____ **State:** _____ **Zip Code:** _____

Phone Number: _____ Fax Number: _____

Email Address: _____

(Rabies Titer Results will be sent to the above email address in 3-4 weeks. All other results will be mailed in 2-3 weeks.)

Rabies Vaccination History: _____

☐ Rabies Titer Screen	☐ Prostate Specific Antigen (PSA)	☐ Thyroid Panel w/TSH
☐ Comprehensive Metabolic + Lipid Panel	☐ Lyme Disease Antibody (test code: 29477)	☐ Brucella antibody, IgG (test code 982)
☐ CBC w/ Differential	☐ Vitamin D	☐ Hepatitis C
☐ Glycohemoglobin A1C	☐ Highly Sensitive C-Reactive Protein	PIL Client ID# 3036 - ONSITE WELLNESS Osgood Kenneth, MD
☐ Lead Levels		

I, the participant named below, have read, understand and agree to the terms of the Rabies Titer Profile/Lab Analysis Notice and Consent provided and attached hereto. No attempts by the participant to modify or amend this form will change its terms or in any way be binding upon the Kansas State University Rabies Laboratory, OnSite Wellness, or other related parties.

Participant's Signature: _____ **Date:** _____

*A signed Rabies Titer Profile/Lab Analysis Consent Form must accompany the lab sample in order for the Kansas State Rabies Laboratory, OnSite Wellness, or other related parties to analyze the sample and release the lab results

Examiner/Collector Information: (To be completed at time of sample collection)

Participant's initials indicate verification the barcode labels on the specimen tubes match the barcode and firt and last name on this form

Serum Draw Date/Time: _____ **Fasting Sample?: Yes:** ___ **Hours** ___ **No** ___

Sample Obtained: **Yes** **No** (If no, please explain: _____)

I, the examiner named above, verify that the enclosed specimens were collected according to the instructions provided by the Kansas State University Rabies Laboratory. I verify that these specimens are the specimens taken from the participant named on this form. I have verified the barcode labels on the specimen tubes match the barcode first and last name on this form.

Examiner's Signature: _____ **Date:** ___

Payment: CashNet Receipt: _____ Check Number: _____ Cash: $_____ by _____

Version 7/2017

Appendix C. Summary of the Process of Preparing a set of Human Laboratory Data for Statistical Evaluation

Source of data

1. VetView is used in KSVDL. It is the laboratory information management system (LIMS) which is a software-based system with features that support a modern laboratory's operations. The features include workflow and data tracking support, flexible architecture, and data exchange interfaces. The excel spreadsheet is a report generated by VetView upon entering the search information of 'client' (the Vet Conference account #) and the output requested (patient name, date of draw, results, etc.). This is one excel that contains all the results. It is named 'RabiesTiterBooth – Excel' and is a summary to list the rabies titer results from all the 'client' rabies titer booth events.
2. Each of the completed rabies titer submission forms called "Rabies Serology for Vaccine Titer Response by RFFIT Screen Method for Human Specimen Only" are associated with each result. The forms are electronically completed by each participant per rabies titer event and printed at the event for signature and sample processing. Next, these forms are saved as scanned pdfs in batches (10 total files), named 'Submission Forms Batch x.pdf' (x representing the batch number).
3. Excel spreadsheet files which are compiled from the data entered into the electronic submission form., named "'Name of conference' 'M-YYYY'", each conference/year spreadsheet contains entered data from all participants in that conference.

Methods

1. Open the RabiesTiterBooth_20210106smm file, the VetView generated report, re-formatted to adjust columns for use in the VLOOKUP formulas, see below, step c.
   This file will be used as source of data to copy to each conference/year excel spreadsheet ("'Name of conference' 'M-YYYY'").
2. Open the conference/year excel spreadsheet file.
   a. Copy the 'Tube ID (Name or ID#)' column to the A column. The Tube ID will be used to link with the RabiesTiterBooth_20210106smm file.

b. Label each column after the last column, which is column O, starting with column P as ID, male, yob, region, conf, date, titer, initial_vx, initial_vx_reason, booster1, booster1_reason, booster2, booster2_reason, booster3, booster3_reason, and Note, respectively.

- ID, this is a number that assigned by VetView, so each sample is unique to only one ID.
- male, this is gender of participants. For female, it will be labelled as 0, and for male, it will be labelled as 1. This data can be found on the submission forms.
- yob, this is the year of birth of participants. This data can be found on the submission forms.
- region, this is the state where participants come from
- conf, this is the conference number which is assigned to each sample in each conference. Each sample is unique to only one conference number.
- date, this is the date that sample was drawn.
- titer, this is the titer of participants. This data can be found in RabiesTiterBooth_20210106smm file.
- initial_vx, this is the year which the initial vaccine was administered.
- initial_vx_reason, this is the reason why the initial vaccine was administered, e.g., post-exposure.
- booster1, this is the year which the first booster was administered.
- booster1_reason, this is the reason why the first booster was administered.
- booster2, this is the year which the second booster was administered.
- booster2_reason, this is the reason why the second booster was administered.
- booster3, this is the year which the third booster was administered.
- booster3_reason, this is the reason why the third booster was administered.
- Last_booster, this is the year which the last booster was administered.
- Last_booster_reason, this is the reason why the last booster was administered.
- Note, this is all the vaccination history that participants have stated in the submission forms.

*Please note that the excel column letter matched with each category can be changed if there are differences on how many columns in each conference excel has; however, the order of columns that we add after the last column on the sheet will be the same.

c. For ID column, in cell P2 enter the VLOOKUP formula:
=VLOOKUP(A2,'[RabiesTiterBooth_20210106smm.xlsx]Sheet 1'!$A:$C,3,0)
Then click enter and select the cell and drag to the last row of data to fill in data.
*Please note that in case that the formula does not work, select table array which is '[RabiesTiterBooth_20210106smm.xlsx]Sheet 1'!$A:$C, then go to RabiesTiterBooth_20210106smm file and click on any of cells. Go back to the conference/year excel spreadsheet and at the table array in the formula, delete what comes after ...'[RabiesTiterBooth_20210106smm.xlsx]Sheet 1'!$ and then add A:$C instead.

d. For male column, the data of each participants can be found in submission forms.

e. For yob column, the data of each participants can be found in submission forms. Only year of birth is used, e.g., 1994.

f. For region column, make a new sheet, named it sheet2, then copy the State name and region number into sheet2 as below.

Connecticut	1	Illinois	5	Nevada	9
Maine	1	Indiana	5	American Samoa	9
Massachusetts	1	Michigan	5	Commonwealth of the Northern Mariana Islands	9
New Hampshire	1	Minnesota	5	Federated States of Micronesia	9
Rhode Island	1	Ohio	5	Guam	9
Vermont	1	Wisconsin	5	Alaska	10
New Jersey	2	Arkansas	6	Idaho	10
New York	2	Louisiana	6	Oregon	10
Puerto Rico	2	New Mexico	6	Washington	10
Virgin Islands	2	Oklahoma	6		
Delaware	3	Texas	6		
District of Columbia	3	Iowa	7		
Maryland	3	Kansas	7		
Pennsylvania	3	Missouri	7		
Virginia	3	Nebraska	7		
West Virginia	3	Colorado	8		
Alabama	4	Montana	8		
Florida	4	North Dakota	8		
Georgia	4	South Dakota	8		
Kentucky	4	Utah	8		
Mississippi	4	Wyoming	8		
North Carolina	4	Arizona	9		
South Carolina	4	California	9		
Tennessee	4	Hawaii	9		

If States label as postal code, this table below will be used instead.

CT	1	KY	4	IA	7	OR	10
ME	1	MS	4	KS	7	WA	10
MA	1	NC	4	MO	7		
NH	1	SC	4	NE	7		
RI	1	TN	4	CO	8		
VT	1	IL	5	MT	8		
NJ	2	IN	5	ND	8		
NY	2	MI	5	SD	8		
DE	3	MN	5	UT	8		
MD	3	OH	5	WY	8		
PA	3	WI	5	AZ	9		
VA	3	AR	6	CA	9		
WV	3	LA	6	HI	9		
AL	4	NM	6	NV	9		
FL	4	OK	6	AK	10		
GA	4	TX	6	ID	10		

*See https://www.hhs.gov/about/agencies/iea/regional-offices/index.html for state's region.

In cell S2 enter the VLOOKUP formula: =VLOOKUP(G2,Sheet2!$A:$B,2,0)

Then click enter and select the cell and drag to the last row of data to fill in data.

* G2 is the first cell in the state column. In this case G column is the state column; however, if the state is in another column, the column has to change after the state column.

*Please note that if there is any state/region which is not in the list, it will be stated as the name of that region, e.g., Ontario.

g. For conf column, copy the conference number from column A in the conference/year excel spreadsheet, and paste into this column.

h. For date column, copy the date which sample was drawn from column M (labelled as date of draw) in the conference/year excel spreadsheet, and paste into this column.

i. For titer column, in cell V2 enter the VLOOKUP formula: =VLOOKUP(A2,'[RabiesTiterBooth_20210106smm.xlsx]Sheet 1'!$A:$B,2,0)
Then click enter and select the cell and drag to the last row of data to fill in data.
*Please note that in case that the formula does not work, select table array which is '[RabiesTiterBooth_20210106smm.xlsx]Sheet 1'!$A:$B, then go to RabiesTiterBooth_20210106smm file and click on any of cells. Go back to the conference/year excel spreadsheet and at the table array in the formula, delete what

comes after ...'[RabiesTiterBooth_20210106smm.xlsx]Sheet 1'!$ and then add A:$B instead.

j. For initial_vx, initial_vx_reason, booster1, booster1_reason, booster2, booster2_reason, booster3, booster3_reason columns, use data in vaccination history from the submission forms to fill in each cell.

k. For Note column, fill in all the vaccination history that participants have stated in the submission forms.

*If there are any cells do not have data, label that cell as N/A.

3. Make a new excel file, named it as ’Name of conference’ ‘M-YYYY’- prepared.
4. Copy columns from conference/year excel spreadsheet starting with ID column to Note column and paste it into the prepared new excel file. It must be pasted as paste value to prevent data missing from using formula.

   *Please note that all participants’ personal information will not be copied in this step. Therefore, the data that is sent to the evaluator/analyzer is blinded to the personal protected information (PPI).
5. Share the prepared spreadsheet to the evaluator.

Difficulties

1. The submission forms did not scan in order, so it is hard to find each sample and fill in the gender, year of birth, and vaccination history.
2. Some of the data used a formula (the format is ‘formula’), so when processing the data, these data is needed to be copied and pasted value to a new sheet first.
3. Some conferences do not have an excel spreadsheet containing data from all participants, so data needs to be pulled out from the VetView manually.
4. Some of the data is missing. E.g., The participants did not fill out in some part or they did not state the vaccination history clearly.

The template for the final file

ID	male	Job	region	conf	date	titer	initial_vx	initial_vx_reason	booster1	booster1_reason	booster2	booster2_reason	booster3	booster3_reason	Last_booster	Last_booster_reason	Note

Appendix D. Summary of Best Practices for Rabies Vaccination and Booster Timing for Personnel Handling Animals

Introduction

Rabies is a zoonotic disease caused by lyssaviruses, almost exclusively by rabies virus (RABV) which occurs worldwide. According to The World Health Organization (WHO), it is estimated that rabies cause 59,000 human deaths annually in over 150 countries. Most rabies deaths in people around the world are caused by bites from rabid dogs. In the United States, rabies infection in humans are rare, where wild animals like bats, raccoons, skunks, and foxes are the most common sources. However, rabies is more prevalent in other parts of the world such as Africa and Asia where dogs are the most common source of rabies. (*Rabies Vaccine Information Statement | CDC*, n.d.)

Rabies is a fatal viral disease. The transmission of the virus occurs through direct contact between infectious saliva and broken skin or mucous membranes in the eyes, nose, or mouth, typically via bites of a rabid animal. (Fisher et al., 2018)It is also possible for people to get rabies from non-bite exposures, including scratches, abrasions, or open wounds that are exposed to saliva or other potentially infectious material from a rabid animal, but the probability of transmission is much less. In contrast, blood, urine, or feces of a rabid animal, are not associated with risk for infection and are not considered to be exposures of concern for rabies. (*How Is Rabies Transmitted? | Transmission | CDC*, n.d.). After exposure, the virus will travel through the body via the nervous system to the brain and cause symptoms. The symptoms include general weakness or discomfort, fever, or headache, then as the disease progresses, the patient may experience delirium, abnormal behavior, hallucinations, hydrophobia, and insomnia. Once patients begin showing clinical signs, the disease nearly always causes death within days. (*What Are the Signs and Symptoms of Rabies? | Symptoms | CDC*, n.d.)

Although there is no effective curative treatment for rabies once clinical signs have shown up, rabies can be prevented by vaccination and appropriate medical care after potential rabies exposure. Rabies vaccination recommendations also depend on risk of rabies exposure regarding to area and occupation. People with a higher occupational risk such as people working with rabies virus in laboratories, and other professions (veterinarians, animal handlers, wildlife

officers etc.) working in rabies endemic areas should know the best practices for rabies vaccination to follow to prevent rabies infection.

Rabies vaccines for humans should meet WHO recommendations for characterization, production, and control, as set out by the WHO Expert Committee on Biological Standardization (World Health Organization, 2014) The WHO recommendations currently apply only to inactivated rabies vaccines produced in cell culture or embryonated eggs. Ideally, vaccines should be prequalified by WHO, to demonstrate the quality, safety and efficacy of vaccines and their suitability for use in national immunization programs in low- and middle-income countries. In addition, a vaccine must also be licensed in its country of manufacture as a prerequisite to prequalification. Current rabies vaccines are produced based on cell culture and embryonated eggs as doses for intramuscular and or intradermal injection. (World Health Organization, 2018) Per the Advisory Committee for Immunization Practices (ACIP) in the United States only intramuscular (IM) injection with an individual dose vaccine used (CDC, 2008).

Pre-exposure prophylaxis (PrEP)

According to ACIP recommendations, there are several reasons why pre-exposure rabies prophylaxis should be administered. First, pre-exposure prophylaxis simplifies management by eliminating the need for RIG and decreasing the number of doses of vaccine needed. Next, it might offer partial immunity to persons whose postexposure prophylaxis is delayed. Finally, pre-exposure prophylaxis might provide some protection to persons at risk for unrecognized exposures to rabies. Therefore, pre-exposure vaccination should be offered to persons in high-risk groups, such as veterinarians and their staff, animal handlers, rabies researchers, and certain laboratory workers. (Manning et al., 2008) The 2008 recommendations are currently under review by the ACIP Rabies Workgroup. Recent changes approved by the ACIP in February 2021, including the pre-exposure prophylaxis (PrEP) recommendations. The below reflect these approved changes to be implemented upon publication of the updated rabies vaccine recommendations expected later in 2021.

- <u>Primary vaccination</u>:

  Two 1.0-mL injections of human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) should be administered IM (deltoid area), one injection per day on days 0 and 7.

- Booster vaccination:

  Booster vaccination and monitoring antibody level titer are recommended in people with high risk of rabies exposure.

  -For people with continuous risk such as rabies research/diagnostic laboratory workers, and rabies biologic production workers, primary course, and serologic testing every 6 months for booster vaccination (intramuscular HDCV or PCECV; 1.0 mL (deltoid area), day 0 only) if antibody is below acceptable level (0.5 IU/mL by the rapid fluorescent focus inhibition test) are recommended.

  - For people with frequent risk such as all persons who frequently handle bats, primary course, and serologic testing every 2 years for booster vaccination if antibody is below acceptable level are recommended.

  - For people with infrequent risk such as person who work with animals (veterinarians, technicians, animal-control workers, wildlife biologists, spelunkers, veterinary students, as well as travelers with increased risk of exposure to rabid dogs, primary course is recommended, and serologic testing at 1-3 years OR a booster vaccine by year 3.

  -For people with rare risk which are population at large, no vaccination is necessary.

Post-exposure prophylaxis (PEP)

Administration of rabies post-exposure prophylaxis is a medical urgency, not a medical emergency, but decisions must not be delayed. (Manning et al., 2008)

Wound treatment is very important after a potential rabies exposure for both previously vaccinated and unvaccinated persons. A proper wound care should be done as soon as possible after exposure. For many types of bite wounds, immediate gentle irrigation with water or a dilute water povidone-iodine solution markedly decrease the risk for bacterial infection. (Callaham, 1978) In addition, tetanus booster vaccine should also be considered. Finally, primary wound closure and antibiotic prophylaxis should be decided regarding to the exposing animal species, size and location of the wound(s), and time interval after the bite individually.

However, rabies post-exposure prophylaxis for vaccination and the use of RIG in people previously vaccinated and unvaccinated are different.

- For previously unvaccinated people:

  First wound treatment should be done as soon as possible. RIG is needed in those who are unvaccinated by administering 20 IU/kg body weight. If anatomically feasible, the full dose globulin (RIG) is infiltrated around the wound(s) and any remaining volume should be administered intramuscularly (IM) at an anatomical site distant from vaccine administration. In addition, RIG should not be administered in the same syringe as vaccine because it might partially suppress active production of antibody. Finally, human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area), one each on days 0, 3, 7, and 14 is given (CDC, 2010).
- For previously vaccinated people:

  First wound treatment should be done as soon as possible. However, RIG should not be given in people who previously vaccinated because it might inhibit the relative strength or rapidity of an expected anamnestic response (Fishbein et al., 1986). Finally, HDCV or PCECV 1.0 mL, IM (deltoid area), one each on days 0 and 3 should be given (CDC, 2010).

Rabies pre-exposure prophylaxis guide – United State, 2008

Risk category	**Nature of risk**	**Typical populations**	**Pre-exposure recommendations**
Continuous	Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, non-bite, aerosol exposure.	Rabies research laboratory workers; rabies biologics production workers.	Primary course. Serologic testing every 6. months; booster vaccination or if antibody titer is below acceptable level. *
Frequent	Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, non-bite, or aerosol exposure	Rabies diagnostic laboratory workers, cavers, veterinarians and staff, and animal-control and wildlife workers in areas where rabies is enzootic. All persons who frequently handle bats.	Primary course Serologic testing every 2 be years; booster vaccination if antibody titer is below acceptable level. *
Infrequent (greater than population at large)	Exposure nearly always episodic with source recognized. Bite or non-bite exposure.	Veterinarians and animal-control staff working with terrestrial animals in areas where rabies is uncommon to rare. Veterinary students. Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including biologics is limited.	Primary course. No serologic testing or booster vaccination.
Rare (population at large)	Exposure always episodic with source recognized. Bite or non-bite exposure.	U.S. population at large, including persons in areas where rabies is epizootic.	No vaccination necessary.

* Per the ACIP 2008 the minimum level of antibody is complete neutralization at a 1:5 serum dilution in the RFFIT. A booster dose should be administered if the titer falls below this level.

Rabies post-exposure prophylaxis schedule – United State, 2010

Vaccination status	**Treatment**	**Regimen***
Not previously vaccinated	Wound cleansing	All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidone-iodine solution should be used to irrigate the wounds.
	Human Rabies immune globulin (HRIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around the wound(s) and any remaining volume should be administered at an anatomical site (intramuscularly [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of antibody, no more than the recommended dose should be administered.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area), 1 each on days 0, 3, 7, and 14.
Previously vaccinated	Wound cleansing	All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidone-iodine solution should be used to irrigate the wounds.
	HRIG	RIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area), 1 each on days 0 and 3.

* These regimens are applicable for all age groups, including children.

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Appendix E. Poster for Educating Animal Handling Staff on Rabies Control and Prevention

RABIES Why is it important?

- Rabies is a disease that can spread between animals and people which occurs worldwide.
- Once clinical signs appear, rabies is deadly and there is no effective treatment.
- However, rabies can be prevented by vaccination and appropriate medical care after potential rabies exposure.

PRE-EXPOSURE PROPHYLAXIS

Risk category	Pre-exposure recommendations
Continuous risk: Rabies research laboratory workers; rabies serum and vaccine production workers.	• 3 shots of rabies vaccines injection on days 0, 7, and 21 or 28 • Immune level testing every 6 months; booster vaccination if the immune level is below the recommended minimum
Frequent risk: Rabies lab workers, cavers, veterinarians and staff, and animal-control and wildlife workers in areas where rabies is always present. All persons who frequently handle bats.	• 3 shots of rabies vaccines injection on days 0, 7, and 21 or 28 • Immune level testing every 2 years; booster vaccination if the immune level is below the recommended minimum.
Infrequent risk: Veterinarians and animal-control staff working with animals in areas where rabies is uncommon to rare. Veterinary students. Travelers visiting areas where rabies is always present and health care is limited.	• 3 shots of rabies vaccines injection on days 0, 7, and 21 or 28. • No immune level testing or booster vaccination
Rare risk: Most US population, including persons in areas that have rabies outbreak.	• No vaccination necessary.

POST-EXPOSURE PROPHYLAXIS

Vaccination status	Treatment
Not previously vaccinated	• Immediate wound cleansing with a solution that can destroy the virus • Serum injected at the wound • Rabies vaccine administered into muscle, 1 each on days 0, 3, 7, and 14.
Previously vaccinated	• Immediate wound cleansing with a solution that can destroy the virus • Serum should not be injected • Rabies vaccine injected into a muscle, 1 each on days 0 and 3.

FOR MORE INFORMATION

- Ask your health care provider.
- Call your local or state health department.
- Contact the Centers for Disease Control and Prevention (CDC):
  - Call 1-800-232-4636 (1-800-CDC-INFO) or
  - Visit CDC's rabies website (https://www.cdc.gov/rabies/index.html)
- Visit https://www.rabiesaware.org to check rabies information by state

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