DEPARTMENT OF DEFENSE BLOGGERS ROUNDTABLE WITH LISA HENSLEY, CHIEF OF VIRAL THERAPEUTICS, VIROLOGY DIVISION, U.S. ARMY INSTITUTE OF INFECTIOUS DISEASES (VIA TELECONFERENCE FROM FORT DETRICK, MARYLAND) SUBJECT: U.S. ARMY RESEARCH IN INFECTIOUS DISEASES TIME: 3:01 P.M. EST DATE: MONDAY, DECEMBER 15, 2008

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LINDY KYZER (Army Public Affairs): Good afternoon, everyone. Thank you so much for joining us for today's Bloggers Roundtable. We're very pleased to have with us Dr. Lisa Hensley. She's the chief of viral therapeutics, Virology Division, U.S. Army Research Institute of Infectious Diseases, Fort Detrick, Maryland.

She has some compelling research to discuss with you today, as well as what it was like to be named one of the most "Outstanding Young People" in the world for 2008. So, after a few minutes of opening remarks from Dr. Hensley, I'll go ahead and turn it over to you all for your questions.

Thank you so much, Lisa, for joining us today. MS. HENSLEY: Okay, thank you. I didn't know I was making opening remarks --

MS. KYZER: Oh.

MS. HENSLEY: -- so I will be shooting from the hip today. As you guys heard from my introduction, I am the chief of viral therapeutics for USAMRID. I've been here for about a decade now. I actually came up in 1997 after graduating from UNC, spending a year at NIH, and then I transitioned to Fort Detrick. And I came up here to really start to look at how viruses cross species, and to look at new and emerging threats.

And I did a post-doc here with Peter Jahrling and Tom Geisbert, and started off looking at Ebola virus and trying to figure out how Ebola causes the disease that it does, and was able to work with them to identify some of the first therapeutics. And then I decided to stay on afterwards, so I must have liked it after 10 years because I'm still here.

And since that time, my work has expanded a little bit. So, not only do we do Ebola virus, we also do work with Marburg virus. We're also working with other viral hemorrhagic fevers, and we're trying to understand how the whole spectrum of viral hemorrhagic fevers are produced, with the idea being if we can understand how the syndrome -- which is caused by multiple viruses, is produced, and if we can find common pathways, perhaps we can find common targets.

And we've also expanded, in addition to therapeutics, to testing vaccines. And then we also do what we call "Virus of the Month," or, actually, just emerging threats. So whenever there's a new and emerging virus that is of relevance to the Army or that the Army thinks could be a potential threat, we are asked to respond to that.

And so one of the more recent examples of that would have been SARS, and so we spent about six months dropping all of our research and taking on SARS. And we were able to develop some of the first sustainable models; as well as team up with my old adviser from UNC, and do the first infectious prong; and then also identify some of the first-candidate therapeutics.

So, that's kind of a little bit about me, and how I got here. And I guess I'll just open it up for discussions, unless -- (inaudible) -- a little bit more background.

MS. KYZER: Great. Thank you so much.

We'll go ahead and go down the list of questions.

Chuck, did you have a question?

Q Oh, yes. I have a lot of questions. MS. KYZER: (Laughs.)

Q Good afternoon, Doctor, my name is Chuck Simmons and I write for America's North Shore Journal.

MS. HENSLEY: Okay.

Q I extensively covered SARS when it was in the public view, and I have a couple of questions with relation to SARS. The first being the numbers that the Mainland Chinese were reporting, of cases -- of fatal cases, were dramatically out of whack, compared to the numbers reported in other nations that had major SARS outbreaks.

I felt that perhaps the original decision by the national government to conceal the epidemic was continuing in their alteration of their statistics. Would that be a possible, fair representation of the numbers that came out of Mainland China?

MS. HENSLEY: You know, I don't think that that's something that I can accurately address, mainly because I wasn't there. I wasn't engaged in those research aspects. And I think that there's a lot of possible scenarios that have been thrown out, including accuracy of the diagnosis; ability to respond; health care; strain differences. So, I don't think it's really fair for me to comment on that.

Q Okay. Then my second question is, what happened to SARS? It vanished, essentially, as quickly as it appeared.

MS. HENSLEY: Yes.

Q Are there any -- are there still cases of SARS, or, you know, what happened to it?

MS. HENSLEY: We're actually very fortunate with SARS. As you mentioned, it exploded onto the scene and then quickly disappeared. So, no,

there haven't been any identified cases in a number of years now. This is not so atypical.

So, most of your infections come about through viruses that jump across the species barrier. And what you tend to see are sometimes these very small outbreaks, and we see that with other emerging infections. And the outbreak will often burn itself out, either because there is not enough people who could become infected -- so in order for the virus to spread, each infected person would have to infect at least one person to keep it at the status quo, or to be maintained, and to infect few people for the epidemic to grow.

And so either the epidemics burn out because there are population densities so low that it can't be effectively transmitted, or the virus doesn't efficiently transmit; or they institute control measures to control the infection. And so what we have with SARS is something where there is a tremendous public health effort -- I mean, global public health effort where they did a tremendous job identifying cases and maintaining them, and then what we saw was the epidemic eventually burn itself out. And we've been very fortunate to have not seen it reemerge.

Q But, you don't really have a good explanation for the die- out, per se?

MS. HENSLEY: So, I think, again, it came back to very good control measures. So, that, I think, is what's critically important when we're responding to epidemics, when we are dealing with things like that is that we isolate the cases or we quickly identify people and treat them. And so most people believe that that's why. If you keep a virus from spreading, the virus will eventually die out. And so that is the best explanation, as well -- you know, the great public health efforts that were mounted.

Q So, that the virus that caused SARS, you're not -- it no longer exists.

MS. HENSLEY: It probably does exist.

It probably exists in the original host. And what happens is, with these emerging infections -- and, again, you have to remember that the reason many of these infections are so severe is that we're not the normal host.

And so when the virus jumps from its normal host -- where maybe it doesn't cause a lot of severe disease, or it may lay dormant, or there's a number of different scenarios -- but, when that virus jumps from its normal host, and it crosses into a new host, and in this case it's us, it causes severe disease.

So the virus probably still exists in -- (inaudible) -- Ebola, or Marburg, or any of these other viruses in its natural host, and it'll be -- it won't be until we see that virus jump the species again that we'll see another epidemic or reemergence of the disease.

Q All right, thank you, Doctor.

MS. KYZER: And, Divi (ph), did you have a question?

Q Yes. I'm wondering -- and I'm not sure exactly how to phrase this correctly, but there's been some recent articles about Gulf War Syndrome

being recognized as real, and possibly linked back to some vaccines, and things of that nature.

I'm wondering if any of the research that you're doing includes not just, you know, fighting the initial infection, but the aftereffects, so that it doesn't -- we don't have another -- you know, if we go back and start re-innoculating people for things like smallpox, which should be gone, so that we don't have another Gulf War Syndrome-type situation on our hands?

MS. HENSLEY: Well, you know, I think I understand what you're asking. So, the work that we do -- And you're worried about that we always run this "risk balance" -- and we factor this in when we're thinking about things like vaccines and preventative measures -- is: What is the risk that somebody will actually get infected? What is the risk that they'll come into contact? And, if they do come into contact, what is the risk of -- say, it's a vaccine, that's a very grate example is smallpox vaccine?

And so the type of work that we do, that is related to that, would be mostly in our vaccine efforts. And what happens -- what is the safety of the vaccines that we're proposing? And what is the long-term durability of the vaccine? So, in other words, how long after we gave the vaccine could we expect it to work, and so how frequently would we have to give it?

And so, we are, of course, always cognizant of the risks of any preventative measure, and we do do the work to make sure that they are very safe before suggesting that they move forward.

Q Thank you.

MS. KYZER: Okay. And Sasha (sp), did you have a question?

Q Yes. My name is Sasha Karbak (sp). I'm a German journalist -- science journalist -- and the MIT, their Knight fellow.

So, I would like to ask, but isn't the lesson from SARS that there is -- there might be hundreds or thousands of viruses sleeping in some hosts, and might come up with a pandemic due to contact between animals and humans? And that we -- that there must be better public health mechanisms to treat these pandemics, and not looking for therapeutics for SARS and stuff like that?

MS. HENSLEY: Absolutely. So there's a number of initiatives that probably are of interest to you. There’s a great effort among many of the people in the scientific community to do pathogen discovery. So the idea is can we get ahead of the curve, and can we identify viruses before they become problematic and before they grow into an epidemic?

And there's a lot of very small efforts that are engaged in that, and they're slowly trying to be linked together. So, some of that is very simple, where investigators may be working in a particular part of the world, and they have cases of disease that they rule out everything that they would expect, and they collect those samples and they look for new viruses in their samples.

There's also something called "Global Viral Surveillance Initiative" (sic) -- I think that's what it's called. Nathan Wolfe, I think, runs it. And so they're actually -- they just got, I think, almost $11 million to look at getting ahead of that curve in identifying new viruses.

So that being said, one of the critical aspects of surveillance and being -- (audio break) -- in active disease surveillance, so catching these things before they spread and reaching out to partner countries and countries where maybe the resources are lacking, where maybe you might see these viruses emerging. And WHO has taken a very active stance in trying to reach out; we've been working with them. There's another -- there are a number of other groups that are working with them to help build diagnostics and to help the surveillance program. And so of course that is the way that -- that's one of the best ways to do it, is to get ahead of the curve.

Q And another question. It's over -- could you please tell me a little bit more about these candidates -- (inaudible) -- you invented for SARS and Ebola? What kind of therapeutics are these, or what stage are you in?

MS. HENSLEY: Sure -- (audio break). Okay, sorry. There was a little bit of feedback.

So for SARS, unfortunately, we were asked to discontinue our work efforts once the virus appeared to die out. But we had been doing work with interferons and interferon data, and we'd been able to show --

Because one of the things that you want to do when a new virus pops onto the scene is you want to look for therapies that might already have a known safety profile. Because viruses will continue to emerge, there's no doubt about that.

And so when something like happens, you want to look to say, well, what do you already have that's approved for other indications that you could rapidly put into use? You know it's safe and you know how it should be administered, et cetera. And so we were working with interferons, and we got very good reductions using interferon beta.

For the filoviruses, our therapeutics really are broken up into three categories. And the first category is the idea of reversing clinical disease. And say, well, viral hemorrhagic fevers, whether you're talking Ebola, Marburg, Lassa, (Hunin ?), they're a syndrome.

They are just -- they're different viruses, but they're grouped together by the disease that they cause, or the clinical picture.

What we believe that happens with the VHF is that basically homeostasis is lost. You develop what's called, often termed a cytokine storm, or a severe inflammatory response syndrome.

And essentially your body's attempt to fight off the virus starts to spiral, and you get an overwhelming inflammatory response. You get activation in the coagulation cascades. You eventually get DIC, shock, and multi-organ failure.

And so the idea is if we can help the host re-set that homeostasis, perhaps we can -- a certain percentage of the people, their immune system will be able to fight it off without any help, or any additional help.

And so we've tested two therapeutics -- or, two of the therapeutics that we have tested, I should put -- that's a little bit more accurate. Two of the therapeutics that we've tested have shown some benefit. One was a drug called rNAPc2, and that was an anti-coagulant. And so we were able to go from

zero percent survival in the non-human primates to 33 percent survival. And the drug was both an anti- coagulant and an anti-inflammatory, so again, we were basically shutting off that cytokine storm.

The second drug that we tried, and that drug also works -- we have also used that drug for Marburg virus, and that now has about a 20 percent -- you go from 0 (percent) to 20 percent in your non-human primate models.

The second drug was Xigris, or recombinant human activated protein C. It's the only approved therapy for septic shock currently on the market.

In that one, we went from about zero percent survival to 20 percent survival with 66 percent of the animals showing substantial delays in the mean time to death. We lost a couple of animals towards the end of the experiment -- not from Ebola, but actually from secondary bacterial infections. So we're probably underestimating the true efficacy.

The second category that we've been working on -- and when I say "we" I should say this is USAMRIID as a whole, has been looking at this whole idea of antisense technology.

And so our group's primarily been focused on siRNAs, so -- small interfering RNAs.

And one of the drawbacks for this technology has always been how do you get the siRNA, and how do you --

(Cross talk.)

MS. HENSLEY: -- yeah, how do you protect it, how do you target it to the right cell, and how do you, once you get it in the cells, do you get it out of the endosome before it's destroyed?

And so we teamed up with a company called Protiva, who has a delivery system that they were starting to put into trials. And we've been testing siRNAs, and we can protect 100 percent of guinea pigs with siRNAs, and we're looking at starting the non-human primate study within the first year.

Another group here, Dr. Arapravari's (ph) group, has been working with PMOs and -- polymorpholino oligonucleotides (sic). I hope I got that right -- and they've also -- it's another antisense strategy, and they've also had a tremendous amount of success and are looking at non-human primates as well.

And the third category of therapeutics that we've been looking at, and these aren't really -- we're not at the point of clinical disease, we're still walking them out -- would be therapeutic vaccines. And I would say probably a better term is post-exposure vaccination.

And somebody brought up smallpox earlier. It's very similar to the idea of smallpox or rabies. After exposure, can you come in with a vaccine and will it have any utility?

And for Ebola and -- a uniformly lethal model, so 100 percent lethal, we can give a vaccine within the first 40 minutes or so post- exposure and protect 50 percent of the animals. With Marburg we can protect 100 percent of the animals.

And what we're doing now is we're starting to walk how far out after we've -- after we expose those animals will this vaccine show any benefit. And then the last comment that I should add to this is that long term, if we're talking about a true therapeutic, and by that I mean trying to intervene after a disease has started, we're probably going to most likely be looking at a combination strategy.

We're probably -- everything that we've learned from these viruses is that it's not just the virus, but it's also the host response. So we're probably going to have to go with a direct antiviral or something to bring that viral load down, as well as something to help the host reestablish the homeostasis.

MS. KYZER: Okay. Did we have one more person join us on the line? Is there anyone out there who hasn't asked a question yet?

Q This is Jonas from The Ball Gunner.

MS. HENSLEY: Hi, Jonas. Did you have a question?

Q I sure did. Dr. Hensley, to get back to your earlier point about a -- what is it, an ounce of prevention beats a pound of cure -- how do you deal with -- I guess I don't want to say backward, but severely superstitious areas. There was something in the news a while back about polio vaccines being vaccinated. What's the -- polio vaccines being boycotted for a variety of superstitious reasons.

How do you do outreach in these sorts of areas in really dealing with areas where modern medicine is dealt with a good deal of suspicion?

MS. HENSLEY: This is rather new territory for us, and I just want to make sure that I'm very up front about this.

I think, mainly -- for some of the reasons you highlight, there is a reluctance of the U.S. Army to be out there to be actively engaged in some of these field sites. So this is something new to us.

And so our experience is quite limited, and I'll tell you our experience as well as some of the other approaches that our collaborators are using.

And with us, it's mainly been a lot of patience as well as trying to find a few key members within the community to bring on board to the program. And I think it helps you a tremendous amount when you do community buy-in, that they realize that you're there to help and that you're there -- that there's somebody from their local community that's also there with you and that has an established relationship with them.

And so that's how we've been approaching it, in our limited work that we've been doing. And of course, we're trying to learn from our collaborators. And some of the other people that we've been working with, and some of the other organizations that are much larger, they'll even bring in cultural anthropologists. It is a significant problem.

So, again, patience and, I think, embracing their beliefs and doing the best that you can to assuage any fears that they have is the right path forward.

MS. KYZER: Okay, great. And we'll go back down the line.

Chuck, did you have another question?

Q Yeah, I do. In looking at all of the virus outbreaks in recent times, are the monkey pox in the Midwest, I believe --

MS. HENSLEY: Yeah.

Q Then there was a Marburg outbreak in Angola.

MS. HENSLEY: Mm hmm. (In affirmation.)

Q And then the bird flu situation. One of the things that seems to be very much key in the prevention is the use of universal precautions.

And when I read, for example, the report on the Canadian health care workers that were exposed and died, I was somewhat horrified at some of the mistakes that were made in their techniques.

Would it be almost as cost-effective to teach and provide health care workers in an epidemic with universal precautions?

MS. HENSLEY: I think that that's already ongoing. And so one of the things, when you see MSF go in or WHO or some of these other organizations go in, is the first thing they'll do is bring universal precautions.

Because you're right, universal -- many of these emerging infections, universal precautions are a great way to go, particularly if you can rapidly identify patients and you can then implement those control measures. And, again, this is what really brings many of these epidemics underneath control are standard public health measures, in combination with good diagnostics.

So, what you often see for many of these outbreaks is them bringing in all of the equipment that you need for universal precautions, as well as -- it's not just bringing the equipment in or the supplies in, it's teaching the community and it's teaching that healthcare workers how to appropriately implement the universal precautions. And doing that, of course accidents will happen, but if you do that you will eliminate a large chunk of the spread.

Q Now, just very quickly, the Marburg outbreak in Angola, is that the largest Marburg outbreak to date? MS. HENSLEY: It is.

Q By a factor of 10 at least, right?

MS. HENSLEY: It was a fairly substantial outbreak, yes.

MS. KYZER: Great. And, Divi (ph), did you have another question?

Q Yes, my question centers around the use of biological weapons. You know, let's say somebody, you know, comes in and, you know, uses some kind of a biological weapon on the United States and releases the anthrax or smallpox or one of these other hemorrhagic fever type of virus in one of our cities. How long do you think it would take to get the treatments manufactured and out to the affected areas?

MS. HENSLEY: That's almost an impossible question to answer because it's going to differ for every specific agent, and it's going to depend, again, on whether or not we have something ready. Is there a therapeutic identified, has it been incorporated into the national stockpile, are there sufficient doses, how many locations is it going to have to go to are all going to factor into that. And of course the worst-case scenario is that you have to make a vaccine or that you have to start from a therapeutic de novo, and it can take months, years if there's nothing in the pipeline.

Q But assuming that we have something that's already there, do we keep -- I mean, would we keep an adequate supply for some kind of a mass-casualty incident?

MS. HENSLEY: Absolutely. That is the goal. I mean, that is the goal that I think everybody in the biodefense field is working for, and the idea behind Bioshield, and it's not only to have the therapeutic there but to have the infrastructure or the logistics worked out to rapidly get it deployed. Basically you've got your pod, the materials ready to go, and to be able to rapidly not only get it to the location but rapidly get it to the people who need it.

Q You mentioned Biosheild?

MS. HENSLEY: Uh-huh.

Q What is that?

MS. HENSLEY: Project Bioshield -- I don't know if Carrie wants to jump in here. I don't know; she might have some standard information about Project Bioshield. Carrie, are you there?

CARRIE VANDER LINDEN (USAMRIID Public Affairs officer.): I'm here.

MS. HENSLEY: Do you have something that perhaps it might be easier to just send them?

MS. VANDER LINDEN: I'm sure I do, but it basically is the initiative to -- it's sort of a multi-government agency effort to prepare countermeasures for an event like this and, as Lisa said, not just to have medical products on hand but to have the systems worked out to get materials to where they're needed. So I think while USAMRIID, you know, certainly is one of the agencies doing biodefense research, there are other agencies involved, the Department of Health and Human Services particularly. They have the Civilian Biodefense Mission. And then of course the Department of Homeland Security would sort of be in charge of the incident management. So it's a multi- agency effort. But basically there have been lots of funds devoted to -- under Bioshield there have been lots of additional funds devoted to biodefense research in the past few years.

MS. HENSLEY: Okay, I'd be interested in seeing that. Thank you.

MS. KYZER: Great. And, Sasha (sp), did you have another question?

Q Yes. What’s for you, personally the difference working at a military institution compared to an institution like CDC? And did anything change after the anthrax cases in 2001 or recently -- yeah, in the recent weeks or -- (inaudible)?

MS. HENSLEY: Okay. So, actually I don't think there is a tremendous amount of difference. I've worked down at CDC as well as at USAMRIID, and so all the work that we do with the variola virus that causes smallpox is actually done in Atlanta, so we all pack our bags and go down there.

Believe it or not, there's actually not a tremendous amount if difference. That could be because many of the folks from Special Pathogens actually came out of RID (ph). There are a few differences, though. The only difference that I would really highlight is the public -- I think the way that we're portrayed sometimes and what exactly our missions are, and I think, working at CDC, they have a broader public health mission, so their ability to respond sometimes is a little bit better than ours in terms of whether or not it's in our scope and whether or not we should be responding, and how involved we can get.

In terms of what changed after 2001, a lot. I will be honest with you; a tremendous amount has changed. And it goes across the board. It goes across the board in terms of simple things like security -- coming on and off post, coming in and out the laboratories, in and out of the building. Our security is much greater than it was. Development of personal reliability programs. And there's also, I think, a greater recognition of the problem, and in a lot of ways I think that's been very helpful. I think there was a time -- and I'll give you a personal example here, which is I think a lot of my friends and family didn't get what I did. They thought, oh, okay, she just goes up to work, wears a blue suit. Oh, she just, like, thinks that it's cool, and then post-2001 and -- my family gets it now. They absolutely get it, and they have a whole new perspective for what we do here.

And so there's a greater, I think, community appreciation, and there's also a greater appreciation amongst the workforce here, and I think that there's a really good team effort at USAMRIID. It's not just the scientists, but the support staff and the people who keep the building running. They really believe in the mission that we're here for. And I think the last way -- one of the other changes was of course the money that got pumped in. The money that's gone into biodefense has been a huge boon. It's allowing facilities to expand, it's allowing us to do more research, and that money, that attention has also allowed us to reach out more into the scientific community to have more collaborators, to bring in some of the best and brightest that are out there, either to come work at USAMRIID or to work with us, and there's no doubt that that critical mass has helped us make some of the progress that we have over the last, you know, seven or eight years.

Q Thank you.

MS. KYZER: Great. And, Jonas, did you have another question?

Q Sure. I'm looking at the counterinsurgency manual right now and it has medical treatment among the populace listed under essential services, for obvious reasons. It's kind of hard to conduct a counterinsurgency when there's cholera outbreaks. So are you finding more and more that some of your work is going to be out among populations in forward-deployed areas?

MS. KYZER: I think we are, and I think a good example of that is Lassa fever. Like I said, I've been here since '97 and it's only been in the last few years that people have really gotten interested Lassa fever and that we've actually seen information called -- or data called "Go out for Lassa Fever." I

think, though, because of our limited resources and our limited capabilities, you'll see is continue to focus on the agents and what could only uniquely be done at a high- containment facility, if that makes sense.

Q Sure, but, I mean, is the Army bringing forward any -- I guess more forward-deployed area for infectious diseases, such as -- I mean, I think, like the cholera outbreak in Iraq a while back, it's small and fairly quickly contained. I guess, is that capability being engendered in the Army?

MS. HENSLEY: My understanding is that it is. I only get to focus on the very small aspects, which are the high-consequence pathogens, and certainly from my personal perspective and my personal work efforts, they are much more -- they are aware of that and they are allowing us to focus on that. And in addition, I will say that USAMRIID is our own little microcosm in some ways, but we've also been quite fortunate here that our commander has allowed us to also support things like the development of models for Nipah virus and Hendra virus and other potential things that may be encountered. But I need to make sure that I also state that you're not going to probably see USAMRIID focusing on cholera or something else that would be at a lower level because that's something that a different facility probably could do with their resources that wouldn't take away from our resources. So the short answer is, yes, but at USAMRIID we're only focusing on the high-consequence ones. MS. VANDER LINDEN: Yeah, if I could just jump in here for a minute. This is Carrie from USAMRIID Public Affairs. Our mission really at USAMRIID is research toward countermeasures, medical countermeasures, to defend against biological threat agents. So in some cases -- you know, obviously many of those agents are also infectious diseases that occur elsewhere in the world, but as Lisa mentioned, we focus more on the agents that require special containment by safety level three and level four. So, for example, an agency like Walter Reed Army Institute of Research would be the one that would study things like malaria, hepatitis, Dengue fever, et cetera, if that makes sense. But the ultimate goal, you know, of the research is to have products that could be used to protect the soldiers and the other service members. It's just that in the case of vaccines and drugs, obviously it takes a long time for the advanced development piece to play out to actually have a licensed product that you could use.

Q Okay, thank you very much.

Q Jonas?

Q Mm hmm?

Q Yeah, there's a Navy hospital in Cairo, Egypt that does a lot with emerging diseases in the Middle East, and they worked on the bird flu when it came to Iraq.

MS. HENSLEY: Right.

Q Okay. All right, thank you.

MS. KYZER: Well, great. We're actually at our time limit, but thank you so much, everyone, for joining us, for asking your questions. And thank you, Dr. Lisa Hensley, for your time, and, Carrie, for jumping in and helping us out with a couple of questions.

You can find the transcript and audio file at defenselink.mil\blogger. This concludes today's roundtable. Thanks so much, everyone.

Q Thank you.

MS. HENSLEY: Thank you.

Q Thank you.

END.