

**Animal Health Institute  
Capitol Hill Antibiotics Briefing  
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**Presentation by Dr. Tom Shryock, Elanco Animal Health**

*Thank you very much Ron. It's a pleasure to be here this afternoon and what I'd like to share with you is a little bit more drilled down in terms of risk assessment. In order to frame this up I need to introduce a few terms, so my background at Indiana State I'll be putting my professorial hat on for just two slides here. First of all, risk analyses, the overall, the overarching word that encompasses risk assessment, risk management and risk communication very simplistically, you've heard about risk assessment and I'll you a little bit more, but that asks the question how bad is it. Risk management is what are you gonna do about it and risk communication what are you gonna say about it. Risk communication also involves getting the risk assessors and the risk managers to interact in dialogue, to talk to one another and that is a very important point. That is one of the reasons that we're here today is trying to get risk managers to talk with risk assessors.*

*Scott has done a very good job under the risk assessment. We've already introduced the concepts of release, exposure and consequence, so we don't need to get into that very much further, but I do want to show in a later slide here how this risk assessment can actually be applied in yet another dimension, not only for product labeling aspects, but also in terms of actually guiding risk management and coming up with risk estimates. Why do risk assessment? Where did this whole idea come from? If we look back in the long history of antibiotic resistance meetings that have occurred there is a number of organizations at the global and international levels all the way down into the US national situation that are all recommending where risk assessment be applied, not just to look for the risk estimate number, but also to guide the decisions that are made about what to do with antibiotic resistance.*

*So what are the two outcomes if you go ahead and do a risk assessment? Well the first would be some kind of one in some million. I think we hear that a lot of times, so we can get a number. What do you do with the number? Is that risk good? Is it bad? Is it relative to anything? So that is one aspect and the second one is can we actually through looking at the process of risk assessment going through that whole food chain continuum through the animal to the food to the people, say what if we started intervening pre harvest with a particular intervention or post harvest on the food. We've got status quo risk, but what would be the affect of our proposed intervention? Will it decrease that risk even more, maybe drop down to 1 in 500,000 from a baseline of 1 in a million or something less or might it actually raise the risk? Those are some of the kinds of applications that risk assessors can provide to the decision making risk managers on how to go about choosing their appropriate interventions. So again, one more time, it's that continuum now. We've got the food animals, which correspond to that release assessment of food from contamination. There is the exposure and the consequence.*

*We don't talk a lot about the consequence. Data is very difficult to find on it, but still it is a very, very important consideration in this whole continuum because risk assessments that are done in*

*the lines of either finding that one in a million estimate or in guiding the risk management in selections and determining those interventions steps becomes very important in a fundamental opportunity to really guide responsible use, not only in veterinary medicine, but also in human medicine, regulatory decision making as well as food safety actions, so it can have a broad base of implications depending on what is done, to what extent and where along that food chain.*

*I'm gonna share with you some data from some publications that look at some of the older antibiotics and their actual risk estimates, so to simplify that whole step here is your three step risk assessment. It's a little more complicated of course, but it follows that release, exposure, consequence. According to the drug need of the animal, how it gets on the meat, contaminated, somebody actually ingests undercooked meat or another product, gets sick and actually then goes to seek medical care. Maybe they're then actually prescribed an antibiotic of the same class, which is used way back on the farm, so you can get a risk estimate if you put all the pieces in place. The neat thing about risk assessments is that they're inductive. You can do these over and over and as you get new information you can add that in. If you identify a data gap that guides research you can get better quality data. You can put boundaries if you go the numerical way of doing this and start to say well I think it's low and somebody says no, it's a high number. Put both in there and see where it comes out at. There is a lot of flexibility in looking at risk estimates.*

*So let's look at four of these published risk assessments. I just have one slide on each. We can provide papers of these and if you want to you can read them when you're – Scott Hurd who is now a professor at Iowa State University formed this one several years ago on macrolides. Macrolides include generic named products such as tylosin, tilmicosin and others in that macrolide class. By going through that release, exposure, consequence paradigm and working with experts from a wide variety of disciplines including human medical doctors, epidemiologists, molecular biologists, food safety experts, veterinarians he was able to model that, take data from sources such as NARMS, such as usage data that was available, looking at current contamination rates, infectious doses, quite the number of data inputs and these are the numbers that he came out with, so 1 in 53 million chance of a person acquiring macrolide resistant campylobacter infection from swine which were treated with macrolide, so it's 1 in 53 million. Chickens are a little higher risk relative to cattle, which were calculated to be a little lower. What does 1 in 53 million really mean? So the bottom for comparison puts other risks or odds if you will the Power Ball, 1 in 120 million to win. It's a relative risk comparison. The bee sting is always a popular one, 1 in a million. That is just some relative risk out there just to try to get a sense of what does that number generated in some of these risk estimates really mean relative to everyday kinds of risks that we encounter.*

*For tetracycline and there is a number of tetracyclines available in the animal health marketplace Tony Cox performed this one and I think it's really very interesting that he couldn't even come up with a numerical risk that was available in part because the published medical literature really does not have any kind of information on documented human treatment failures with tetracycline and it mentioned potentially here [INAUDIBLE] as one of those, so didn't take that out to a numerical outcome on this. So if you look at the literature out there a very old drug now mainline human use antibiotic the risk becomes very, very small if you can even calculate it.*

*And for penicillin Tony Cox also did this one. If you were looking at ampicillin [INAUDIBLE] or penicillin might be one for the resistance of enterococcus faecium. Now enterococcus faecium is not a food borne pathogen by itself. It can be transmitted by the food borne route, but most often it's due to a hospital acquired infection. You have surgery, an invasive procedure, something along those lines, so for those individuals that would find themselves in that sort of a circumstance, a very serious medical condition, in an intensive care unit for example the number here in the middle bullet indicate 0.135 chances over 350,000. If you just multiply that to make the math a little more understandable it would be 1 in 3.15 million, so you can start to look at some of these kinds of numbers and the relative risks that are involved on that, so penicillin being around for awhile very low risk and other antibiotics that are used to treat severe enterococcal infections in human patients.*

*And the last class that I'll look at, which is myosin Streptogramin and there is two risk assessments that were done here. One is from the Center for Veterinary Medicine. It's available on their website if you choose to download it and they looked at a very specific type of enterococcus faecium here, Vancomycin – resistant and quinupristin – dalfopristin. That is the Streptogramin molecule. Vancomycin that has been the traditional drug of last resort for treating enterococcal infections. There are other options available today that are used with vancomycin and several others. In trying to put this in context when this risk assessment was lined up in the early 2000's CBM came up with some risk scenarios, which you can read here on this slide and their estimates here looking at 6 to 120 chances in 100 million in a year and then if you're looking at general populations that risk goes down even further, so by going through the risk continuum we've looked at going from the food, from the farm to the food, to the human clinical. These risk assessments started with that hospitalized high risk patient population and working backwards, so it can go either way.*

*To reconfirm that this finding was also very low numbered Tony Cox again did some work and his model here shows that if you took away the use of Virginiamycin product in food animals you would reduce average treatment failures by .18 cases over five years, mortality by 0.29. Those are model estimates. We don't know if those will actually translate or not into real patient events. That is what comes out when you do the math.*

*So those are some of the risk estimate applications looking at specifically at some of the older products, some of which are used for the intention of growth promotion, some of which also have therapeutic claims. What is the real value then of saying OK well even there is a risk we still need do something. Another value of the risk assessment process now is for risk management to guide the appropriate interventions, so it can come back just as a refresher to our food chain continuum, release, exposure, consequence and looking at this time what are the options out there. Shall we restrict the use of a product pre harvest? Should we have veterinary oversight? Should we just discontinue the antibiotic all together? What other the risk management options on farm and pre harvest can we come up with? Here are some others or if you relook at post harvest, at our carcass processing to reduce the potential for microbial contamination, thermal treatment, carcass rinses, etcetera. There is a number of interventions there or even looking at human medical consequences, better diagnostics, better selection of antibiotics. All sorts of*

*things could be in play there. So choose what you want to use as an intervention. Work through a risk assessment process, evaluate those options. Whatever is chosen by the risk managers should be implemented. We may have more than one intervention, so [INAUDIBLE] or barrier [INAUDIBLE], but once it's implemented that is not the end of the story because the real question then is well how do you know that what you actually did is working and that is where this monitoring review process is so critical. You've got to have the tools in place to know that what we've now managed we can measure and does that measurement say that we had successes, reduced our infectious rate appropriately. The food supply has been safeguarded again. What is the outcome on that? So we – by following these risk management steps it helps to guide not only choice, but the implementation from that monitoring review process.*

*So just to wrap it up here, the three key points that this process offers a lot of value and I think there is a lot of folks that would be very glad to participate in this and share their expertise and to provide some perspectives how it can be applied. The looking back in terms of risk estimates on some of the older established animal health products it looks like from the current feed additive from this perspective that risk to human health is very, very low. And then by taking that same process and looking at those interventions that are being proposed perhaps we can identify several that are appropriate, maybe some are easier to do than others. At least we can get started. And then this idea that as we're going through this whole risk assessment process we can identify data gaps. If we just had better data on, insert whatever you need there. Then we can direct some of the research agencies and academic organizations to go out and get that data to fill in the missing blanks.*

*So in total the opportunities here for applying risk analysis is yet another layer of protection in a multifold. So I hope that this has been somewhat useful to give you perspective on yet another way of not just making a decision, but to make an informed decision about the future or animal health products.*