Second China-U.S. Workshop on the Challenges of Emerging Infections, Laboratory Safety and Global Health Security

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Meeting Report

During the welcome session the Chair of the meeting for the Chinese Academy of Sciences (CAS) **Zhiming Yuan** (Principal Investigator, Wuhan Institute of Virology, CAS) thanked the assembled audience of about 100 experts and noted that the meeting would focus on the importance of good science and good policy for controlling emerging disease. Yuan said the meeting is a milestone for Sino-U.S. cooperation on emerging infections, laboratory safety and global health and security and would lead to further cooperation between the U.S. National Academy of Sciences (NAS) and CAS and between the United States and China. **Xinwen Chen** (Director General/ Principal Investigator, Wuhan Institute of Virology, CAS) said that the Wuhan Institute of Virology, a key sponsor of the workshop, and an operator of one of China's Biological Safety Level Four (BSL-4) high containment laboratories, aims to improve fundamental research in virology and other areas of basic science by doing fundamental research to combat emerging infections and outbreaks in China and around the world to ensure global health security and safety in China. **Yaping Zhang** (Vice President/ Academician, CAS) was not available due to a family emergency so **Qingquan Zhang** (Department of International Affairs, CAS) gave short opening remarks on behalf of CAS. He extended congratulations to the assembled group on behalf of the CAS Bureau of International Cooperation (who provided some of the funding for the meeting) and said that science in China is booming but groups like CAS and NAS need to look back to see how well we have done in the past and provide guidance and advice for the future.

Linda Saif (Professor, The Ohio State University) opened the meeting on behalf of the NAS. The institution has 2290 members, 460 foreign associates as affiliates and counts 200 noble prize winners among its members. NAS was established in 1863 to provide independent advice to the U.S. government and has done so for over 150 years including advice on building the Panama Canal and the launch of the first U.S. satellite. NAS was involved in organizing the 1975 Asilomar, California conference to establish a common understanding of risk and sensible precautionary measures related to recombinant DNA research. NAS produces two types of reports, workshop proceedings and consensus reports with findings and commendations, with the majority requested by government agencies. This year NAS published a report on research guidelines for human gene editing and posted the proceedings of an international human gene editing summit. She noted that NAS recently reorganized its divisions to form the National Academies of Science, Engineering, and Medicine, (NAS, NAM, NAE).

After the introduction she explained that the current workshop is designed to help Chinese

and American experts better cooperate to respond to emerging infectious diseases, promote lab and global health biosecurity, and address impediments to cooperation and collaboration between the U.S. and China. She outlined the goals of the current workshop as:

1) Establish communication and scientific relationships within the region
2) Exchange scientific knowledge and best safety and security practices for research
3) Foster future China-U.S. cooperation and collaboration

She noted that CAS and NAS would produce documents summarizing the meeting and plan to organize future workshops on these topics.

David Relman (Professor, Stanford University) greeted the group on behalf of the U.S. National Academy of Medicine (NAM) president and foreign secretary. He described NAM as a 2000 member organization, created under the NAS charter in 1970, focusing on improving health and setting the agenda in medicine and health in the United States. As the chair of the NAM Forum on Microbial Threats he focuses on why infectious diseases occur, the microbe/host environment, and the framework for emerging infectious disease. NAM is also interested in microbial forensics and global health security and is promoting a global health risk framework. He sees three broad areas for further collaboration between the U.S. and China:

1) *Emerging infections*, understanding disease reservoirs, disease emergence, disease surveillance, natural versus human origin of disease, data sharing, and building capacity for research during public health emergencies.
2) *Anticipating Risk* in the life sciences and medicine related to biotechnology innovation, such as identifying certain experiments that are too risky to conduct.
3) *Governance of Science* to reduce risk, such as doing research in centralized laboratories versus distributed labs, managing research costs, learning from the past technical and bureaucratic mistakes, best ways to diminish risk without hindering science and address technical risk for the laboratory versus social risk for the community.

At the end of the introductions the audience was curious about how NAS and NAM reports are produced and asked how to ensure that the government will take the advice given. Dr. Relman answered that NAS and NAM produce independent reports for the U.S. Government and other sponsors; it is up to the sponsor to use or implement the advice in the report, but they are not required to do so. A participant noted that it is important for groups like NAS and NAM to catalyze and convene groups of the best minds to agree on a suitable path forward for others to implement but noted that CAS is somewhat different than the NAS. CAS advises and convenes but has a basic research mission as well. He said perhaps CAS can benefit from NAS experience on how to provide sound advice to the government on science.

James Le Duc (Professor, Galveston National Laboratory) then summarized the technical aspects and challenges associated with high-containment laboratories. Le Duc noted that China is on the verge of opening three BSL-4 high-containment laboratories and offered thoughts and advice from his perspective as the head of the University of Texas Medical Branch Galveston National Laboratory (GNL). He described high containment labs as

valuable resources that often employ the best people addressing the most difficult problems of global health. GNL is designed to handle all BSL-4 agents and has been in operation for about a decade. The lab cost 175 million USD to build and had significant ongoing operations expenses independent of the cost of research activities. These include utility costs, maintenance, and training the large onsite security force. The yearly operation costs equals about 11.5-15 million USD or about 7-9% of the construction costs. Other key issues of concern are the preparation for and proper management of laboratory accidents. Some accidents are inevitable so it is import to take precaution not only to reduce the likelihood of their occurrence but to manage and minimize the consequences. Labs should have a preexisting plan for many adverse situations. This plan should especially include a strategy for communication with the public and policy makers. Labs are a source of pride for the local community but when things go bad, opinion can change. It is important to build up a 'bank account' of good will by talking about important scientific contributions made by the researchers at the facility and how valuable research is to domestic and global health, and then be open and transparent if something goes wrong.

When asked how he defends and secures the large budget needed to run the lab year to year, Le Duc said this is a constant struggle, as costs go up and political leadership changes, the best strategy is to maintain lines of communication between the lab and the community and to politicians. In the U.S. it's not possible to guarantee the budget each year. The U.S. NIH helps offset the some of the operations costs, but it is not practical to recoup all of this money from the NIH alone. NIH just provides costs for operations of labs, but all research expenses are funded through individual competitive grants and contracts. About 2/3 of the initial construction costs were provided by NIH and the remainder by the State of Texas and the University of Texas, with some philanthropic contributions. In the U.S. the long-term sustainability of a BSL-4 laboratory requires constant vigilance regarding the cost of operations and maintenance of the facility.

Session 1: Gain-of-function research, gene editing, targeting, and delivery and other novel biotechnology was chaired by **Yanyi Wang** (Deputy Director General/ Principal Investigator, Wuhan Institute of Virology, CAS). Participants discussed gain-of-function research, gene editing, targeting and delivery, other novel biotechnology and other recent advances in technology and their applications.

David Relman (Academician, Stanford University) spoke about the challenges and opportunities of genome engineering and other novel life sciences technologies. He said that responding appropriately to emerging infections has not changed, what has changed is the kind of science that is done. Today, scientists have a profoundly better ability to study and manipulate life at the genetic level but collectively, the scientific community has not given enough thought to what these new science capabilities mean. He described the process-based classification of life sciences technologies as the acquisition of novel biological or molecular diversity (e.g., DNA synthesis, DNA shuffling, combinatorial chemistry), directed design (e.g., synthetic biology, reverse genetic engineering), understanding and manipulating biological systems (e.g., "systems biology", RNAi, modulators of homeostatic systems), and production, packaging, delivery (e.g., microfluidics / microfabrication, nanotechnology, microencapsulation, gene therapy/targeting). He said that today individuals have increasing

power in the life sciences due to the low barrier of entry and the lower costs and more efficient and rapid processes described above. For example most RNA viruses can be re-synthesized using just the sequence so possession of a sequence allows an individual to make a virus.

When considering risk from the misuse of biology he asked if certain experiments should not be undertaken because the risks outweigh the benefits or because benefits will only be realized in the indefinite future? A key risk factor is the possibility of unusually large consequences if an accident were to occur (like the inability to contain a release and prevent illness and death, especially in resource-poor areas). Misuse can take many forms, from accidental or benign, to unwitting infections or release all the way to callous or deliberate (the most likely being accidental).

There is currently a vigorous discussion in the U.S. about experiments that enhance the virulence of influenza virus and genetic manipulation associated with gain-of-function research. He suggested that scientists should think carefully about strategies to minimize risk before doing such experiments, and to factor risk into decisions about research plans. Benefits almost always can be achieved with other experimental approaches. Other ways to address this problem include:

- More transparency in the scientific process
- The regulation of access to reagents and information
- Sensitizing relevant communities and establishing norms for the role of individuals, professional organizations, academia, industry, national leadership, and international organizations.
- Anticipating and preempting threats
- Response if something goes wrong (detection, reversal, attribution, etc.)

To achieve any of this strong scientific leadership is needed and should involve the entire scientific community. Consider the 1975 Asilomar Conference on Recombinant DNA as an example, scientists designed guidelines to ensure safe ways to work with recombinant DNA before an emerging era of research became a more public problem.

The audience asked about the U.S. approval process for gain-of-function research. Relman said that United States is in process of determining what to do about this. The audience asked how to engage the public on these issues. He said that this is also a challenge. In general most people are confused about the reasons for doing experiments like these in the first place therefore we need to explain the value of the work as well as the risks. An audience member asked if there are U.S. laws on gain-of-function research. Relman said no, law and regulation could control some research, but any evaluation system will not be able to catch everything, especially a rogue individual. An audience member suggested that we can raise awareness among the scientific community to inspire more scientists to think about the risks before they undertake an experiment to address a scientific problem.

Zhihong Hu (Principal Investigator, Wuhan Institute of Virology, CAS) discussed the construction and rescue of a functional synthetic baculovirus as an example of the capabilities of modern synthetic biology. She noted the massive uptick in reference to synthetic biology in scientific journals this century and the many advances in the filed since polio virus was first synthesized in 2002. Her research focuses on baculovirus co-evolution with insect hosts,

a system with a very unique lifecycle and could be used as a bio-control agent to control pest outbreaks. Her research suggests that Baculovirus, a large DNA virus, can be synthesized and that it is a powerful platform for virus modification and engineering and for fundamental studies. She said that virus synthesis is a unique tool to study the viruses with only genome information or uncultured viruses. She noted that there is a low risk for synthesizing baculovirus because the virus has a large flexible genome that is easy to manipulate where researcher can delete genes without risk. She concluded by asking the audience if the scientific community should regulate synthetic biology and if so how?

The audience asked about reproducibility of her baculovirus virus synthesis and she said that a very skilled student can synthesize baculovirus in one month; others in two months. An audience member asked her to predict when Zika virus would be synthesized. She said any flavivirus lab could do it right now. Another member of the audience asked if having the original virus made the process easier? She said yes, it is harder to do from a database sequence and more difficult without the original virus. An audience member mentioned safety concerns noting that in the United States the NIH publishes regulations on modified genetic organisms.Hu said that she participated in the discussions to destroy small pox stocks; labs now can only possess 30% of the small pox genome but asked how can you control and regulate that in an era of synthetic biology? She said she knows that she will face public questions about her research and wants to make sure her viruses stay safe and secure.

Wensheng Wei (Professor, Peking University) spoke about high-throughput functional genomics: coding, non-coding and beyond. He described his research as using bio technology to address anthrax toxicity, Clostridium difficile bacterial infections (CDIs) and viral infection. He also discussed the use of gene editing tools and gain of function research. He uses gene editing systems, like CRISPR to address bacterial antibiotic resistance, a large problem in China because gene editing has many applications for drug target identification. His current research focuses on CDIs that are more resistant to antibiotics and how synthetic and natural systems for editing can be turned into a high throughput strategy to produce better antibiotics. He is also working to produce Zika virus antivirals and is developing high throughput methods to identify non-coding elements on the chromosome to get better tools to study the whole genome. The new gene editing tools are useful for addressing drug resistance but new techniques still needed to get the drugs through clinical trials. An audience member asked if he had found any new roles for RNA in the infectious disease process. Wei said not yet but that this is a promising area.

Session 2: Public health response to outbreaks and issues. The session chair **James Le Duc** (Professor, Galveston National Laboratory) noted that the panelists would present three technical talks demonstrating collaborative research concerning Dengue, Zika, Ebola, and influenza, including Avian Influenza, and host-pathogen interaction (pathogenesis).

Xia Jin (Principal Investigator, Institute Pasteur of Shanghai, CAS) spoke about observations that Dengue immune sera enhances Zika virus infection in human peripheral blood monocytes. He noted that dengue antibodies enhance Zika infection and explained the mechanism and how this is being considered as researchers work to produce a Zika vaccine. Audience members asked if Dengue would enhance infection in infants and toddlers and he

noted that a baby born of a Dengue infected mother will have more severe infection. However he said that there is no epidemiological data that overlays Dengue and Zika infections showing severe Zika in populations with Dengue. He also noted that Zika vaccine would be ready soon and that Zika vaccine development would be easier than a Dengue vaccine.

Rui Gong (Principal Investigator, Wuhan Institute of Virology, CAS) spoke about engineered human antibody constant domain as a candidate against Ebola virus. He said that therapeutic antibodies are invaluable tools for control of viral infection, they are the most effective tools for prevention of pathogen infection after exposure. He discussed techniques for using therapeutic antibodies and updated the group on "ZMapp" and other current neutralizing antibody therapies against Ebola. Monoclonal antibodies ZMapp were used for therapy in infected patients during the Ebola epidemic in West Africa. The sera from convalescent patients were used for therapy in MERS-CoV infected patients in Korea. He said that the therapeutic antibody market remains one of the fastest-growing segments in the pharmaceutical industry, with a growth rate of approximately 30% per year. He explained his research focus and the possible next steps in the therapeutic antibodies research process including, the further optimization on 7c2M antibodies, animal studies, understanding the neutralization mechanism in antibodies, neutralization experiment in protection from Ebola virus infection at the cell level, and the evaluation of the "drugability" of the 7c2 antibody.

Pei-Yong Shi (Professor, University of Texas) discussed antiviral drug discovery and development. He noted his diverse background in science, public health and administration and more recent work on antiviral drug discovery. His presentation outlined antiviral drug discovery strategy to target viral and host proteins, stimulate immune systems, and modulate molecular pathways that lead to diseases. Two antiviral approaches could be taken: a target based approach and a cell based approach. Next, he presented two dengue antiviral projects. One project used crystal structure to rationally design inhibitors of dengue viral polymerase. Another project used cell-based screening to identify inhibitors of dengue NS4B protein. He said that future research would determine the mechanism of NS4B inhibitors and develop compound with pan-serotype activity. An audience member asked if in clinical use, the prompt for initiating treatment would likely be a sign, like fever then asked how he envisioned timing of use in humans? Shi noted that by the time the patient reports to a clinic viremia already starts to drop. An audience member asked if the virus will clear faster if you increase the dose? He said that the hope is to get the immune system to kick in to mitigate the disease. The session chair asked about the location of his collaborators. He said they are all over the world and in Brazil since that is Zika ground zero; they report progress in real time to the Brazilian government to promote transparency.

James Le Duc (Professor, Galveston National Laboratory) the chair of the session, then discussed improving the BSL-4 laboratory's role in emergency health response and the importance of communications during a crisis. He changed the focus of the session from technical talks on research to discussing the labs where some of the research takes place and how best to response and communicate during and after an outbreak.

At the beginning of the talk he noted that every aspect of outbreak response can be complicated, for example, at what level and for how long should we screen people after exposure? Ebola can live in the body for months after recovery. It's important to take precaution but size the precaution to the risk. The time to think about question like this is before the outbreak. He noted that GNL is one of nine regional facilities that can treat Ebola in the U.S. and has 6 hospital type rooms to treat infected patients while in containment.

During a crisis the focus should be on laboratories providing transparent, accurate and timely diagnostics of patients during an outbreak or exposure. When the community is not informed the situation tends to get out of hand. Much can be done to manage the perception of risk in advance. Proper education should happen early. During a crisis leaders should know the facts and have something to say and convey it clearly. We learned that it is important to have clear leadership and manage communication with the public and with politicians while responding to the recent Ebola case in Dallas, Texas. During the crisis in Dallas then Governor Rick Perry created a taskforce that brought everyone together to respond. Later other problems had to be solved. The patient generated a huge amount of medical waste, treatment generated eight 55 gallon drums of waste every day. The state of Texas trucked the waste to GNL and we disposed of it properly. Other issues include cleaning secondary facilities and dealing with pets. An outbreak can be a time when you demonstrate the value of your facility to your country, be prepared to help, plan a communication strategy, use a trusted spokesperson and stay on message. Use the right people to do this, for example, Thomas Ksiazek, senior leader at GNL has experience responding to outbreaks going back to 1977. Anticipate and welcome involvement of political leaders. Be prepared to provide definitive diagnostics. Train lab and clinical staff on PPE and patient management before the need arises and don't forget waste management.

During the question and answer session a Chinese participant asked about GNL's "official" responsibilities during the crisis, where there problems delegating authority when making

official statements? Le Duc said that he did not have the responsibility to speak on behalf of the U.S. Government (even though the lab is a “national” lab) and also that he did not get paid extra for any of this, he said that it was part of our duty, to the community, state and nation. During the response GNL had to reprioritize some of its basic research, like vaccine development. That said, extra investment paid off in the good will and support that GNL received. Good statements by public officials help preserve the prestige of lab. He also said that the community was very supportive from the beginning because GNL leaders spend a lot of time communicating and maintaining a dialogue with local leaders and frequently notes the economic value that the facility creates. For example GNL did a 20 year economic forecast, noting that GNL generates more than 1billion for the community. An audience member noted that China was also prepared to respond to Ebola. Government leaders across agencies and ministries have had many meetings but the response would have been organized by the Ministry of Health and Family Planning if there was an Ebola case in China. An audience member asked for more details about how to treat clinical medical waste. Le Duc explained that the waste generated by the Ebola patient was initially treated with chemicals and not autoclave because Dallas did not have a large enough facility. Chinese audience members noted that China does not have a large autoclave clinical waste capability and needs to come up with a strategy. In China the emergency response is organized by the Chinese CDC. Le Duc noted that GNL played a supporting role in the Ebola patient response, the U.S. CDC had primary responsibility for the national response but because the case happened in the state of Texas GNL naturally had a larger role. A Chinese participant noted that the U.S. system is different than in China but noted that if anything happens in Wuhan, the first sample would go to Hubei province CDC first and that the local facilities would also have a larger role.

The first day ended with a round table discussion chaired by **Zhiming Yuan** (Principal Investigator, Wuhan Institute of Virology, CAS) and **James Le Duc** (Professor, Galveston National Laboratory).The chairs reviewed the discussion from day one. Yuan noted that excellent science is going forward in China and in the United States but that new research techniques and risks associated with certain research are raising some policy issues at the national and international level. How do we work together to create regulations that will not hinder the good science going on? He say many opportunities for collaboration and exchange between China and the United States but looked to the future by asking how do we educate students on technical issues but help them understand the context of global challenges going forward? He noted that several BSL-4 labs are about to open in China and asked about how to best share virus stocks, reagents and the tools and techniques necessary to do the critical scientific work the labs were designed to do?

Yuan first noted that the day one presentations on combating emerging disease control are good basis for future communication and collaboration; the United States and China can find common interests in these areas. He noted that NAS and NAM and CAS, while different types of organizations, have the same basic objectives to promote science for the development of the world. However our communities have different ways to approach crisis; China should do a better job explaining our system and what happens when there is a

problem in China and how it is addressed. We have lots of processes in place but we can learn a lot from the American side on understanding how to effectively manage crisis. He said he was concerned about how scientists can manage advances of new technology. Scientists have mostly used modern technology and science to do good work but today some research proses risks that should be acknowledged and addressed. He asked how our communities can better understand risks to prevent accidents or misuse not blocking research pathways that can produce real benefit. Finally he noted that scientists have a duty to help the public understand the value of scientific research and demystify their work.

An audience member agreed with the theme of his summary, and said that the problem of controlling emerging infections is a difficult problem that we share. One important problem to consider is how scientists can better understand natural disease reservoirs and interpret sequence data from nature? Today it is easy to generate sequences but it remains hard to understand what a given sequence means regarding phenotype. What other kinds of information do we need to collect to solve this problem? Regarding research that carries some risk, we should also think about the kinds of experiments that warrant further discussion or review and address the problem before outsiders challenge the rational to do the science.

A Chinese participant said that we know that bats and birds host potential pathogens and that the scientific research community is working across China to map reservoirs. We have generated a lot of sequence information over the past several years but we don’t understand why diseases emerge when they do; more collaboration on reservoirs is needed. They said that there is a lot China can learn from the GNL, but not just scientifically. When managing a laboratory transparency and trust are important. BSL-4 labs are huge investments and require millions of dollars to run, we want the world to understand what we are doing so they will support what we do. The participant said that it would be good to see institutional level collaboration between The Wuhan National Institute of Virology (NIV) and GNL and that CAS could spend money to help support the collaboration. CAS has several mechanisms to support international engagement and collaboration including funding international exchanges and fellowships for people from abroad to come to China and do research. Also scientists in China can propose international projects that CAS can fund, something could be done jointly on the ecology and evolution of infectious disease. CAS is already working with the U.S. NSF and NIH, the program manager will visit NIV next month. We can use all these resources.

Another Chinese participant said that the group should be most interested in collaborating on pathogenic viruses and should focus on significant viral threats to human health. China CDC is working to discover unknown pathogens. He also stated that the U.S. and China should share their experience responding to emergencies. Scientists will have to work with the policy makers to prepare for infectious disease emergencies. This could be a topic for a joint report.

A Chinese participant noted that sharing viruses even domestically is difficult and asked how the scientific community can overcome this logistical problem? They have created a consortium to share samples within China, but sharing samples across international borders is

more difficult. Another participant said that there are many issues to solve at the policy level, for example shipping live virus is an especially big problem; however there are techniques to ship parts of the viral genomes. More science can be done to overcome the policy problems. An American participant noted that the group is focused on public health and science but should remember to engage the veterinary and the agriculture production sector (in the spirit of One Health). The U.S. and China can expand this collaboration like they have with the long-standing collaboration on influenza.

Yuan said that on the second day the group would hear more about China's new BSL-4 facilities, biosafety, biosecurity and regulation and management of research in both China and the United States. These topics might also be the basis for future collaboration. Also to better accommodate collaboration we should consider a more formal linkage between our groups, like a memorandum of understanding. After the meeting we should identify priorities and write joint remarks to our academy presidents about the meeting and what our two academies can do together on these issues to provide a channel and bridge for future.

Day 2

Session 3: Emerging infectious diseases and global health security. The chair, **Pei-yong Shi** (Professor, University of Texas, GNL) noted that the session would cover anti-viral countermeasures (strategy and R&D) and improving the high containment laboratory's role in emergency health response.

George Gao (Academician, Institute of Microbiology, CAS) discussed biosafety, biorisk, and biosecurity pathogens and human behavior. Gao said he has experience responding to natural outbreaks all over the world, and played a leading role in China's response to the 2014 West African Ebola outbreak but has less experience addressing or thinking about deliberate misuse of biology. He stated that the meetings between Chinese and American experts are important because more and better collaboration can help prevent accidents and has the potential to prevent misuse. He started his presentation by asking two questions, why do we have so many new viruses and why do we have periodic disease outbreaks? Gao noted that today the world is more interconnected, human behavior has been a driving force for many of the changes. He spoke of the H7N9 outbreak of 2013 and the difference between low pathogenic and highly pathogenic avian influenza. He said we do not know what HxNy flu virus will causes the next significant loss of human life but we do know that that it will come eventually. China is a place where the mixing occurs. Influenza continues to evolve and is very complex, in China new flu strains circulate and evolve in live poultry markets. What is the solution; close the markets? He said Ebola, Nipa, and MERS, viruses also spill over from natural reservoir to humans. MERS is especially troublesome; coronavirus recombination is common. Will MERS become like flu? It is a constant struggle to control the effects of virus evolution and adaption into new hosts. Looking at how viruses adapt to new hosts is a key area where we can cooperate. We can exchange methods for studying adaptation and work with the international community. He has advocated for younger people to address emerging communicable disease especially in Africa and noted that China CDC is thinking and

working more internationally and providing aid and financial support to efforts in other countries. He helped establish the Sierra Leone China Friendship Biological Safety Association. Gao also discussed the disease surveillance context of the announced Chinese government Belt and Road Initiative, the Chinese effort to create an economic zone through the historic Silk Road region of central Asia.

Gao stated that the U.S. and China should have a real discussion on how to work together to consider the risks from gain of function and loss of function research, it is not in either of our countries interest to create disastrous viruses. Going forward, to maintain and increase public trust transparency by scientists is critical.

An audience member working on MERS said he found a very high viral presence in camels in Pakistan and also found evidence of the virus in humans, but did not see clinical cases. He asked Gao why this might be the case? Gao was not sure; he suggested maybe virus mutation? He proposed that maybe the virus population in Pakistan has low pathogenicity? An American participant said that he did not see the Ebola outbreak virus become more virulent during the 2014 outbreak. Gao stated that they have no evidence one way or the other but are still doing sequencing. An audience member asked if Gao was trying to say that bats carry a MERS-like virus and what might be the real host of MERS, bats or camels? Another also asked if we are likely to see an influenza like MERS virus in the future? Gao said that camels are just intermediate hosts and that he thinks that MERS may evolve to be more flu-like in the future.

Jiahai Lu (Professor, Zhongshan School of Medicine, Sun Yat-Sen University) spoke about China's use of the One Health strategy to respond to emerging infectious diseases (EIDs). Lu described One Health as a strategy that considers all related contact between humans and animals to combat and possibly predict EIDs. He explained that One Health is a particularly appropriate strategy in Guangdong province. Guangdong is vulnerable to EIDs due to its location, culture and high population. Because of the emphasis on freshness in Cantonese food, animals are kept alive until just before they are consumed. This makes Guangdong province, and especially the live animal markets a hotbed of vector borne zoonotic disease outbreaks. Many are actively working to implement One Health in Guangdong. The first SARS outbreak was in Guangdong. Infected bats came into contact with civet cats and then the virus evolved and jumped to humans. Another reemerging infectious disease of concern in the region is brucellosis, associated with imported sheep. Lu also detailed the five waves of H7N9 outbreak in China. 95% of human cases followed exposure to live poultry. He noted a recent novel mutation (in March 2017) that showed a new high pathogenicity avian flu. China has examined the impact of closing the live poultry markets to curb future outbreaks but noted the negative impact on the local economy. He cited an article that details China's response to EIDs and the need for a One Health approach in future responses. An audience member agreed that people in Guangdong eat "everything" which poses a unique disease control problem.

Zhengli Shi (Principal Investigator, Wuhan Institute of Virology, CAS) spoke about the

evolution and pathogenesis of bat SARS like coronavirus (SL CoV). Shi is working on corona virus and other emerging infections and said that bat SL CoV could be the next pandemic. He described the cases and countries involved in the 2003 SARs outbreak. For bat corona virus to cause the next SL CoV outbreak many factors will have to be involved. His research looks at the pathogenesis of SL CoV in transgenic mice. It replicates very well in mice and human tissue. The virus can easily enter human cells but in the animal model the virus has less pathogenesis; this is good news. His research shows that some bat SL CoVs have potential interspecies transmission to other animals and humans. An audience member asked if one could clear an infected bat of this virus? Zhengli said that he tried this with Nipah virus in bats and bats could produce antibodies, clear within seven days. In nature we found that bats produce antibodies to some viruses but not all. SL CoV can exist in bats for several months. An audience member said that you cannot be sure that this pathogen will cause human disease and that more data are needed. Right now infections are very mild and there is no clinical syndrome. Further studies are needed.

Mifang Liang (Principal Investigator, National Institute for Viral Disease Control and Prevention) discussed the epidemiological characteristics of severe fever with thrombocytopenia syndrome (SFTS) in China from first discovery to current knowledge. SFTS in china recently emerged; it was discovered in 2009 and 2010.

She said that it has been very hard to find the virus in nature. It was only recently added to the International Committee on Taxonomy of Viruses (ICTV) catalog. In the catalogue it is described as a highly pathogenic phlebovirus in the family bunyaviridae. It is now listed by the World Health Organization as a special pathogen of concern. She recently mapped the genome structure of the virusThe number of cases are increasing every year but the case fatality rate is decreasing every year. Most patients are from the Chinese countryside, about 86% are farmers. Over 10,000 cases in 25 provinces were reported since the first discovery of SFTS virus. Peak time for exposure and infection is May to Aug due to weather.

An audience member asked how do people become infected? Mifang said that is unknown, so far only local endemic investigations and we have isolated virus from ticks. It has been determined that it is transmitted by ticks and person to person. Ticks may act as a major vector for SFTSV transmission and domestic animals are widely infected by SFTSV, but reservoirs or hosts are not known. Person to person transmission of SFTSV has occurred through direct contact with patient blood containing high virus load. They have not done studies to understand how humans have become infected. She did note that most patients do

not have tick bites or exposure recently to slaughtered animals. In the future they plan to do experiments to determine how humans get the virus.

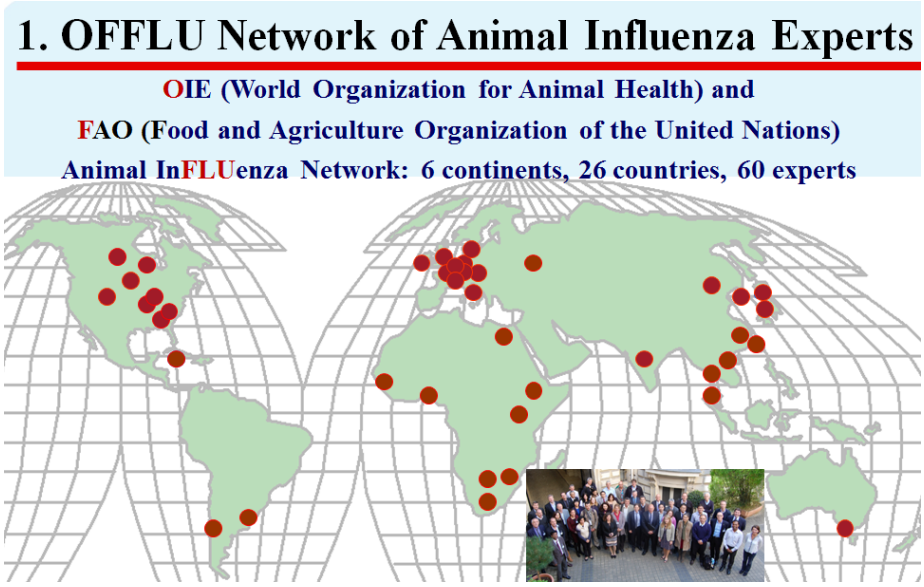
Linda Saif (Professor, The Ohio State University) talked about animal coronaviruses as a global threat to humans and animals. Coronaviruses (CoV) continue to evolve and emerge globally as a cause of fatal respiratory and enteric infections of young animals and humans. Saif's talk covered SARS and MERS coronaviruses. She explained the basic morphology of the virus and the diversity of avian and mammalian CoVs. Coronaviruses are genetically diverse due to frequent mutation and recombination. The viruses can be transmitted among wild ruminants and to domestic ruminants or vice versa. She cited two historical examples for the predicted transmission of bovine CoV to humans and described how bovine CoVs, MERS CoV and SARS CoV infect their hosts and whether camels are the host or intermediate reservoir for MERS infection of humans. She provided data documenting that humans on statins (for hypercholesterolemia) are more susceptible to Norovirus as an example of how co-morbidities or drugs to treat them could affect the high susceptibility of the elderly to MERS and SARS. Because SARS CoVs are documented in bat reservoir hosts, she expressed a concern that SARS could reemerge from an animal reservoir and cause another pandemic. It is also important to determine how MERS CoV is transmitted (camel to human or human to human) so that the scientific community can better target the virus, design preventive measures and prevent such a pandemic. Right now the strategy is to manage and reduce contact with infected camels or camel products, but there are many unresolved questions. The epidemiology of MERS CoV infections in camels and its zoonotic transmission is poorly understood, but it resembles respiratory coronavirus infections in cattle. To date no vaccines have been licensed for any respiratory CoV infection.

An audience member asked about the closest relative to MERS? Saif stated it is bat and camel genogroup C betacoronaviruses. An audience member said that they were trying to determine if all coronaviruses originated from bats. What is the origin of swine porcine epidemic diarrhea (PEDV) coronavirus? Saif said we don't know, but added that PEDV died out after its initial discovery in Europe in the late 1970's, until it re-emerged there recently. One theory is that it was originally not completely swine adapted. A Chinese participant suggested that if SARS is gone why should the government keep doing SARS research? What is your suggestion on how to prepare for another attack of SARS? Saif said that labs should keep all reagents available and continue to research CoV vaccines and antivirals as the bat reservoir is still there. We still may see isolated spillover events, but only when the virus acquires the ability to transmit efficiently from human to human and persist will it result in further pandemics and high morbidity and mortality as was the initial case for SARS and continues for MERS. It is important to stay vigilant. An audience member asked about farmed civet cats relationship to spread? Saif said there was genetic evidence of SARS interspecies transmission between civet cats and humans and that this is another argument for closing live animal markets; when the Chinese government got rid of civets in live animal markets, this appeared to aid in stopping SARS transmission and the epidemic in China. An audience member supported this statement and said that Chinese data supports transmission between bats and civets in a market environment but studies indicate that there is no SARS CoV in wild civets.

Chengfeng Qin (Professor, the Academy of Military Medical Sciences) described existing weapons against the emerging Zika virus. Chengfeng discussed the original discovery and spread of Zika from Africa to more recent regional epidemics and detailed isolating the

Chinese Zika virus strain. He published a paper in January 2016 about Zika in China and is working with Pei-yong and George Gao to do further work on the virus. He noted that there is currently no case of Zika infection reported in mainland China but there are examples of several imported cases. He is looking for further collaboration and communication on Zika with American researchers. Audience members noted that much of the population of Brazil might have Dengue already and asked about the relationship between Dengue and Zika. Chengfeng suggested that the answer is related to how the antibodies interact.

David Swayne (Director, USDA Southeast Poultry Research Laboratory) discussed avian influenza at the animal-human interface and global challenges for scientific contributions to control. Swayne works to combat animal flu issues and also implements the One Health concept to prevent animal health issues from becoming human health problems. He introduced the World Organization for Animal Health and Food and Agriculture Organization for the United Nations (OIE/FAO) Network of Expertise on Animal Influenza (OFFLU) and discussed the importance of combating the influenza virus at the animal-human interface. He then discussed the 42 specific highly pathogenic avian influenza (HPAI) epidemic cases. He said that animal flu continues to be a threat to humans, with 453 recorded deaths since 2003 for H5N1 bird flu. He reported a significant number of H3N2 infections at agricultural fairs in the United States and 534 H7N9 HPAI deaths in China since 2013. He explained that we know little about what virus may cause the next pandemic. OFFLU works with WHO and OIE to track outbreaks and prepare for epidemics and pandemics; the group helps WHO identify appropriate prepandemic vaccine candidates by providing genetic and antigenic data, and epidemiological information on circulating animal flu strains.



Swayne described several avian influenza poultry vaccines strategies and the many different seed strains licensed around the world. A major function of the OFFLU is to help collect and analyze influenza virus data to assist countries and companies in the decision process on what to produce and when.

An audience member asked about reasons for changes to the strains over time and if he attributed changes to vaccination or natural drift over time? Swayne did not have a single

explanation for the changes as the drifting of field viruses is different for HPAI verses low pathogenic avian influenza (LPAI) viruses, but noted that we see different types of changes in countries that are doing vaccinations compared to countries with endemic infection with LPAI viruses. Before large poultry vaccination programs, changes in the hemagglutinin antigenic sites were random, now they are driven at specific sites on the surface of the hemagglutinin protein.

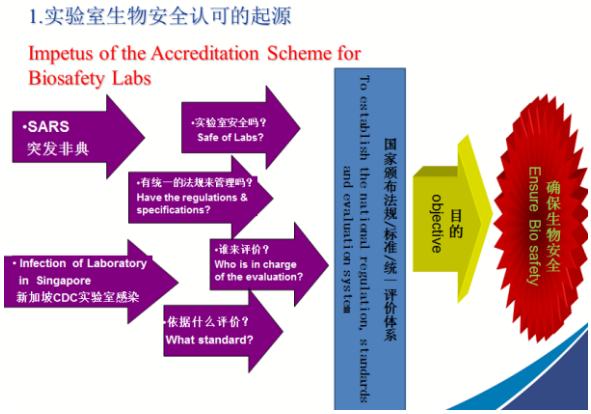
Gong Cheng (Professor, Qinghua University) presented his research on non-structural protein 1 a key for flavivirus transfer from host to vector. The discussion centered around flavivirus, particularly Dengue and the Dengue virus transmission process and the prevalence of Zika infected mosquitoes via a "mosquito-host-mosquito" transmission cycle. He is studying transmission of Dengue from human to mosquito, and hypothesizes that factors in human blood affect transmission.

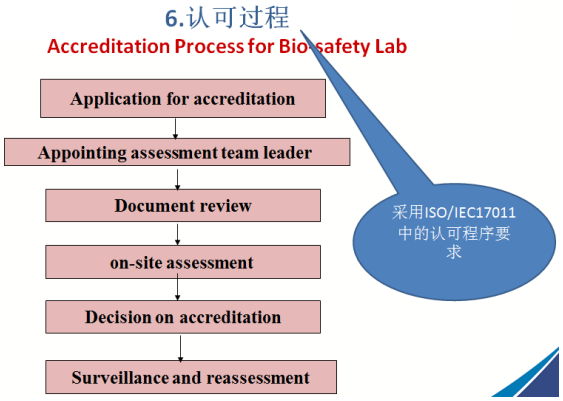
Pei-Yong Shi (Professor, University of Texas) discussed the rapid response to Zika virus emergence including diagnostics and the state of vaccine development. He addressed the devastating clinical outcomes of Zika virus infection: microcephaly. He noted that virus can persist in the male sexual reproductive tract well after clinical symptoms cease and that 80% of individuals are asymptomatic throughout disease. There are two way to diagnose Zika now: detect virus or detect antibodies. He added that there are two Zika vaccines in phase 1 trials and discussed platforms to manufacture inactivated Zika vaccine and experiments to test vaccines. One of the live-attenuated vaccines has been proven to protect monkeys from Zika infection but more work is needed.

Session 4: High-level biosafety Laboratory: construction, commissioning, and sustainment was chaired by **Zhiming Yuan** (Principal Investigator, Wuhan Institute of Virology, CAS). Presenters discussed some of the BSL-4 high containment labs in China and the United States, the importance of community relations and public communication between the laboratories and the surrounding community, the importance of clinical facilities in biocontainment labs, special maintenance and operational issues associated with BSL-4 labs, the role of BSL-4 labs in outbreak response and the importance of maintaining reference collections and reagents.

Peijun Zhai (Division Director, China National Accreditation Service for Conformity Assessment) discussed the process of accrediting biological safety labs in China. He first detailed China National Accreditation Service (CNAS) the authorized accreditation body in China. CNAS has more than 1000 members and 4000 technical experts on call with 260 technical staff, it is the largest national laboratory accreditation body in the world. The SARs outbreak provided the impetus for biosafety lab accreditation in China. He listed the laws and regulations and standards related to biosafety and for biosafety labs in China and described the accreditation process CNAS runs for biosafety labs. Accreditation schemes for labs for biosafety and laboratories start with the Chinese code for laboratories – General Requirements for Biosafety GB 19489. The objective is to ensure biosafety of all labs. Currently 71 biosafety labs of various types are accredited by CNAS in China. Article 20 of

national accreditation says that labs at the BSL-3 and BSL-4 levels require national accreditation in China. He also discussed the difference between certification and accreditation in China.





An audience member asked whether unannounced inspections take place during the five-year period after initial laboratory accreditation. Peijun said that during the interval from assessment to reassessment CNAS does surveillance at the facility on a regular basis. Usually, the first inspection takes place after 1-1.5 years and then approximately every six months.

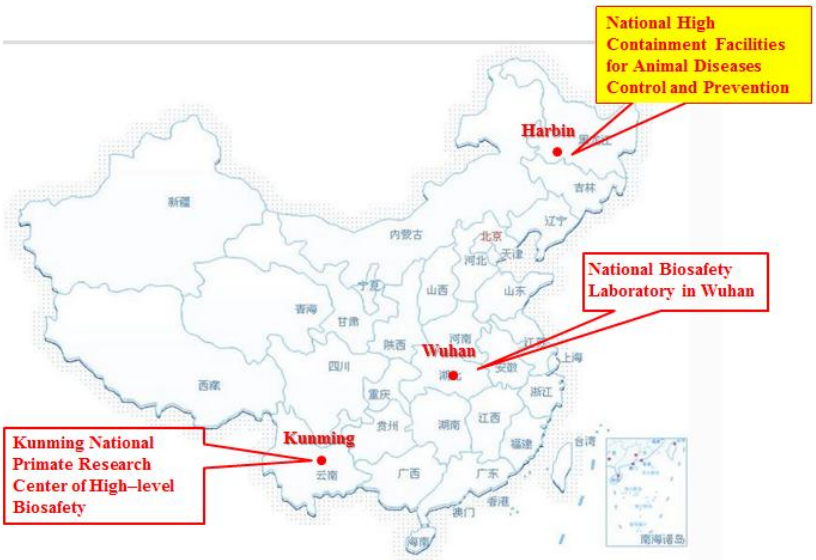
Thomas Ksiazek (Professor, Galveston National Laboratory) talked about biocontainment operations and maintenance and UTMB GNL and training personnel to work at other containment facilities. Ksiazek discussed BSL-4 biocontainment operation and maintenance at the GNL, noting that a lot goes on behind the scenes. The cornerstone is compliance with the current version of the CDC Biosafety in Microbiological and Biomedical Laboratories (BMBL) guidelines, the select agent law adds additional requirements and yearly inspections in order to maintain certification. Key concerns of BSL-4 lab operations are reoccurring expenses, like security costs, utility payment and training. GNL is unique in the United States in that it is operated by a university (the Boston University National Emerging Infectious Diseases Laboratory is not operating yet).

Ksiazek described the unique safety, maintenance and information technology operations at the lab. GNL works with operators and researchers from many other countries, it had maintained a worldwide biosafety training center, but funds for the center have recently dried up and directors are working on options to sustain the program. Still have some interaction with Chinese institutes like NIV.

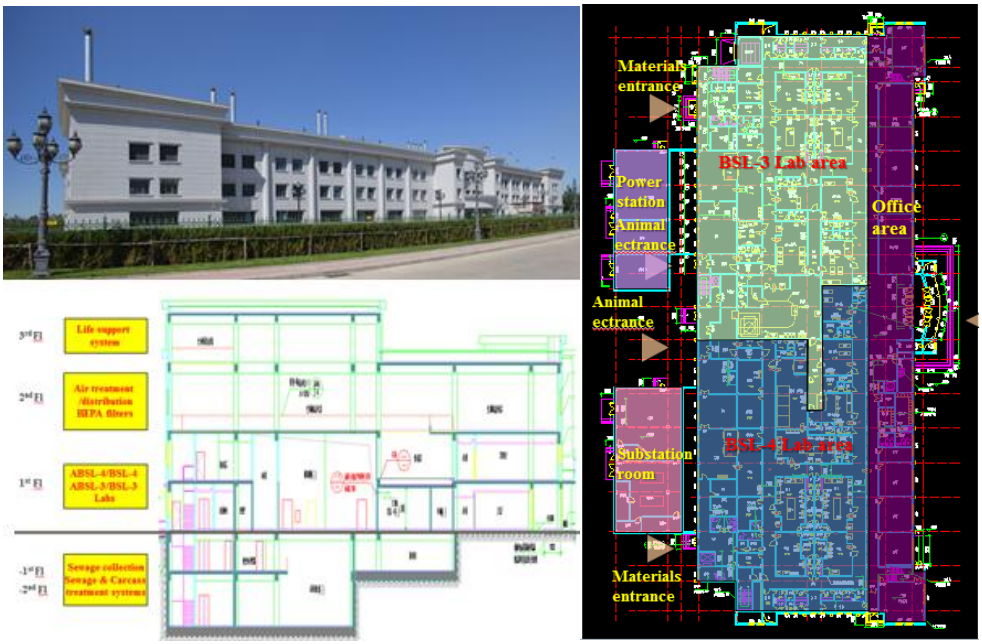
An audience member ask how long before a person can operate in the high containment space unsupervised? Ksiazek said it takes about 100 hours of mentored training per person but it depends a lot on the individual in getting to the mentored training tier of the overall BSL-4 training regimen. An audience member asked how countries with limited resources, like in Africa, should undertake diagnostic lab response to support outbreak control. Ksiazek said don't establish a BSL-4 in that kind of environment but rather set up a field laboratory in which personal protective equipment (PPE) is used to protect the individuals handling the clinical materials from patients, who are being cared for in the same environment. An audience member asked about GNLs precautions against flooding and severe weather and their waste management procedures and record back up. Ksiazek said that Hurricane Ike did inundate Galveston Island in 2008 but that the GNL building was not affected; GNL had power and actually acted as a life boat for the remainder of campus. Waste stream is done as

standard disposal for these facilities. Also GNL incinerates solid waste and everything coming from the laboratory is autoclaved prior to going to the incinerator. When asked about potential for losing the viruses stored in the lab, the GNL serves as a reference center with emergency backup power and the viruses in the reference center collection are lyophilized and he said he is reasonably sure that the viruses would survive a problem. In conclusion he said that some labs are in rural areas some are in population centers. High containment facilities have shown that they can operate safely in populated areas.

Zhigao Bu (Director General/Principal Investigator, Harbin Veterinary Research Institute, the Chinese Academy of Agricultural Sciences) discussed the design, construction and operation of Chinese National High Containment Facilities for Animal Diseases Control and Prevention (NHCFADCP) at the Harbin Veterinary Research Institute. Zhigao said that his institute, the Harbin Veterinary Research Institute is the most active institute for animal disease control in China. It is important to have such a facility because China has a significant percentage of the worlds livestock (fifty percent [800m] of the worlds pigs for example), and numerous agricultural health challenges due to its diverse and large population. He described SARs as a huge shock to the agricultural sector. After the SARS outbreak in 2004 China launched a plan to build three ABSL/BSL-4 facilities; in Harbin, Kunming and Wuhan. The Harbin lab was designated to focus on animal disease control and prevention.



He said that when they started, they had no idea how to construct BSL-4 lab buildings and facilities so formed lots of partnerships. They worked closely with labs in Australia, Japan and Canada, the USDA National Animal Disease Center and Kansas State University in the U.S., labs in Hamburg and Reims in Germany and the Jean Mérieux BSL-4 Laboratory in Lyon, France. He showed pictures of the construction of the NHCFADCP.



Construction of the Harbin lab was completed in 2016. The lab is composed of 5 floors with two below ground. The Lab has nine working areas for BSL-4 and 10 for BSL-3. He discussed security measures for the facility, including access and monitoring of personal. They hope to have CNAS certification by the end of this year.

An audience member asked which pathogens they anticipate studying at in the BSL-4 portion of the lab? Zhigao said that is currently difficult to answer, interested in many pathogens, but need to get approved for each by Ministry of Health and Family Planning and it can be difficult to get approved. They work with many pathogens at the BSL-3 portion of the lab already; Brucella, flavivirus, SARs, and avian influenza. An audience member pointed out that Zhigao's photos showed workers using two types of suites in the lab. He said that the blue suits are made in China and the white ones are made in France. He stated that there is a big difference in the price between the domestic and foreign manufactured suits. Chinese suits are not yet certified for use in BSL-4 space.

Longding Liu (Institute of Medical Biology Chinese Academy of Medical Sciences) [represented Dr. Yunzhang Hu, the Principal Investigator and the head of the BSL-4 lab at the Kunming Institute of Medical Biology who was unable to attend the meeting.] Longding spoke about the Kunming Institute of Medical Biology National Primate Research Center of High-level Biosafety. Like the NHCFADCP he said that the lab was created after SARS in 2004 to focus on basic research to combat animal and human disease.

The facility was originally designed as a production facility for vaccines. He said at first they did not have any idea on how to create a BSL-4 lab but worked closely with other countries and institutes to complete the construction. The lab cost 300m CNY and includes almost 3000 sqm of BSL-4 workspace. The campus includes a monkey breeding facility built 15km from Kunming city. Longding described the security for the facility, and showed photos of BSL-2, BSL-3, and BSL-4 suites. In the 3 and 4 rooms they use secondary negative pressure cabinets for housing monkeys. Like Harbin and at other BSL-4 facilities they have an extensive staff for maintenance and engineering support, air handling and cleaning.

ABSL/BSL-4 Labs

He said that the new BSL-4 lab and existing vaccine R&D platform will make the campus a more efficient producer of vaccines for infectious disease control.

An audience member asked about his thought on collaboration? He said that the facility doesn’t have any experiments ongoing in BSL-3 right now but that they are seeking collaboration to facilitate work in the BSL-3 and BSL-4 spaces.

Session 5: Biosafety, biosecurity and bioethics chair **David R. Franz** (Former Commander, US Army Medical Research Institute of Infectious Diseases) introduced the session on new technology for laboratory biological risk management, improving response to incidents at the lab, improving biosafety and biosecurity training, laboratory leadership, and culture and ethics.

Zhiming Yuan (Principal Investigator, Wuhan Institute of Virology, CAS) described the Wuhan Institute of Virology BSL-4 laboratory. He noted that some of the participants would visit the facility the following day. He said that he hoped to have a license soon so the lab could begin research in the BSL-4 areas. He stated that they had learned a lot from SARS and naturally occurring disease outbreaks but China still has a weak understanding of intentional misuse and how to deal with the dual use dilemma. Scientists have different motivation for doing research. Most scientists around the world who do gain-of-function research have good reasons to do the research but their needs to be a risk benefit balance. He asked how to make this balance and suggested several questions that might be asked when considering the benefit and risk of certain experiments. Law and regulation cannot answer all these questions. We must first consider biosafety in the laboratory. China has a biosafety legislation framework which includes regulation measures and codes related to all aspects of biosafety. But not everything can be easily regulated, like whether to do certain new experiments. He listed existing laws and ethical codes that could guide biomedical research and bioethics and discussed how laws and ethics overlap in biology and areas of bio ethics related to medical experiments on people. Zhiming further noted that CAS has its own bio ethics committee. He suggested that we combine biosafety, biosecurity, and bioethics as a way to address the spectrum of bio risk more broadly. He said that the life science community needs to establish science code of conduct and promote joint work on ethics, and create a culture and philosophy of ethics.

A Chinese participant said that some institutes already teach biosafety courses and therefore, some students already have a strong ethical understanding. They know the dangers inherent in the pathogens that are contained in the BSL-3 and 4 labs. An audience member suggested that biosafety and biosecurity are different and asked which is most important for China today? Zhiming said that they are equally important and should be giving significant attention.

Thomas Ksiazek (Professor, Galveston National Laboratory) discussed regulatory issues affecting the operation of a functional high containment lab including obtaining, shipping, maintaining and exchanging high hazard pathogens. Ksiazek focused on biosafety and biosecurity and the regulatory environment in the United States; he said that the U.S. was the first country that had a national standard for biosafety. The impetus for this began at the Asilomar conference in 1975. In 1984 the U.S. CDC produced the first Biosafety in Microbiological and Biomedical Laboratories (BMBL) handbook that categorized pathogens into risk groups; they are now working on the 6th addition of the BMBL. It sets the operating principles for biocontainment labs. When asked he often says that he “doesn’t do safety for a living but does safety to keep on living.” However he said that there is not enough focus on how safety regulations effect the science that the labs are designed to do. In the United States, the regulations that have been put in place since the 9/11 terrorist attack are mostly about

security, not safety. One of his key concerns is shipping samples; in the U.S. it was simple until about 5 years ago. Shipping of pathogen isolates is becoming prohibitively expensive. Now World Courier is the only group left that routinely ships select and BSL-4 agents in the U.S. He is seeking to get the United States Government to pressure the FedEx company to start shipping again. Another problem is that aircraft captains have the right to refuse dangerous goods shipments; the pilot has the final word on what goes on the plane. This has prevented shipping samples out of outbreak areas in the past. For example it was really difficult during the 2014 Ebola epidemic to get samples from West Africa; the U.S. chartered a jet to get Ebola isolates back to U.S. and the British Government utilized a ship. It has also become difficult to get necessary permits (through the U.S. department of Agriculture and the U.S. Public Health Service) to allow the efficient operation of a reference facility in the U.S. In addition we have to deal with regulators who have responsibility for laboratory certification and necessary permits; they usually have no practical experience working with high containment pathogens. Intellectual property issues are also becoming increasingly difficult; institutional lawyers are delaying exchange of viruses and reagents and not abiding by older principles of scientific cooperation between investigators doing non-commercial research. Collectively we can make a difference; scientists need to address the trend of over securitization. A Chinese audience member said that in China internal movement of samples between CCDC and CAS is really difficult as well with lots of bureaucratic hurdles. China only uses one group for international shipping.

David R. Franz (Former Commander, U.S. Army Medical Research Institute of Infectious Diseases) spoke about laboratory leadership, responsibility and progress. He said that his goal as an institutional leader was to create a functional ethical organizational cultural so the institution could do good work. In the laboratory environment the key is to balance regulation with progress. He stated that biosafety is much easier than biosecurity, because it is difficult to define the risk or to measure success in biosecurity. The NAS "Fink committee" report *Biotechnology Research in an Age of Terrorism* that discussed dual use research was ahead of its time. The committee ultimately concluded that education and awareness are key to addressing the threat. Following that study, the U.S. Government put together the National Science Advisory Board for Biosecurity (NSABB) to address dual use research. Franz discussed the evolution of biosecurity thinking in the U.S. noting only one accidental death—and not from a true select agent— is associated with the U.S. Select Agent program (and three deaths before 1969 when the U.S. offensive biological program was halted). He compared that to the more than 700,000 hospital acquired infections and 400,000 deaths due to medical mistakes in recent years.

He pointed out that leaders and scientists in the high-containment lab community must understand that the actions by a few affect the many. A negative incident in one laboratory can impact the ability of many laboratories to function. An audience member asked how best to balance security with transparency and how to build trust when accidents happen all the time? What about deep rooted mistrust due to social structure? What is your strategy to build trust with the Chinese and with other countries? Franz said it is important to create "nodes of trust" globally between individuals. Building networks and nodes is the model we use at NAS, the strategy is called "Track II diplomacy," (with Track I being formal government meetings between officials) interaction and meetings between nongovernmental technical experts in the U.S. and in other countries. He noted that we can do the same thing within any country by

reaching out to others and forming personal connections to share advice and best practices in areas of mutual concern and interest, but there is no perfect solution to eliminating biosafety and, particularly, biosecurity incidents, we can only minimize the risk. A Chinese participant agreed that more enlightened leadership is key for safety and without sacrificing productivity and there is a need to build trust between people, directors and workers at these facilities. But, he asked, for BSL-4 labs, how could we collaborate together to be more productive? The participant suggested that collaboration occur between the three new labs in China.

Zhiming Yuan (Principal Investigator, Wuhan Institute of Virology, CAS) and **David R. Franz** (Former Commander, US Army Medical Research Institute of Infectious Diseases) presented conclusions from the meeting and led a discussion on possible roles of CAS and NAS to enhance cooperation between the U.S. and China on emerging infections, laboratory safety and global health security and other topics discussed at the meeting.

Franz presented summary thoughts from the meeting to the group. He first identified some key topics that came up during the presentations and discussions:

- Role of scientists in balancing regulation, safety, security and productivity
- Popularizing Science (helping the non-science community understand science)
- Emerging infections (reservoirs, natural populations and sequence data)
- The importance of transparency within and between countries
- The importance of trust within and between organizations and nations
- The One Health (animal health, the economy, human health) concept
- Responsibility of the science community to self-police and in some cases, regulate

He also presented some possible joint project ideas which had arisen during the meeting:

- Direct cooperation between CAS and NAS like formal institutional partnering and scientific collaboration
- Joint “Table Top Exercise” detailing hypothetical response to an outbreak
- Outbreak and incident response training
- How to make decisions regarding “Dangerous Research” on certain pathogens and gain of function research in general
- A joint manuscript of shared values and concerns
- Overcoming barriers to sharing strain collections and transport of pathogens
- Exchange and training of students

The audience suggested other issues including exchanging reference strains as many strains in China are interesting to researchers in other parts of the world. NAS and CAS representatives could jointly write a paper addressing how best to facilitate strain exchange. Others said that would be very useful but we must follow international guidelines like the Nagoya Protocol on Access to Genetic Resources. Also domestic property rights become an issue; if an outbreak occurs in a third country and we isolate virus, the virus belongs to country where sample is from. This makes exchange difficult.

Zhiming offered several additional suggestions:

- Create an official agreement between BSL-4 operating institutions to promote institutional collaboration.
- Chinese and American groups could work together to encourage scientists to create a culture of trust, safety and bioethics. NAS and CAS should provide a platform for cooperation.
- The U.S. could do more scientists training and train the trainer training for Chinese institution staff and students.
- Support efforts to improve the free movement of sample material.
- NAS and CAS could write a joint report and from that we can extract important information to provide to CAS and NAS leadership.
- CAS can form a core group for NAS to talk to about future activities. NAS will work with CAS to bring scientist to the U.S. to continue the discussion.

In discussions after the meeting the chairs decided on the following list of near term action items as priorities:

- Scientist exchange and training, particular for BSL-4 laboratories.
- Identifying joint BSL-4 research projects that are beneficial for both the U.S. and China.
- A memorandum between UTMB GNL and the Wuhan Institute of Virology (and also the other two Chinese BSL-4 laboratories) for both long-term and short-term collaboration and partnership.
- Hold further face-to-face meetings in the United States at the Galveston National Laboratory. Topics for the workshop will likely center around specific high biocontainment “operational” issues such as:
    - An overall strategy and creating centers for effective high containment laboratory staff training.
    - Creating and maintaining clinical care facilities in BSL-4 space and training clinical staff.
    - Conducting “well-documented” studies under BSL-4 conditions. including practical aspects of non-human primate experimentation in the BSL-4 space.
    - Development and maintenance of best practices for long-term safe and productive BSL-4 operations.
    - Community relations and outreach efforts and the differences and similarities between interacting with the communities surrounding laboratories in China and the U.S.
    - Conducting vector studies to identify animal virus reservoirs and combat emerging infections caused by viral agents requiring high-containment facilities.

Longer terms priorities:

- Enhancing our ability to share strain collections.
- Joint white paper that each side could use to educate political leaders and others.

- Promote international collaboration via China-US joint projects.
- Joint training programs between labs.
- Joint manuscript between individuals and institutions.
- Support improving biosafety and biosecurity at labs and trust building between scientists.