less GI effects." Something clearly is wrong in the risk/benefits communication process between the manufacturer/distributor, the veterinarian, and the consumer/owner of the animal receiving the drug.

A veterinary drug database. Many users don't understand possible risks without personally conducting exhaustive research which they may or may not be able to pursue. Information about new human drugs is readily accessible by consumers from the FDA home page, a database of veterinary prescription drug information that can be accessed from the CVM home page we recommend should be created. The FOI summaries don't answer the need. Consumers cannot readily access information about a new animal drugs like Etogesic as they can about a new human drug like Celobrex (phonetics).

U.S. approval status reports. We believe the FDA can do a better job of informing the public about the U.S. approval status of drugs approved and being used successfully in other countries. Cartofovet, penicillin polysulfate sodium (phonetics), for example, has been available in Australia, New Zealand, Canada, the United Kingdom and Ireland for years. This therapy for

osteoarthritis in dogs is not available in the United States, and we do not know how to determine its status.

We think the public needs to know. We think the CVM could explain its position on fighting this promotional advertising works advising material to the American public.

Here are four copies -- or copies of four letters from the Agency to Pfizer dated April 4, October 8, December 19 and December 21, 1998. Each of these letters discussed fair balance and advised that Pfizer was found in violation of the FFDC act and applicable regulations. The public, we believe, deserves to know the results of these actions. Pfizer has claimed Rimidil is safer than aspirin. This is a bogus claim.

And I'll skip. I'm getting signs telling me to stop talking. So I'll again edit further on the fly.

The claim that Rimidil is safer than aspirin is wrong. That was documented in the October '98 summary of '97 ADE reports highlighted in the January-February issue of the FDA Veterinarian and discussed in articles appearing in recent issues of APC Veterinary News and Dog

World.

The Pfizer commercials continue. The golden retriever is still jumping over garbage cans, leaping to the second floor and sliding down banisters. We think that and merchandising materials, toy dogs, desk pads, calendars, lack fair balance of risk/benefit information.

We'd also like to know why -- we'd like CVM to comment on why the U.S. Dosage for Rimidil after one week is twice that in Australia, the United Kingdom and Europe where adverse experiences seem to be less than in this national market.

Let me close by describing a personal experience that occurred in March at a specialty show the day before the Detroit Dog Show. A lady that we met brought her six-year-old dog for obedience trials and a beautiful fourteen-year-old along for the ride. In conversation, the owner said that her vet had just put the older dog on Rimidil. We asked why. Her answer? "Oh, no symptoms. She just slowing down a little and the vet said Rimidil is very popular now."

Jean, Jane and I are here in part

seeking closure and for those who record the remote, statistically insignificant judgment, I say that for Misty and George and many others, it was a hundred percent.

As you people in CVM well know, the premarket testing rarely indicates the full range of problems. Our plea is simply one for better communications, improvements in the exchange of information about animal drugs.

The so-called action plan for the provision of useful prescription medicine information approved for human drugs by Secretary Shalala January 13, '97, we recommend be adopted for animal drugs. What we miss today is the guarantee that information about the drugs we give to our animals is timely, accurate, up-to-date, unbiased, specific, and comprehensive and is presented in an understandable and legible format and is useful.

Thank you very much for your time.

(Applause.)

MR. BREEN: Does the CVM panel have any clarifying questions it wishes to ask?

(No response.)

MR. BREEN: Then let's proceed

with the questions. Some of them have been -- excuse me a second.

Thank you very much to all speakers.

(Applause.)

MR. BREEN: Dr. Sundlof will take care of the questions.

MR. SUNDLOF: We have one that was originally submitted to the -- by the American Veterinary Medical Association to the telecast and, unfortunately, was not addressed at the telecast. Because it was very specific, the CVM, I thought we would be able to address this question first. It's one to which a number of people alluded to. It talks about the risk assessment. New concept.

It says risk assessment is well-recognized as a tool that supports the decision, i.e. the risk management tool. The discipline uses scientific data to evaluate risk and was introduced in the 1970s to evaluate human cancer risk. Risk assessment provides what has been qualified by Anne Lammerding of Health Canada, a common, unified work space for people of different backgrounds to contribute to a better understanding of the whole system.

Risk assessment shows where there are data gaps, serve as a storage vehicle for valuable knowledge as it is accumulated and describe a chain of cause-and-effect events where proposed changes can be evaluated.

That's the prologue. And then the first question is given the complexity and the importance of managing potential human health impact of antimicrobial use in food animals, is the FDA planning to conduct a risk assessment to define these risks to human health and derive these benefits associated with risk assessment in concert with its intention to the proposed antimicrobial framework? And the answer is yes.

Next question -- maybe I should expand. Yeah, we expect to have our risk assessment completed this summer, and so we'll be coming out -- we are very far along in it. In fact, we had two of our people down at CDC just this week going through their files collecting the kind of data that is going to be required to try and associate the actual human health problems with antimicrobial resistance, we'll go back and use the data from the NARM system to look at animals, look at human resistance, and we will have a risk

assessment that we'll go out and we want a lot of input from all our stakeholders, especially in the scientific community, on that risk assessment so that we're sure that we feel confident that it was done properly. We're doing this in conjunction with a consultant who is very well respected within the risk assessment community. His name is David Voss.

And let me just say that this risk assessment will apply to food-borne pathogens and will not address commensal organisms like enterococcus. That's a more difficult and challenging risk assessment to perform. We intend to do that subsequent to getting this first one out, which we think the food-borne entero-pathogens are easier to model. So, yes, we certainly support that. We think we have the actual data so that we can minimize the uncertainty in that risk assessment. So that's the answer to that question.

The second one, USDA has recently, recently completed a risk assessment on Salmonella enteritidis that will serve as a prototype for future risk assessments of microbial hazards. The risk assessment for E. coli is being conducted by the same agency. The USDA and FDA since then are

cooperating on a complete risk assessment of Escherichia in food. Question: Do you envision the Center for Veterinary Medicine working cooperatively with the USDA to conduct the risk assessment on the human health impact of antimicrobial use in food-producing animals?

Let me say that, as I indicated earlier, we are working with a consultant. We are participating with the USDA in their risk assessment consortium. In fact, our risk assessment model, I think, has been addressed at that consortium. So a number of the people working in USDA on risk assessment, in addition to the Office of Risk Assessment Analysis within USDA certainly have been informed about the risk assessment, the basis for the risk assessment, and we are seeking your input on this as we will seek broad input. And also, yes, the Center is also looking at it. So we are addressing the issue of risk assessment and we do agree that it's very important to do that, and we certainly concur that the decisions that we make that lead to regulations guidance, et cetera, are based on the best science available. That's first one.

I haven't read these in advance,

so we'll take one more of the ones that have been written and then maybe go to the microphone and kind of go back and forth.

This one, it says, "How does CVC propose to focus resources on areas of greatest risk in those areas where risk has not been adequately assessed? For example, antimicrobial use. The answer is the FDA, I think we just did that. I'm going to say that we really do try and focus our enforcement efforts on those areas of highest risk. But not totally. And the reason is because we can't let the -- it's like the broken window theory of crime, that if you allow some minor indiscretions to continue, it escalates and you have a deteriorating system that loses credibility. So we try and focus on those with the greatest risk, but we don't ignore some of the other ones as well.

So since we already did that one, I'll just read one more and then we will go to the floor.

This one says, "What can or will be done to improve consumer veterinarian manufacturers' relationship with regard to informing consumers about possible adverse effects

of medications so that veterinarian -- so often veterinarians administer drugs, particularly newly introduced ones, without accompanying literature that gives sufficient warning about what side effects to be on the alert for and really emphasizes the side effects to watch for." And that's very consistent with the presentation that we just heard from Mr. Sinclair. And Dr. Tollefson?

DR. TOLLEFSON: I'll answer this one, too. There is another submission by Bob Sinclair, who you just heard speak, and it had to do -- he actually had some very excellent points -- with improving the availability and timeliness of ADE reports, particularly for the newly approved products, and I think the, as many of you know, the adverse events, the adverse reactions that we receive come in the initial stages of the marketing of the product -- at least the great majority of them -- and that's been associated with the level of use, the advertising, the fact that it's now getting out into the market where a lot of animals are using the drug, and we discover the adverse reactions.

We have been trying to improve the

timeliness of reporting those adverse reaction reports, the summaries, et cetera. It's directly linked to resources. The FY 2000 budget is not going to give us much relief on that. We will be submitting information for the 2001 link report on adverse reactions. It's directly linked to the consumer advertising. We're becoming overwhelmed with the amount of information that's getting out there. The request for the new products, although maybe it wasn't accurately expressed at this meeting but Office of New Animal Drugs' proficiency at approving new products, and it's becoming very critical that we do that.

Your ideas about creating more animal health information for the consumer is well received. We want to do that in general, you know, link our home page. We think that maybe that's one way to counteract a lot of information that's becoming widespread on the internet where consumers -- anybody can get information that's not always accurate, not so much for approved products as for unapproved products. It's difficult to regulate that area. So we're thinking that if FDA serves as a source of the neutral information, that will induce people to come to us to check the

claims and so on. But we do appreciate your input.

DR. SUNDLOF: Let's go to the audience. If anybody has any questions, let's go to the microphones. I think there are two there. Let's try to come up and ask those questions.

In fact, why don't I read another, because I don't see people flocking. I'll go ahead and read. But while I'm doing one, if you think of a burning question, please walk over to the microphones and we'll get to you.

This one says, "What is the agency's role" -- I think that's "role" -- "in regulating animal feed additives? Does current science support restricting some drugs, or is it mostly perception? If it's mostly perception, will FDA bow to pressure for regulation anyway?"

Well, as I think is well known that there have been some severe restrictions, especially in some European union where certain products were simply banned without a full scientific review. Whether those products were contributing resistance is still an open question, has not been resolved. CVM's position is that we look at drugs and make regulatory actions based on

their risks to the public. If that risk is unacceptable, then we would take action.

Once a drug is approved, though, the burden of proof is on the FDA to establish that it is unsafe. So any action that we would take on any feed additives would have to be based on our true ability to demonstrate that there was a risk.

We do have a petition before us right now to take some similar action to banning certain growth-promoting antibiotics in feeds, which was -- there was more than forty organizations and individuals, including a Nobel laureate that was a co-signator to that citizens' petition. So regardless, it is still the responsibility of the FDA to demonstrate that those products are unsafe, and that's our mandate within the law, and we will make those decisions based on data and science.

Dr. Jarrett?

DR. JARRETT: Further to the comments I made about compliance and enforcement, I noticed in the slides and the overheads that you used compliance and enforcement based on your wishes had the lowest funding and the greatest desire for funding, and I commend you for that.

Would you like to comment on that further?

DR. TOLLEFSON: Yes, it's always been on our wish list. It's difficult. Frequently that concept doesn't sell very well to FDA stakeholders, the increased compliance, and it never really has. We are now addressing it under the brooder term of product quality assurance, so that you bring in to the issue the preapproval instructions, the GMP issues, that sort of thing, so that everything is lumped into one, and we think it may sell better in a congressional format. Again, our funding requests are being broken down into two areas under food safety initiative enhancements and under regular base line FDA requirements. The inspections component and enforcement issues are under both for FY 2001. And I probably sound like a broken record in saying that our hopes are up for 2001, but that is the case. And we're not alone. The other senators also want to do that. So we're hopeful.

Does that answer your question at all or do you want specifics?

DR. JARRETT: No, no, no. My inference, though, was more to existing regulations and at the field level, product usage and so forth,

not those -- the professionals that are out there doing it right. The few that are not doing it right --

DR. TOLLEFSON: Correct. We get information own those types of activities from a number of sources. We get an awful lot of information from veterinarians, from organizations, practitioner groups, from competing drug sponsors. We do follow those up. We categorize them in terms of the activity, like compounding pharmaceuticals that you mentioned, internet advertisement and sales. And we request to the field; the field follows up on them based on the priority. And we need to compete against all the other agencies. Representatives from the field can tell you that their priorities follow the lines of the user investigations that have to be done. They're under a mandate to be done, so they come first. Then it's prioritized based on public health. We actually have a pretty good relationship with the field. They do a lot of our work.

The other part of that problem is you won't get specific information fed back to you on what is going on if the case is developed or warning labels are issued and so on.

There's actually a fairly good description of that in the folder on our response to the last stakeholders meeting that addresses some of those specific issues.

But our request for additional funding will, of course, help that problem, but it's not specifically addressing enforcing current regulations. It's more for statutory inspections that which are not necessarily overlapping.

DR. JARRETT: Thank you.

MS. LAVENBERG: My name is Donna Lavenberg, and I'm with Bayer. I noticed in one of the handouts that CVM is starting some third-party reviews, and I just had some questions. Are the sponsors aware that a portion of their application may be under review by a third party? Is this -- in what areas are you working? Are you going to continue this effort? Just some more basic information about the program.

DR. BEAULIEU: Yes. We're now working on the Food Safety section, particularly the pathology reviews associated with the tox studies. We lost our tox -- our path expertise, and the general consensus was that, resources being as limited at they were, we could not afford to

invest one complete FDT in keeping that expertise within the organization. So that was an obvious place to reach outside the organization to get that expertise. We are paying for that. So it's still a resource that's counted against our operating budget. It's working well to the extent we have resources to do it. I think we're very happy with the way that process is working and something on the order of half a dozen reviews, maybe, a year is about what we can afford in that.

We're interested in expanding that process possibly into other areas of expertise that we're currently deficient in. But the resources to support that are going to have to come from our budget at this point. So our ability to do that is limited. But so far it's available. It's been a favorable experience. We would very much like to expand it. Part of what we would do with our additional resources in the future, if we get them, would be to expand that program.

If you guys have -- I know that you suggested one area that we might consider for going outside for expertise was the statistical area because I think you folks viewed that as a potential roadblock. Where we didn't have

sufficient resources we dealt with that by investing in more in-house resources in that area, and we hope to deal with that situation in the future, too.

But if there are other specific areas of expertise that you perceive that are bottlenecks because -- that are holding the applications up, or you would suggest maybe going outside, we would certainly be interested in hearing about those.

The food safety portion of the application, in our judgment right now, tends to lend itself best to that approach. We're not looking for a clinical judgment, we're not looking at any effectiveness evaluation, we're looking for the ability to look for someone to make a fairly specific and concrete determination with respect to what a specific study says.

MS. LAVENBERGER: Thank you.

MR. RIGGS: David Riggs from Watkinsville, Georgia.

I attended a conference that was held at the Centers for Disease Control back earlier in the year, and this is a group of molecular scientists that were discussing their

findings, and I was very impressed with the content of the meeting and the presentations. But the thing that also hit me is that when people are asked, Where did this resistance that these scientists had recognized and had identified, the question came up, Well, where did they come from? And they gave their opinion -- not fact -- as to what the origin of that resistance was, and the thing that I left that meeting with is a very strong suggestion that we need to get the molecular scientists, the epidemiologists and the people in the field, the end users, together, and have those three groups discuss their findings and be challenged when they make particular statements about -- particularly about the origin and evolution of the antimicrobial resistance issue.

That being said, my question to CVM is: Do you have any plans at all to bring these groups together? Would this be a part of your working group plan that you have -- that you had mentioned, and, more specifically, in your research priorities, do you have any long-range plans to look more closely at the origin and the evolution of antimicrobial resistance specifically as to the frequency of transfer within related and

even unrelated bacterial populations?

DR. ALDERSON: Within CVM, there are two resources: The intramural and the extramural. And I think if you'll look at what we're doing, particularly in the intramural side, I think it's very basic just addressing the issue that you're talking about. We have hired three outstanding scientists already, fixing to hire two more. We failed last year. We made two offers, and they got more money to stay where they were. So in one way we failed, but in another way we did select good candidates because they got more money to stay where they were. So we are starting down that path again.

But the short answer to your question is: We're very focused intramurally particularly and will become more focused extramurally in the next year's round of funding on just the issue you're talking about. Because that's the evolution of resistance. We've got within our facility now the means for us to take samples when they lie down -- well, anywhere in the GI tract without being able to follow that evolution of resistance beginning in the gut of the animal and following the same animals through that

process. That's where we are. I think our focus is on how do we help the industry address the problems they have and the problems that we're trying to grasp and give advice to the industry on what do we need to do to address the antibiotic resistance issue to make these products available?

There was one other part of the question.

DR. SUNDLOF: You were wanting to the know if we're going to bring the different disciplines together, the molecular microbiologists and the epidemiologists and other groups that may have particular expertise that could be brought to bear on this issue. And I would just say that we don't have any formal plans right now to convene such a conference, but I think that in the future we will -- we certainly may.

It is our intention to bring as many diverse scientific opinions together on this issue as possible. One of the presenters implied that we were only listening to one faction and that that might be epidemiology, and you should be listening more towards people that are bench scientists' point of view.

The whole area of antimicrobial

resistance is extremely complex. It encompasses a wide variety of scientific disciplines and expertise, and we certainly try and listen to all of those to the extent possible. I think some of the comments that Norris was making was in reference to the fact that we need to be bringing more of that expertise into the Center so that we can understand what's being on out there in the scientific community. If you don't understand molecular biology very well, it's hard to take the newest science into account when you're forming regulations or policies or making decisions. So we're trying to build up our own expertise internally just so we can better understand all of the complexities and new science that's going on out there.

I think that's a very important comment, and I appreciate it.

Did that address your --

We have just one more.

DR. JARRETT: Are you also going to address the frequency of transfer of resistance from one bacteria to another? Are you going to look at frequency.

DR. ALDERSON: Yes, that's part of

what we're looking at within our research program. Again, I think the issue, as you notice particularly later in the year, and of course the next year our announcements coming up are for extramural funding. You'll see that particular factor very prominent in the advertisement for extramural funds.

DR. SUNDLOF: I'd just add to that that the reason that we're not doing a risk assessment on those types of potential resistance issues -- that is, the transfer of resistance from one organism to another organism -- is because we don't feel we have enough science to define that process very readily in risk assessment modeling. So we are very interested in getting more of that information so that when we do our risk assessment as Phase 2, it will be based on a lot more knowledge than we presently have.

We have one more question here, and it says: What role do you see for the office of criminal investigation in your science-based regulatory agency?

Norris, do you want to take that one?

DR. ALDERSON: You don't want me

to answer that one.

DR. SUNDLOF: Well, I think one of the things we were talking about, whether it's the Office of Criminal Investigation or the field, that we're dealing with a lot of very sophisticated issues that deal with the products that we regulate. And certainly the field needs to be able to keep up with all of the latest changes in science and manufacturing technology and et cetera so that they can do an adequate job. I would assume it would be the same for the Office of Criminal Investigations where they are investigating potential criminal activities that involve some fairly sophisticated mechanisms. My favorite one -- this is the one of the cow, where they wired a cow and traced it through a number of sale barns where individuals had told them that they actually used drugs on them and had all this stuff on tape and had video cameras. It was really neat.

DR. TOLLEFSON: It's true.

(Laughter.)

DR. SUNDLOF: It's true. So they do use some fairly sophisticated techniques that you seldom hear about because they want to keep

that activity away from the public, for obvious reasons.

But we certainly think that the issues that we deal with are technically complex and challenging, and that the Office of Criminal Investigations would need some kind of training to maintain currency as the other component.

Charles, I am going to turn it back over to you.

MR. BREEN: I'd like to thank everybody very much for your attendance and participation here today.

Did you have anything more to say?

DR. SUNDLOF: I'm supposed to summarize.

Dave Lynch and company have been faithfully taking down notes, too, and trying to summarize what they thought the main points that were raised today are. And Jackie Pace was also involved in that.

There was broad support for strong science base, and we're encouraged by that, since that's one of the Commission's major emphasis.

The risk assessment was very

important, and there seems to be a lot of support for CVM making sure that their decisions are based on a valid risk assessment.

Continued partnering with stakeholders. We heard a strong sense that partnering was an essential part of doing business.

Continued development of judicious use of principles. Absolutely CVM supports that.

Support and enhancement and expansion of the National Antimicrobial Monitoring System and surveillance, that is also a view that we certainly share and we will be asking for additional funds through the Food Safety Initiative to increase the robustness of that program.

Enforce current regulations. We heard this a lot at our last stakeholders meeting, and we heard it again today. We will go back and again discuss this and try and apply the resources necessary against the -- where we think the enforcement activities need to be.

Inclusion of veterinarians and practitioners and producers in the decision-making process. We heard that today, and we certainly support broad public input into decisions.

Support for the use of

compassionate investigation of new animal drug applications, where certain diseases impact a relatively small percentage of the animals, but when diseases do occur, people need drugs, and anything we can do to help with that process is something that we've tried to do and will continue to do.

Request for regulations on VFDs, licensing and minor species document. I think we'll be seeing some of those fairly soon because we have come quite a long way on those.

Veterinary drug database on the worldwide web. That's something that we need to be considering. I'll be very honest that CVM has not had a lot of requests for this kind of information before, but we've been approving a lot of new drugs for companion animals lately, and as a result of that, maybe this is an area that we haven't spent enough time on.

We really appreciate your coming out and making those statements. We may not have been as responsive as we should had you not been here. So certainly we'll try and work on that. Better communication between FDA and consumers. And, again, good suggestions.

So that's it.

Okay, Charles.

MR. BREEN: Thank you.

I won't repeat myself, but having the last word is a privilege. I would just like to say the stakeholder meetings isn't just a walk, it's a good idea.

Thank you.

(Applause.)

(The proceedings concluded at 4:54 p.m.)

# C E R T I F I C A T E

I, LINDA R. BURT, a Certified Shorthand Reporter of the State of Kansas, do hereby certify:

That said proceedings were was taken down by me in shorthand at the time and place hereinbefore stated and was thereafter reduced to typewriting under my direction;

That the foregoing transcript is a true record to the best of my ability of the statements given;

That I am not a relative or employee or attorney or counsel of any of the parties or a relative or employee of such attorney or counsel or financially interested in the action.

WITNESS my hand and seal this _____ day of _____, 1999.

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LINDA R. BURT, C.S.R.
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State of Kansas