HIGHLIGHTS OF A ROUNDTABLE DISCUSSION

PIG HEALTH TODAY®

AMR SURVEILLANCE

Mapping a course for responsible, effective antimicrobial use in swine

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welcome

With few alternatives today for treating life-threatening bacterial infections in pigs and other animals, antibiotics remain essential tools for maintaining high levels of herd health and welfare. Veterinarians and producers must use them responsibly, however — not only to preserve their efficacy in animals but also in humans. Likewise, human medicine must be part of an action plan to preserve the efficacy of antibiotics.

For this reason, Zoetis is a strong advocate of One Health — a science-based, holistic approach that encourages collaboration and communication across all sectors to address this common goal. In addition, we believe veterinarians should be involved with all antibiotic decisions for animals.

Responsible usage is not enough, however. To help the food-animal industry be good antibiotic stewards, we are vigorous proponents of antimicrobial-resistance (AMR) surveillance to monitor efficacy of these valuable tools.

Since 1998, Zoetis has made significant investments in AMR surveillance. In that time, we have collected more than 80,000 bacteria isolates, which have helped increase our understanding of both the development and the mechanisms of AMR.

Most importantly, we have routinely shared our findings with program participants and the industries we serve. This in turn has helped veterinarians select the appropriate antimicrobial agent for treating sick pigs and other animals.

To shed more light on this important topic, we recently assembled a panel of swine-health experts for a roundtable discussion on AMR and what steps we can take to preserve antibiotics for the pork industry. We are pleased to share these highlights from that discussion.

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PIG HEALTH TODAY®

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TRIUMPH FOODS

Who's monitoring for antimicrobial resistance (AMR) and how?

DAVIES

Our mission is to have a broad, interactive discussion about antimicrobial resistance (AMR) with an emphasis on surveillance and how AMR affects the pork industry. The way we evaluate resistance has changed a lot, but many questions remain. For example:

- **What antimicrobials should we be including for susceptibility testing?**
- **AMR involves public health, so should we look at the panels of antimicrobials included in the National Antibiotic Resistance Monitoring System (NARMS), which tracks changes in antimicrobial susceptibility of certain bacteria in people, retail meats and food animals?**
- **Or do we want to test only antibiotics veterinarians can use to treat conditions?**
- **What are we really trying to achieve with surveillance in the swine industry?**

With these questions in mind, let's turn the discussion over to the panelists. Let's start with Dr. Nerem of Pipestone Veterinary Service. Please tell us about your involvement developing practical surveillance programs for the swine industry.

• NEREM

Our veterinary practice has been engaged in surveillance work. It started in 2017 and coincided with the new veterinary feed directive (VFD) rules and increase in veterinary oversight for medically important antibiotics — an initiative that we've welcomed.

We recognized the high level of societal concern about antibiotic-resistant infections. According to statistics from the Centers for Disease Control and Prevention (CDC), these infections cause 35,000 deaths in people annually.[1] As veterinarians, and recognizing the oath we took to protect public health while guarding animal welfare, we could not ignore the issue of antibiotic resistance nor should we be defensive about how we've used antibiotics in the past.

We determined we needed to do more AMR surveillance on the farm, with the full understanding that just because we're veterinarians doesn't make us experts in the field of antibiotic resistance.

There are a lot of resistance data available based on outbreak investigations conducted by CDC, the Food and Drug Administration (FDA) and other groups regarding nosocomial infections in hospitals and pathogens that might be within the food-supply chain. And unfortunately, the implication has been that a lot of this resistance is happening at the farm level, yet at the farm level, there doesn't seem to be a lot of data to support that.

Consequently, we created a surveillance program called Pipestone Antibiotic Resistance Tracker. That program has two pilot projects.

The first pilot project focuses on resistance for pathogens of veterinary importance. We discovered we had a great data set of submissions by Pipestone veterinarians over the past 17 or 18 years. There are three major veterinary diagnostic laboratories we've worked with, so we went back and looked at the culture and sensitivity data from the swine submissions we'd made and developed what we called a resistance index. Within this project, we looked at the five pathogens of interest: *Streptococcus suis, Haemophilus parasuis, Escherichia coli, Salmonella* and *Actinobacillosis suis*.

DAVIES

How many cases have you accumulated?

• NEREM

Today, there are about 4,500 cases included in that data set over a 17- or 18-year period. For each of those five pathogens, a value of 0 is assigned for a drug it is sensitive to and a 1 is assigned for each drug it is resistant to. A graph is created showing resistance over time.

DAVIES

Tell us about the second pilot program.

• NEREM

We looked at four pathogens that NARMS is concerned about: *Enterococcus, Salmonella, E. coli* and *Campylobacter*. We sampled swine farms and some alternative sites — specifically, our clinic's companion-animal exam room, a community playground and a municipal wastewater-treatment plant.

> At the Minnesota Veterinary Diagnostic Laboratory, we have about 60,000 or so isolates that have been mined by different researchers and used for genotypic testing. That's a significant amount.
>
> **JERRY TORRISON, DVM, PhD**

Each month we collected a sample from each location and submitted them to South Dakota State University for culture and sensitivity. Then we tracked our ability to isolate those four pathogens from each of those sampling locations. If we did isolate those pathogens, we looked at the resistance profiles for those organisms.

My colleague, at Pipestone, Scott Dee, DVM, was the leader of that project. We're hoping to use the information to help guide us in other surveillance projects we might launch in the future. We used the NARMS diagnostic panels for this project.

• RISSER

At Country View Farms, we're not tracking resistance extensively, but we do obtain antibiotic-susceptibility testing for comparison to clinical susceptibility and resistance. We compare that to our history of what's occurred in those pigs in the past.

Whether we obtain that testing depends on the clinical picture, who sent in the sample and the pathogens found in affected pigs. If a production service manager sends in samples, we're not necessarily going to rely on those isolates. We like the samples to come from a veterinarian.

• SWEENEY

The Zoetis surveillance program dates back to 1998. Diagnostic labs throughout North America and Canada participate. As of 2019, we had 18 US and six Canadian diagnostic laboratories participating. We get bacteria from sick or dead animals only, so it's a passive, not active, surveillance program. The bacteria we collect are *Pasteurella multocida, Actinobacillus pleuropneumonia*, *S. suis* and *Bordetella bronchiseptica*. We also request *E. coli* and *Salmonella*.

We test against 10 antibiotics using a MIC [minimum inhibitory concentration] panel. We take the data and crunch them down to MIC50, MIC90 and SIR [susceptible, intermediate or resistant] based on breakpoints. We present those data reports to the FDA's Center for Veterinary Medicine on a yearly basis. We also try to publish the data every 5 to 10 years as well.

• DAVIES

Do you use Clinical and Laboratory Standards Institute (CLSI) breakpoints?

• SWEENEY

Yes, I'm a voting member on CLSI's subcommittee on Veterinary Antimicrobial Susceptibility Testing. The group has done a really good job at increasing the number of available clinical breakpoints for swine and bovine pathogens over the last 5 to 6 years.

So yes, in our program we exclusively use the 10 CLSI breakpoints available for animals. There isn't a breakpoint for trimethoprim, however, so we simply report MIC50 or 90. No SIR [susceptible, intermediate or resistant].

• TORRISON

At the Minnesota Veterinary Diagnostic Laboratory, we have about 60,000 or so isolates that have been mined by different researchers and used for genotypic testing. That's a significant amount.

We're also involved in projects, including one with USDA that involves a number of diagnostic labs across the country that are submitting isolates, which are sequenced.

Another project is with FDA. It's called "Vet-LIRN" [Veterinary Laboratory Investigation and Response Network] and is part of an initial pilot group of 20 labs; it's very much whole-genome sequencing based. The objective is to test for resistance and to come up with standardized, repeatable methods that heretofore have not really been attempted much in terms of the whole genome-sequencing world.

So, hats off to FDA to consider that an important objective. It's important to develop an infrastructure before we try to proceed with some means of assessing the resistance situation. That's a very important first step.

continued

Who's monitoring for antimicrobial resistance (AMR) and how?

DAVIES

I can't count how many meetings I've been in where consumer-group representatives ask why the FDA can't just report all the VFD data on antibiotic use to the public. Dr. Holck, you and your colleagues at GlobalVetLink (GVL) probably have a better read on that than anyone. What data are available, or potentially available, from GVL to help the pork industry answer this question?

HOLCK

The vast majority of electronic VFDs are going through GVL, so there's a substantial database. Due to the updated regulations that took effect January 1 of 2017, there was a dramatic increase in the number of VFDs in 2017, but then we saw about a 15% reduction in the number of VFDs in 2018. The number of VFDs written in 2019 was similar to 2018. Obviously, the use of medically important feed antibiotics is going down. But there are a lot of nuances to consider.

VFDs are written by a veterinarian under a veterinary-client-patient relationship to allow for the use of the medicated feed containing antibiotics considered by FDA to be medically important to human medicine. However, that's not directly tied to fulfillment. There are opportunities to link into some other databases where we can get use or fulfillment data. GVL and Prairie Systems — another software company — are working to tie VFD, use/fulfillment and diagnostic data together, which will be tremendously valuable for the veterinarian and producer.

> "Obviously, the use of medically important feed antibiotics is going down. But there are a lot of nuances to consider."
>
> TYLER HOLCK, DVM

Resistance findings

DAVIES

What have we learned about AMR patterns in the pork industry?

NEREM

From the Pipestone Antibiotic Resistance Tracker data set, we've found that the resistance graph goes up and down a bit, but to date it's been a pretty flat line. In our second project, isolation of the four NARMS pathogens was similar across sites, as were the levels of AMR.

HOLCK

Interpretation is a bit difficult, but I did look at resistance data for a few pathogens in the GVL diagnostic database over just the last 4 years. Similar to Dr. Nerem's comments, I did not see any change in the resistance patterns over that relatively short time frame. There is a tremendous amount of data, but it's not all connected yet. An issue is whether measuring antibiotic use is a good surrogate for antibiotic resistance. I continue to be frustrated at conferences where antibiotic use is the focus, and we don't even discuss resistance.

SWEENEY

At the Zoetis lab, we see low rates of resistance for swine. Put another way, we're seeing high rates of susceptibility for a majority of medications that we test on our panel, except for tetracycline and *S. suis*. That's a big one right there.

RISSER

There's one severe resistance case I can think of, and it was in a traditional pig flow. It involved *S. suis* bacteria resistant to our normally used antibiotics.

TORRISON

We've published some of our results with cattle and pigs. Specifically, it involves *Salmonella* and *E. coli* trends with resistance, both phenotypic and genotypic over time. As others have said here, it's mostly flat with the exception of maybe some *Salmonella* resistance to enrofloxacin measured and observed in swine only.

DUDLEY

We are not tracking AMR patterns at this time. Empirically, from a clinical standpoint, however, *E. coli* resistance to enrofloxacin is a concern.

> "...we're seeing high rates of susceptibility for a majority of medications that we test on our panel, except for tetracycline and *S. suis*."
>
> **MICHAEL SWEENEY, MS**

Genotyping versus phenotyping

DAVIES
Has anyone looked at results with genotyping versus phenotyping?

SWEENEY
Yes, we took a serious look at that. We found that genotyping is still expensive for what we'd like to do, and the database just isn't there yet. In another 5 or 10 years, I think it's going to be really powerful.

NEREM
We looked at genotyping as well in one of our pilot projects and compared it to phenotypic testing of cultures and sensitivity from the lab. We found there was about a 92% agreement. The cost of genotyping was way too expensive though for our small budget. So, we've continued with culture and sensitivity.

TORRISON
There's been some variation with both genotypic and phenotypic results. There is also unpublished genotypic work by others involving the expansion of resistance genes throughout bacterial populations. That can potentially raise a concern that there may be more resistance-gene distribution among the population of bacteria than we have at the lab.

> "We looked at genotyping as well in one of our pilot projects and compared it to phenotypic testing of cultures and sensitivity from the lab. We found there was about a 92% agreement."
>
> JOEL NEREM, DVM

IV Linking resistance data to clinical experience

DAVIES

Has anyone been able to link resistance data to the clinical experience or diagnostic background?

• **HOLCK**

The answer would be that it's as good as what the submission form says. Everyone here can quickly relate to that, right? There are no specific criteria nor a classification scheme that would go along with the clinical scenario. But on any given case, there could be a lot of information there regarding clinical presentation.

• **SWEENEY**

For us, the diagnostic labs own the isolates they send us. We provide them with the data on a yearly basis, so they have access to all that information. That's all we have available.

DAVIES

Let's talk about surveillance technology. Dr. Torrison, can you please comment about what you've observed at the Minnesota Veterinary Diagnostic Laboratory and what changes you anticipate going forward?

• **TORRISON**

Up to now, the traditional methods of getting submissions from sick or dead pigs — growing what will grow from animals that were probably treated, selecting single pure colonies from the garden that grows and then performing antimicrobial susceptibility testing on those individual colonies — has actually worked pretty well, even considering all the biases built in to that regarding individual case management.

That information is submitted, and we test for fairly specific purposes. My concern would be extrapolating that same information for broader use. We need to take a step back and look at our objectives regarding different surveillance methods.

DAVIES

Dr. Dudley, as a manager of a large mixed-animal veterinary practice in southern Minnesota, can you comment on your approach as a clinician and user of data from the diagnostic laboratories? In my experience, a lot of people on the human medical side aren't aware that veterinarians do quite a lot of resistance testing — often more so than some physicians.

• **DUDLEY**

It's correct that we veterinary practitioners do a lot of diagnostics and resistance testing. All of that would be phenotypic, primarily to determine what treatment we're going to utilize. If individual clients won't obtain the testing, we look to universities for published data.

DAVIES

Dr. Risser, how do you use available data in practice?

• **RISSER**

We have pretty consistent flows of pigs, so we have a lot of history we can develop within a flow, and we have an idea of what antibiotics are going to be useful in those pigs versus others.

Today we have many pigs that are not given any water or feed medications; we strictly use injectable antibiotics in about half of our pigs raised in a program without antibiotics. That gives us some opportunity to get a lot of samples from pigs not treated with antibiotics. It's interesting because when you take away antibiotics in feed and water, you just never know what impact it's going to have on bacteria in that environment.

> "...we veterinary practitioners do a lot of diagnostics and resistance testing. All of that would be phenotypic, primarily to determine what treatment we're going to utilize."
>
> **STEVEN DUDLEY, DVM**

V Managing resistance in the field

DAVIES

Let's focus on the clinical problem of resistance in the field. We read every day about the concerns with AMR in human medicine and about the profligate use of antibiotics in food-animal systems.

Personally, I've spent time trying to seek out data on how often treatment failures are documented. There are very few examples I've found where we've obtained useful information over time for particular pathogens. It is a really hard thing to work out because of all the complicating factors.

With that in mind, I'm interested in getting opinions from the practitioners on the panel on how big a problem AMR is in the field and whether it's a constraint on your ability to practice medicine.

• RISSER

Regarding the one case of resistance we had — *S. suis* was resistant to our normally used antibiotic — we had to raise the bar and go to a different antibiotic class. It's not that we didn't find an antibiotic that worked; it just wasn't the first choice we went with. Once we figured out what antibiotic was needed, it worked.

Based on my experience raising pigs without antibiotics, management is more critical than anything. The animal husbandry starting with those pigs on day 1 can change your bacterial profile and the immune status through the life of that pig. It really limits your room for error when you take away prevention- and control-use antibiotics and rely solely on individual treatment.

DAVIES

Did the resistance problem become apparent due to a clinical failure of response to treatment, versus shifts in susceptibility testing?

• RISSER

In the field, looking at the clinical picture, we weren't getting a response to our treatment. And that's when we started really looking at susceptibility information from the labs, which confirmed what we were seeing in the field. I think that's really important, even with measuring usage or resistance. We have to be correlating it back to what's happening in the field clinically and the outcome — the results of our practice.

What is the survivability rate? If resistance goes down, our survivability should get better. But if usage goes down, then our survivability gets worse. That's not a good message for our industry.

> "...if usage goes down, then our survivability gets worse. That's not a good message for our industry."
>
> JESSICA RISSER, DVM

• DUDLEY

I ran across an *S. suis* situation. Pigs were treated with amoxicillin in the water and clinically responded, even though phenotypic testing results at the laboratory came back resistant.

I continue to be confused on clinical versus phenotypical information. The other big challenge regarding treatment failures typically involves combination infections with viral and bacterial pathogens. That's where clinical responses are not what we would desire. I would say that's where we've had some of the biggest challenges addressing resistance and clinical responses to bacterial problems.

DAVIES

I think that's a really important observation. It also speaks to why things might be a little bit different in veterinary versus human medicine. In swine, we might see less resistance as a clinical problem because most of our patients are in their prime. On the other hand, in humans, physicians are dealing with generally geriatric and immunocompromised patients.

• NEREM

Clinically we're not seeing an appreciable increase or decrease in our ability to treat bacterial infections in swine herds. Yes, we've got the issue of co-infections with viruses. We deal with porcine reproductive and respiratory syndrome and swine influenza, but I would say we're not seeing an issue as it relates to resistance that way.

VI Aligning surveillance needs and goals

DAVIES

How should we establish a baseline, specifically for resistance rather than for use? What are the approaches for sampling? Do they differ in conventional versus antibiotic-free systems? Does geography matter? And in the end, what are we trying to achieve?

WISEMAN

It's important to assess what we do as an industry. In the slaughter plant, we have Food Safety and Inspection Service (FSIS) taking samples for AMR a couple of times per month. Typically, these samples are taken as cecal contents and sent for further analysis, starting in FSIS laboratories in Athens, Georgia. I assume they end up with further analysis in CDC. In a plant harvesting more than 20,000 head per day, two to four samples per month seems small. But I guess over time and over many plants, the data would be better than nothing, although we haven't seen anything yet.

SWEENEY

When the Zoetis surveillance program was initiated back in 1998, we thought the results would prompt us to do more research on newer antibiotics. Back then, judicious or responsible use wasn't a hot topic, but certainly in the last 5 to 10 years it has become one. The good news is that after more than 20 years, we're seeing very low incidence of resistance in swine.

HOLCK

It would be nice to take that one extra step and, as it was mentioned earlier, have a standardized method for adding clinical information with submissions. A lot of the submissions are done by production teams, but that's where I think veterinary oversight, at least in training, would be helpful. Whether the submissions come to the University of Minnesota, Iowa State University or wherever, we can start gathering field information, especially for clinical cases. We could have some alignment on the most important information relative to the history or the clinical situation of that farm.

> "It's important to assess what we do as an industry."
>
> **BARRY WISEMAN, DVM, PhD**

DAVIES

Yes, that's a good point. We have NARMS with its public-health perspective looking at four organisms coming in through the food chain. But again, it's a pretty small window, both in the intensity of sampling and a relatively small number of organisms.

We look at *Campylobacter* in swine because it's an important foodborne pathogen, even though there's almost no evidence that swine has any role in human *Campylobacter* infections.

In Denmark, they've published trends of macrolide resistance going down in *Campylobacter* infections, but there's not really any evidence it has any impact on the world. If our industry and veterinarians don't integrate that information, other people are likely to do it. Veterinarians are a unique group in terms of being able to provide context to surveillance data. One of the biggest concerns I would have is if people [out of our industry] set up streams of surveillance related to the food industry and put out nonsense.

TORRISON

I want to pick up on one of the things you said in terms of the data stream — specifically, what happens when it all comes together and advocates for us?

We need to take an active role in coming up with information and participating in understanding the correlations that may, or may not, be present between human health, animal health and antibiotic use. The One Health concept is something we're trying to paddle really hard on at the University of Minnesota, as are many other institutions.

Consider that fresh produce is becoming a leading cause of foodborne illness. Some of that is derived from animal-farm run-off or groundwater or surface water. Even among people not consuming animal products, there are elements of risk that are being ascribed that could well be true in some instances, but they might have other causes. For us to track trends, I'm interested to see where we'll wind up with some of the resistome work.*

continued

**Resistome is the collection of all the antibiotic-resistance genes, including those usually associated with pathogenic bacteria isolated in the clinics, non-pathogenic antibiotic-producing bacteria and all other resistance genes.*

VI Aligning surveillance needs and goals

> If we are up front with our surveillance and our reporting of our surveillance, we will get closer to the truth and be able to defend what we do, or change what we do so that it works better for everybody.
>
> JERRY TORRISON, DVM, PhD

It will be helpful to keep track of some of the gene loci or other genetic evaluations of resistance and then just the percentage of isolates that have resistance to different agents. Surveillance is all about counting. So, count how many bugs have how much resistance. Count how many resistant genes there are present and then track what's happening in the environment, associated or not associated with animal agriculture. Then see how it all winds up.

If we are up front with our surveillance and our reporting of our surveillance, we will get closer to the truth and be able to defend what we do, or change what we do so that it works better for everybody.

• NEREM

I fully agree. As an industry, we shouldn't look at the topic of antibiotic resistance to defend our current practices. We need to determine, particularly as it relates to surveillance for resistance, what the best methods are for "counting," as you say, and then take an honest look at the data we collect.

If there are things we're doing in practice as it relates to our current practices — whether it's how production systems are designed or how veterinarians are prescribing medications — we need to own up to that. By putting our foot forward, we're going to continue to build trust with the consumer, and that's ultimately the reason we're raising pigs to begin with.

It's critical for veterinarians to stand in the middle and provide leadership to help us better understand antibiotic resistance and what happens if the farm may or may not be contributing to that. If we're doing something to contribute to resistance, then we should change. If we're not, then we should obviously continue to make the best decisions for animals and for the public health.

DAVIES

The source of AMR data and, of course, who collected the samples affect our confidence in the information collected. So, whether we're 1) looking at consolidating data that might reflect information of importance to public health, or 2) trying to look at data to understand how our own practices might be influencing resistance in a broad sense, how important is it to set up an organized sampling structure and bring more consistency to the process worldwide?

• SWEENEY

I think one of the biggest problems with surveillance in general is a lack of harmonization. We've touched on that. It's difficult for human-health programs to compare their data; it's also difficult for animal health. A report recommending how to harmonize data with other programs would be a big step forward, but it's tough to do.

DAVIES

Harmonization could happen at multiple levels, although at the laboratory level it probably would still be a challenge. It's my understanding that many lab errors happen in the pre-testing, sampling environment. Dr. Risser, you raised the issue of sample quality.

• RISSER

We have to rely on production teams that are on the farms every week when they see the clinical signs of disease. We need to get the samples as soon as we can in an acute break. We use it as a teaching moment to correlate what we find at the lab with the quality of samples that they send in to what they're seeing in the farm. And over time, we've come a long way.

It goes back to who's going to pay for it. I've recently had customers ask about antibiotic-usage information. But is usage an indicator of resistance? Is it an indicator of the pigs' well-being?

> ...you can't have it both ways. If you don't treat pigs, it may increase the risk of abscesses or other defects.
>
> **BARRY WISEMAN, DVM, PhD**

I think there's going to come a time when consumers and customers want to know. It seems they want to know more and more every day. Country View Farms has always been very transparent and tried to answer all customer questions. It's difficult at times when we get questions from customers about antibiotic usage and mortality rates, because you can't always explain the situation or provide a good answer in a simple email. You need to have a conversation. How do we as an industry make that work? Will it become a right to entry into the marketplace?

• HOLCK

That's a very good point, Dr. Risser. What is the message to the consumer that's simple and straightforward? Do we know scientifically if AMR and antibiotic use are always linked? What about the intentional non-use of antibiotics in production? What impact does that have on food safety? We certainly can't make sense out of it yet, but we are building databases and need to be able to tell that story. On the one hand, at the production level, we need to get busy, get our boots dirty and understand what's really happening on the farm. On the other hand, the consumer needs to hear a story that's real.

• WISEMAN

This year the city of San Francisco enforced a 2017 ordinance which required grocers selling raw meat products to report and document antibiotic usage in the animals used in production, with the specific intent of reducing usage. This required us to look at levels of antibiotics individual producers were using and also allowed us to correlate these levels to carcass defects, such as abscesses. Our initial findings would suggest that reduced antibiotics will yield increased abscesses. So, I guess the point I'm trying to get across is that you can't have it both ways. If you don't treat pigs, it may increase the risk of abscesses or other defects.

• HOLCK

I fully agree, but I don't know if the consumer would see it that way. Generally speaking, consumers think less antibiotic use is good. Period. And as you pointed out from a health standpoint, from a product standpoint, that's not necessarily the story.

Back to today's topic — resistance — I'm not sure we know that clearly as well. I'd like to see us develop more information at the group level.

? DAVIES

Dr. Holck, please elaborate on what you mean by working at the group level.

• HOLCK

We have data from the GVL VFD database (Figure 1), gathered since the new VFD rule took affect in January 2017. About three-fourths of VFDs for swine are written at 5,000 head or less per VFD. I would equate that to a "group." One-quarter of them are written for more than 5,000 head, and in fact, 5% are written for 25,000 head or more. It's really hard to get data that's meaningful or allows an opportunity to assess issues like AMR when it does not specify a group or lot of pigs. I would like to see us get more information at the group level — that is, to know more about what actually happened in that group, whether it's a VFD or whether it's a prescription.

Just for context, it is my understanding that medicated feed or VFDs represent about 70% of antibiotic usage in livestock. Is that correct, Dr. Davies?

continued

VI Aligning surveillance needs and goals

DAVIES

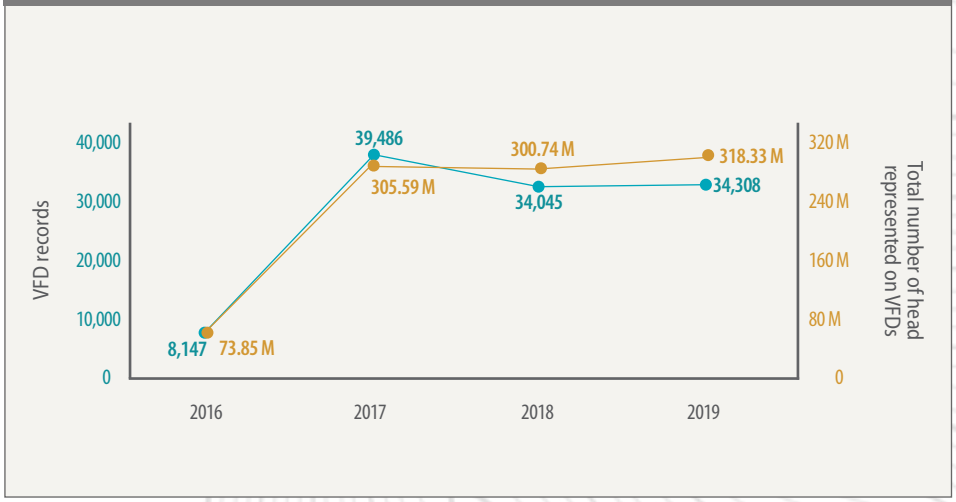
Yes, probably 60% to 70% of the antibiotic-usage data are from VFDs.

HOLCK

One other issue is that the labeled indications for use for some VFD products are ancient. Take, for example, the treatment options for bacterial enteritis caused by *E. coli, Salmonella* or *S. suis* — that's the most common indication for use selected for chlortetracycline (CTC) in swine in the GVL database. When we then look at the resistance patterns for those same pathogens, they tend to be resistant to CTC in the GVL database.

When the updated VFD rule took effect in 2017, we heard a lot of veterinarians, especially bovine veterinarians, express concern that their options for treatment were limited because some products were not indicated for the health problems they encountered in the field. Veterinarians didn't know what to do. I think that's also an issue to consider, although I know the pharmaceutical companies are in a quandary about what to do because it takes a lot of resources and some risk to update for indications for these older medications.

Figure 1. Veterinary feed directives issued for US swine 2016-2019



Source: GlobalVetLink

Note: According to USDA, there were 77.3 million hogs and pigs in the US as of December 1, 2019, up from 71.5 million as of December 1, 2016.

> One other issue is that the labeled indications for use for some VFD products are ancient.
>
> **TYLER HOLCK, DVM**

VII Justifying antimicrobial use to customers and consumers

DAVIES

Let's transition to discussion of whether measuring antibiotic use should be used as an indicator of antibiotic resistance. The FDA is now annually reporting pharmaceutical-industry sales data and instances of species use. The 2017 report showed a 33% reduction across species, with a 35% reduction in swine.[3] That was for total sales, and I think those numbers have been positive indicators for both FDA and the pork industry.

I'm also involved with a pilot project with FDA looking at antimicrobial usage across systems in the US. As you're all aware, many of the European countries have a lot more granular approaches, and even regulatory approaches, to how they're dealing with antibiotic use. But in the eyes of the public and others, how far down that road should we go? What gains can be made from surveillance, both within the pork industry and beyond it?

• TORRISON

There are many news stories circulating that make us question why a few people can impose their will on how we raise and care for livestock and what food-animal veterinarians should or shouldn't be allowed to do.

For example, we've read articles about the drilling in the Antarctic and pulling up 20,000-year-old bacteria that are antimicrobial resistant, indicating resistance is natural. That's an intriguing discovery, but we can't fall for that argument, however. Likewise, we can't assume that AMR in people is a bigger problem than it is in food animals and leave it to human medicine to fix. We need to consider pharmacokinetics.

> "We need more data to understand the pharmacokinetics and pharmacodynamics to help veterinarians make good decisions. And that's just the starting point."
>
> **JERRY TORRISON, DVM, PhD**

DAVIES

Can you give an example?

• TORRISON

Here's a case in point: We vacationed with some family who all came down with whooping cough. We were all put on antibiotics and were all given exactly the same dose, even though I weighed much more than many of the children at that time. I thought, "Well, that's an interesting way to manage the pharmacological aspect of it." We need more data to understand the pharmacokinetics and pharmacodynamics to help veterinarians make good decisions. And that's just the starting point.

We talk a lot today about precision farming, but what about precision *pharming*? How high of a tissue level can we get if we're dealing with respiratory disease in sick pigs? That's come up a number of times, but we're still lacking data for different aged pigs.

When I talk to veterinarians, some of them have some confidence, but nobody's completely confident they can take a product out in the field, treat pigs with it and really evaluate whether it was effective. If you have successive groups and you've got a *Streptococcus* that shows up resistant, that's clear. *E. coli* post-weaning seems to be harder. Because it's so complex with pig flows, barn cleaning, disinfecting and other factors that affect pig performance and the effectiveness of the drugs, it's pretty hard to get your arms around whether or not drugs are effective in the field. It's therefore a challenge for us to help guide people, because there are so many factors affecting performance of the pigs and disease dynamics.

• NEREM

My personal opinion is that we should be demonstrating to the consumer that we, as veterinarians and farmers, are responsible when it comes to the use of these tools. We also need to communicate that we disagree with the approach that many of the European markets have taken, which is to assume that society's concerns about AMR are basically met by arbitrary reductions in use. We don't personally believe that's the right thing for the animal.

As a group, we should continue to look for ways to use antibiotics more responsibly. We should also look for other tools — vaccines, for example — and other management practices that might allow us to manage diseases effectively. That will allow us to manage health in a better way without always

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relying on antibiotics. We fully support that, but we think arbitrary reductions are wrong.

In my opinion, we need to continue to tell a story to the public and to consumers about how we use antibiotics responsibly and what that means. Part of that, we believe, is that we need to monitor usage, but not for the sake of simply arbitrary reductions. Unfortunately, it's difficult to convince somebody you're being responsible with antibiotics if you can't tell them how much antibiotic you're actually using. That's a mindset that we, as an industry, are going to have to accept.

• RISSER

How critical is it to correlate antibiotic usage to the clinical outcome? Do we point to the survivability of the pigs? If consumers want usage to go down and we can't report it, is it important to then correlate it to how we're doing with other metrics so they can see and understand the impact of our responsible approach?

• NEREM

Yes, it's very important to be able to do that — and the veterinarian is the person that has the best perspective on that, right? When I look at the farmers we work with, as they monitor their antibiotic use, some years usage will be at a certain level and then the next year it might go up. We can put context to that if an increase in usage was due to a health challenge. But we can't simply not measure because we don't want to tell somebody how much we're using. It's hard to say that you're being responsible if you don't know which antibiotics or how much are being used.

• DAVIES

There's been some work done in different places showing that you've got more antibiotic use in situations where there's higher mortality or where you have more problems. Context is also important regarding treatment of pigs before they're clinically ill. For example, we may know that pigs arriving on the farm are from a sow farm with problems. Those things are really complex.

Another issue to consider is routine use of injectable antibiotics at processing and the need for post-weaning medications. Does that have any impact downstream?

Some of these discussions haven't occurred. I'm interested in any comments about the need for metaphylaxis — let's call it that for the moment — and the need for routine uses that may have downstream benefits and, as a result, reduce the need to treat animals later in life. I'll put that on the clinicians.

• DUDLEY

I would echo comments that we're always looking at different alternatives including vaccines, husbandry, management, flows, etc., to try and decrease antibiotic needs. I think as we self-reflect, there's no doubt that some antibiotic use is a habit.

To be able to step away and try to decrease antibiotic use, or at least question an antibiotic's use, is our responsibility. It's a bit more of a challenge with some producers than others. But I think we do have to push ourselves to take a look at some of those metaphylactic uses and re-evaluate how we correlate that to less antibiotic usage downstream.

> "...I think we do have to push ourselves to take a look at some of those metaphylactic uses and re-evaluate how we correlate that to less antibiotic usage downstream."
>
> **STEVEN DUDLEY, DVM**

Currently, the production systems or farms that I work with look at it on return on investment and don't necessarily tie it in to AMR. Resistance isn't part of the equation at all. They're looking at their return.

• TORRISON

There can be economies of scale that allow people to accomplish some improvements that aren't necessarily available to everybody. For example, on the poultry side, there's a tremendous movement afoot to raise birds without antibiotics. Much of the poultry industry is integrated, so they can completely depopulate a breeding herd if it gets contaminated with a bug they can't manage in an antibiotic-free system, which is fantastic if they have the wherewithal to do that. But if you only

have one breeding farm and you only supply a certain number of houses with birds, you're done.

Large, integrated producers can accommodate consumer demands by understanding the technology and by having the ability to use data to make changes that can be incorporated systematically through their systems. They have financial resources to weather the storms versus independent producers, who are doing the best they can but don't have all those options or access to the information or technology needed to make those changes. It squeezes the small- and medium-sized independent producers, which isn't necessarily fair, but it's the reality.

• RISSER

About routine usage: We have pigs we're raising without antibiotics. It wasn't something we did overnight. It's only half of our system, and it took about 15 years to implement effectively. We had to get a lot of good management practices in place. But when you start pulling away routine antibiotic use, you very clearly see room for improvements in animal husbandry and management. When you remove antibiotics, it removes all room for error and quickly displays where you need more cleaning and disinfection, or where you need iodine for spraying umbilical cords to prevent belly ruptures.

I think there is a need for metaphylactic use, but I don't want to say "routine usage" because you need to test that theory and question your antibiotic usage. Is this considered responsible use? What are the welfare ramifications if I don't? For that reason, I'm still a strong advocate for judicious, preventive usage in some situations, as long as it's under veterinary supervision. I've seen what happens when you arbitrarily take the antibiotic away and the impact that has on the health and welfare of the herd downstream.

> "I've seen what happens when you arbitrarily take the antibiotic away and the impact that has on the health and welfare of the herd downstream."
>
> **JESSICA RISSER, DVM**

• NEREM

I agree with that. I've certainly seen the benefits of responsibly using antibiotics for disease-prevention purposes or metaphylaxis-type treatments. There is certainly medical value there when we look at the outcome. I've also probably not had as many conversations with consumers as you have, Dr. Risser. I have had some engagement with retailers we've brought in to help their sustainability teams view modern pig farming.

When we brought in the retailers and were explaining how we use antibiotics, we were able to provide exquisite records from a producer that showed exactly when and how animals were treated.

Despite our good records, adherence to the Animal Medicinal Drug Use Clarification Act of 1994 and use of good diagnostic data, the retailers were ultimately most concerned about the routine use of antibiotics in feed or water to all groups of pigs in a particular production flow. We as a profession need to be prepared to address this concern as well.

• RISSER

In some of the conversations I've had with non-governmental organizations, there isn't as much concern about antibiotic usage for surgical procedures like castrating or tail-docking as there is about antibiotic use in water and feed post-weaning.

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DAVIES

I think it's getting more difficult because of the developments in Europe, where they've put out more stringent rules regarding prophylaxis and metaphylaxis, which some consumer groups perceived as "evils" because, unlike veterinarians, they didn't understand the practice and didn't see it as responsible use.

Using antimicrobials to prevent or control an infection is sometimes a difficult conversation to have with people outside of agriculture, because it winds back to, "Well, if you weren't producing the animals on these large commercial farms, you wouldn't have to do this." That's a really tough part of the argument.

With that in mind, I'd like to cover one other important topic related to antimicrobial use — specifically, the need to re-evaluate treatment protocols and their frequency.

Recently, I spoke with a Dutch veterinarian about mandatory reductions in antibiotic use. He said they saw a 50% reduction under the new laws, and most of the decrease resulted from discontinuing antibiotics they were "using out of habit." They realized they didn't have to use them.

So, regarding our own judicious-use guidelines, is there any emphasis on how often we need to re-evaluate? It may be difficult for independent producer clients versus the large integrators who can spread risk over multiple sites.

• **DUDLEY**

Well, in my world, living in southwestern Minnesota, biosecurity is a huge deal. But we've also got a tremendous population of other animals that makes arbitrary reductions a little bit more of a challenge. If I could get improved husbandry and health and repopulate herds and do all of those things, that would quickly reduce antibiotic use. But as mentioned, it's a different decision if they have one farm versus 50.

DAVIES

In Denmark, they're measuring not only the producer's antibiotic use but also each veterinarian's use across their client base — and they've got benchmarks for that.

One of the ways veterinarians stay under the critical limit is to get rid of clients who are ruining their average. That's a stark reality. If we go down that road — and let's and say there's going to be a subset of farms and producers out there where biosecurity, management and everything else isn't what it should be — that's going to be difficult to manage with some independent producers.

To me, it's ironic that some of these consumer-motivated initiatives that are critical of large systems actually cause more hardship on the smaller, independent operations and, as a result, shift the industry toward larger systems. It's easier to guarantee food safety to customers when you control your supply chain.

• **DUDLEY**

I would agree 100% with that. It's an interesting dichotomy. A lot of the folks who are super-concerned about AMR are also opposed to large, corporate entities, but increased regulation makes it more challenging for small, independent producers to be competitive.

• **TORRISON**

We haven't discussed environmental health. There's not only the resistance question but also the primary product, metabolites and the impact on the environment. That's part of the equation that we can't just write off as insignificant. And I don't have answers for that.

> "...in my world, living in southwestern Minnesota, biosecurity is a huge deal."
>
> **STEVEN DUDLEY, DVM**

VIII Closing remarks

> Consumers and customers want more and more transparency. We need to find ways to streamline it so that systems, independent producers and all stakeholders in the industry can participate.
>
> JESSICA RISSER, DVM

DAVIES

It's been an informative and thought-provoking discussion. Before we adjourn, would you each briefly predict where you think the pork industry will be in the next 5 or 10 years from now, regarding antimicrobial surveillance and the issue of resistance?

WISEMAN

I would hope that the issues of antibiotic surveillance would be resolved through additional recordkeeping. There will be a new market for antibiotic substitutes that will not be seen as promoting resistance. As the New Swine Inspection System is further defined by USDA, opportunities will be created for liveside veterinarians to assume more responsibility for pathology seen at post-mortem examination in the plant. This will create new challenges to reduce disease in both the farm and the plant. Food safety and reduction of food pathogens will become more important both through economic and regulatory pressures.

RISSER

Look at what's happened already in Europe. There's a pattern. US pork customers ask for similar information from 8 to 15 years after EU customers. We'd better get working on how we're going to report antibiotic use as an industry. I know we've been working on it, but how are we going to streamline reporting, so we have information available?

Consumers and customers want more and more transparency. We need to find ways to streamline it so that systems, independent producers and all stakeholders in the industry can participate. And we need to do it in a way that tells our story from an ethical standpoint. What does it mean to food safety and to animal well-being? That's the challenge.

DUDLEY

I believe there will be increased surveillance over the next 5 to 10 years. I agree with Dr. Risser's comment that we tend to follow whatever happens in Europe. I think that VFD and changes to water-medication prescriptions were a first step toward evaluating antibiotic use in the swine industry. In veterinary medicine, I think that in the next 5 years we'll see some sort of evaluation by criteria, either by production system or by veterinarian.

We also need consistency among species so that the poultry or cattle industry doesn't throw us under the bus, despite our good record for using antibiotics responsibly. It's important for us in the pork industry to work with all production-species groups to have that conversation.

Labor is a challenge for most pork producers, and I don't see that changing. I think we have to be mindful that labor is a component of feed and water as opposed to individual injection. And if it's easy people will do it, and if it's not they won't. So again, how we tie that in to welfare and mortality — that's a message that's hard to take back to the public. Is it okay if we have 10% mortality and decreased antibiotic use? How does that tie into resistance? So those are concerns I have.

The last concern would be how our information will be used by anti-agriculture or anti-meat groups. Will they spin it in a way that's anti-agriculture? We have to be mindful of that as we talk about all these issues and remind people we have a very safe, wholesome and abundant food supply.

TORRISON

Sometimes students ask where they should take their career in research. I like to tell them that microbiome is actually a Greek word that means "your grant will get funded."

So, partly we have to follow where people are investing money, whether it's from the governments or other entities. The CDC, USDA and FDA seem happy to be exploring the potential for using various molecular methods to characterize what's going on with AMR, and I expect that will grow, at least in the short term.

continued

VIII Closing Remarks

I think our job is to make sure we're swimming alongside as hard and fast as we can to make sure we bring the practical realities of animal agriculture and how science interfaces with agriculture, the environment and the public, because we have a corner on that in the veterinary world.

Unfortunately, we haven't brought the human medical side along with us maybe as fast as we would like. It will be our job to make sure we pull all that information together with really good science but also with a really good understanding of how all this fits together.

• HOLCK

I continue to be excited about precision "pharming," and before today, I was thinking that was spelled with an "f," but I guess for this issue it is with a "ph."

I think we've got a lot of good information to make informed decisions. Labor is an issue, but with our mobile technology, we can gather more information.

So, where are we going to go? I think we're going to get more precise, but again, I think we need to work at the group level where we can measure outcomes. Whether it's performance, whether it's resistance, whether it's welfare issues — all of these can then be linked together.

The other point I want to make is about the consumer: I don't see them distinguishing between antibiotic resistance and antibiotic use. We need to be cognizant of that and communicate accordingly.

• NEREM

Considering the trajectory we're on, consumers are interested in transparency — about where their food comes from and the practices we're using to produce it.

Certainly, they have a concern about antibiotic resistance, and we, as farmers, veterinarians and the pork industry, need to continue fostering a genuine effort at transparency in how we're raising pigs. We need to also demonstrate very well that we are being responsible and have the public's best interest in mind.

I think we're going to have to continue to do more and more work on surveilling resistance as well as tracking and being transparent about the amount of antibiotics we're using and why. I think that's the general direction and we're going to have to all do that.

• SWEENEY

I'm encouraged by the pork industry's direction and commitment to responsible antibiotic use. Even within our advanced surveillance program at Zoetis, we continue to see low resistance in the pig sector. We have the luxury of comparing that data to other programs. We see high rates of resistance in the bovine program.

I am often asked why there's low resistance among swine versus high resistance among cattle. I don't know the answer. My guess, though, is management. It might have something to do with all-in/all-out management in the swine industry.

But make no mistake, surveillance is an opportunity, especially in swine, to look more closely at management practices versus bovine management, where we see higher resistance rates. Surveillance will challenge all of us to look at management practices for animals.

"I'm encouraged by the pork industry's direction and commitment to responsible antibiotic use. Even within our advanced surveillance program at Zoetis, we continue to see low resistance in the pig sector."

MICHAEL SWEENEY, MS

DAVIES

Our time is up, so I thank everyone for their enthusiastic participation. I've learned a lot from all of you. It was a great conversation.

[1] Centers for Disease Control and Prevention. https://www.cdc.gov/drugresistance/index.html

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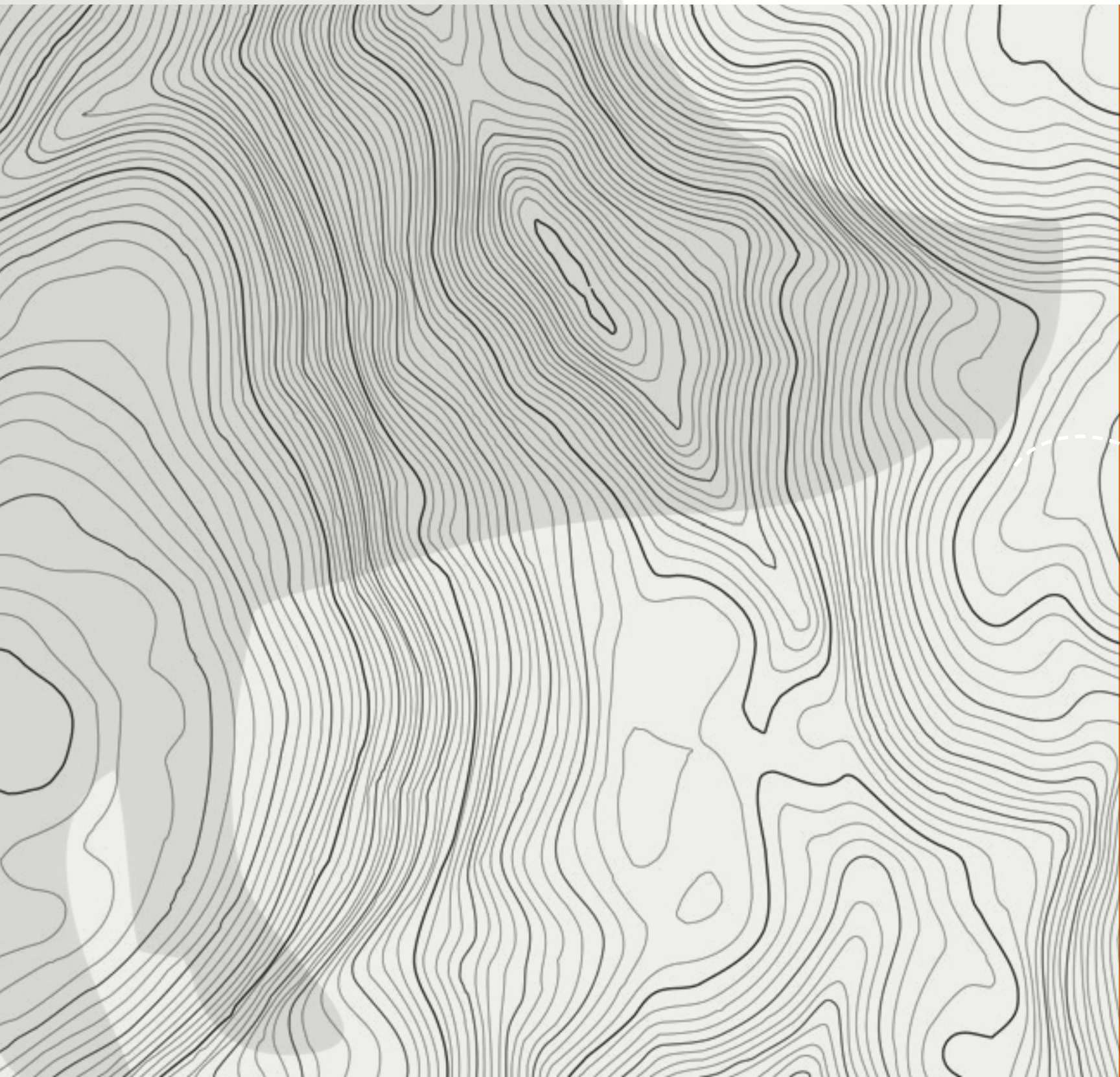
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