recombinant DNA technology can lead to useful products and processes. Because this is a basic methodology, the unforeseen applications may very well be more important than any of those that have been proposed so far to date. The underlying science of molecular biology and molecular genetics is dynamic and it is reasonable to assume that new opportunities will be created as the depth of our scientific understanding increases. This new technology is surely no panacea. On the other hand, it carries the realizable potential of contributing significantly to the solution of some of the most difficult problems facing animal health and production today.

Panel Discussion

Question: The question is directed to Dr. Ardans regarding the use of modified live BVD viruses in dairy herds.

Answer: When I first got out of school that was a question that I thought I pretty well understood and I find myself, I think, as I go along saying more and more, I don't know. I've gone the full circle, I think, with BVD. Unless an outfit has had a significant problem with BVD, it hasn't been in our areas—I've been really pushing BVD vaccines. I know that I am going to get torn apart by some of the biologics people for this thing. But that has been our feeling. The inactivated ones, especially the ones using the Singer strain, I don't think have been out long enough really—I haven't made any decisions in my own mind about it. There's a lot of talk about which strain is the better strain to use and I guess I have not really seen anything that is definitive that says the NADL strain is better than the Singer, or the Singer is better than that. I think some of the problems that we had with some of the early vaccines were that there were some contaminating factors in some of those vaccines. I think that is where we got into some problems and I think that's the beauty of what Dr. Muscoplat was talking about. In the future we can produce, or hopefully produce, vaccines that will be noninfectious and hopefully not have the effect on the immune systems that BVD certainly in some instances seems to really have. I realize that's a long way around the bush saying I don't know, but I really don't have any firm recommendations on that. To take the last question, the question with the half-life of maternal antibodies being such as they are, the recommendations at times have been to prolong vaccination schedules until these antibodies have diminished and in many cases they're not. In certain diseases, persistence of paternal immunoglobulins have been shown for 6, 7, 8 or 9 months; 9 months would be stretching it somewhat, but BVD has been shown to go out that far. What about recommendations for vaccine? And the second one was, what antibody can be absorbed in the adult cow? My feeling is what antibody isn't absorbed in the adult animal because they don't have this mechanism that the young calf does so that they can absorb it orally. So I don't think it is an efficacious way. Going back to the immunization schedules, I think the situation that we get into with young calves, an area where we really need some good work to see what kind of schedules we might be able to develop for these baby calves, even though we give calves a vaccine, for example, and they don't necessarily make a response, in the serum that we can measure, there's probably pretty good evidence that those calves have been primed. So that when they are immunized the next time or they're given the vaccine there have already been some memory cells set up so that you get a quicker response. We have some trials that we are trying to get going now with some baby calves to see what type of intervals. I think we're probably going to come to using a multiple type approach or some thing, vaccinating over a more frequent schedule to see if we can get over the effect of the maternal immunity, and there's no doubt there is going to be some effect of the maternal immunity as far as inhibiting these organisms, say for a live virus, to go ahead and replicate. But there probably is going to be a little priming and that is the thing we are going to study. Lavamisole has been used. That is probably the one, if you want to call them immunomodulators, immunopotentiators, that are available that had been used in cattle. The problem is that we don't have from an experimental standpoint real good assays yet to really define what effects levamisole does have on say some of these subsets of the t-lymphocytes. Now in certain situations there have been good examples where levamisole seems to be associated with an increased t-cell response. But the thing to stress is that it seems to be only effective in those animals that have a t-suppression. It doesn't seem to do anything for the animal that seemingly has normal response. When you start looking at the area of how it affects antibody production, there are some individuals that have said they have seen better antibody production. There was an individual that was a graduate student at Davis a few years ago who used it along with an IBR vaccine trial and he actually saw a suppression in the antibody response in the particular situation when he used levamisole. So I think it can be used, but I don't think we fully understand it.

Second Answer: Let me just give two comments, maybe three. Dr. Don Johnson at the University of Minnesota, about 5 years ago, made some experiments on cattle that came into the veterinary clinic that really had what you would call chronic BVD, really non-responsive, and was able to get them to turn around with levamisole therapy. The information was never published but I believe it was sound. There was a recent report in the Amer. J. of Vet. Res., about 2-3 months ago, from Saskatoon showing that administration of levamisole to feedlot cattle significantly improved antibody responses to IBR. The third point would be that there are over 600 published reports in the literature documenting the immune-cementing properties of levamisole in the laboratory or some controlled situation. The problem would be to translate that into economic benefits to the cattle producer. It has been a most difficult thing to extrapolate. Given the fact that there

have been almost 10 years of experimentation, we still don't know the real cost benefit on the farm and those types of experiments take 3-4 years, year after year of doing double blind trials. I might add that it is not too different from asking questions like, does Vitamin C prevent the common cold? After all these years we don't have the answer to that and maybe one day we will have a definitive answer on levamisole. I don't know that anyone has seen any harmful effects, immunologically, from it. Would you agree with that?

Dr. Osborn: I probably won't agree with that. I don't think levamisole, per se, is necessarily harmful, but in some studies that we will describe tomorrow on bluetongue we find that with levamisole we do see an increased cell-mediated response to bluetongue viral antigens, but one of the unfortunate side effects is that it can set the stage for hyper-sensitivity which will allow for expression of disease.

Question: We have a two part question. The first part deals with the cow that is milked throughout her entire gestation. Does she produce any colostrum? The second part is, does stored colostrum provide the same effective passive antibody that fresh colostrum does?

Dr. Ardans: The cow that is milked continuously, does produce colostrum, and it has pretty well been demonstrated that the cow starts selectively transferring the IgG-1 about 4-5 weeks before she calves, into the udder. So if you've got a cow that is being milked continuously, that is going to be diluted out and you're going to be losing it. Again, the cow does it once and once only. The more effective transfer comes the closer to calving they are. Regarding effectiveness of using stored colostrum, I'm talking about frozen colostrum, verses the colostrum they would get fresh, I am not aware of any studies that have really looked at that critically and I have seen the studies where you can get good passive transfer of immunoglobulins, but how that relates on to susceptibility to disease I don't know

Question: The question has to do with hand milking versus machine milking and the resultant antibody level in the colostrum.

Answer: I am not aware of that study but I do want to add to what I said this morning regarding chronic "Shedders" and BVD. In experimental work, when the virus has been inoculated into fetuses prior to the time that they are immunologically competent, the experimental evidence would suggest that you cannot produce a tolerance state with this replicating virus. In studies on lambs that have Border Disease, which is caused by a border disease virus which may be one of the strains of BVD or something very similar to it, it is possible that the persistently infected animals shed virus up until 2½ years, or as long as we followed them, after birth. Now these animals do not have detectable neutralizing antibody. However, we do have some evidence that there are probably low levels of antibody being produced but the antigen excess is tying up the antibody and so we do not have a measurable immune response. So this in effect is a form of treadmill tolerence in which the antigen excess is over-riding any immune response that can be detected. I think that one of the problems, at least if I go back and try to compare this to studies that have been done in mice with lymphocytic virus, originally they felt there was tolerence in those animals to the virus. As they began later to follow them they again found there were low levels of the antibody being produced. I think that most of the tolerence is seen in certain strains of mice which may be genetically programmed not to produce as great an immune response to the virus as some other strains. This gets back to something that Dr. Ardans was pointing out earlier, studies are just beginning on the bovine species to determine whether we can define if there are immune response genes that are going to modulate or regulate the degree of responsiveness to any particular agent and although I don't have evidence of this, I wonder if some of the cases of chronic BVD are not, in fact, a combination of the immunosuppressive effect of the virus plus a failure on the part of the calf to mount a sufficient immune response to overcome it.

Dr. Ardans' paper will be published in the 1983 issue of Bovine Practitioner.