Ractopamine Free Pork and Implications for Use in Growing Pigs: Frequently Asked Questions

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In order to gain and preserve access to international markets that have banned the use of ractopamine in swine, several United States processors announced their intention to process only pigs that are free of ractopamine. There have not been recent changes to the regulatory status of ractopamine in the United States and processor approaches to eliminating ractopamine from their pig supply have varied. What follows represents an attempt to summarize the relevant scientific data about ractopamine in the pig, producer experiences and anecdotal information to guide producers adjusting to the new requirements. This document will be updated as new information is available. Specific references are available on request.

Q1: What is ractopamine, what does it do, and how long do the effects last?
A1: Ractopamine (Paylean®, Engain®) is a feed additive that changes how the pig partitions nutrients and energy to muscle and fat cells. It increases the amount of protein deposited in muscle cells and increases the rate that fat is removed from storage. The net effect is that a greater portion of the carcass is lean protein. The drug accomplishes this by activating a receptor on the surface of cells in the pig. Ractopamine is fed in the period immediately prior to marketing because these effects peak after a few weeks of continuous feeding and begin to subside. The changes to protein and fat deposition are not permanent and the rate of protein and fat deposition gradually returns to near baseline levels when ractopamine is no longer binding the cellular receptor. Although gradual, changes can be observed as quickly as seven days after removal of ractopamine from feed.

Q2: What is the difference between the United States Food and Drug Administration (FDA) "tolerance level" and being completely free of ractopamine?
A2: The FDA tolerance level is the level above which it is illegal to market a pig into the human food chain. This is a federal standard and applies to all pigs processed for consumption by humans. Pigs with levels above the tolerance are considered adulterated and cannot enter the food supply. The FDA tolerance level is based on an "acceptable daily intake" (ADI) by humans that would not cause any effects when consumed. This level is determined by scientific studies, includes a safety factor, and considers both average human body weight and average pork portion size of edible tissue. The resulting level in pork that allows consumption by humans and results in human levels below the ADI is the tolerance level in pork.

Note that this does not consider non-edible tissues (such as urine or hair). In the case of ractopamine, the target tissues that were important to the determination of the tolerance level were pork liver and muscle. Additional studies demonstrated that nearly as soon as ractopamine treated pig food is removed, pork liver and muscle fall below these tolerance levels for human consumption. However, the edible tissues are not completely free of ractopamine and it is possible that non-edible tissues (such as urine and hair) have

higher levels than liver or meat. When processors require pigs to be completely free of ractopamine and test the pigs to confirm this, levels must be lower than the sensitivity of the test used in the tissue tested. While the FDA tolerance in muscle is 0.05 parts per **Million**, there are tests available that can detect ractopamine in swine tissues at 0.25 parts per **Billion**. There is approximately a 1000-fold difference between what is safe to market per the FDA tolerance and what can be detected in the pig by most tests including those that could be used by processors to verify that pigs they purchase are truly free of ractopamine.

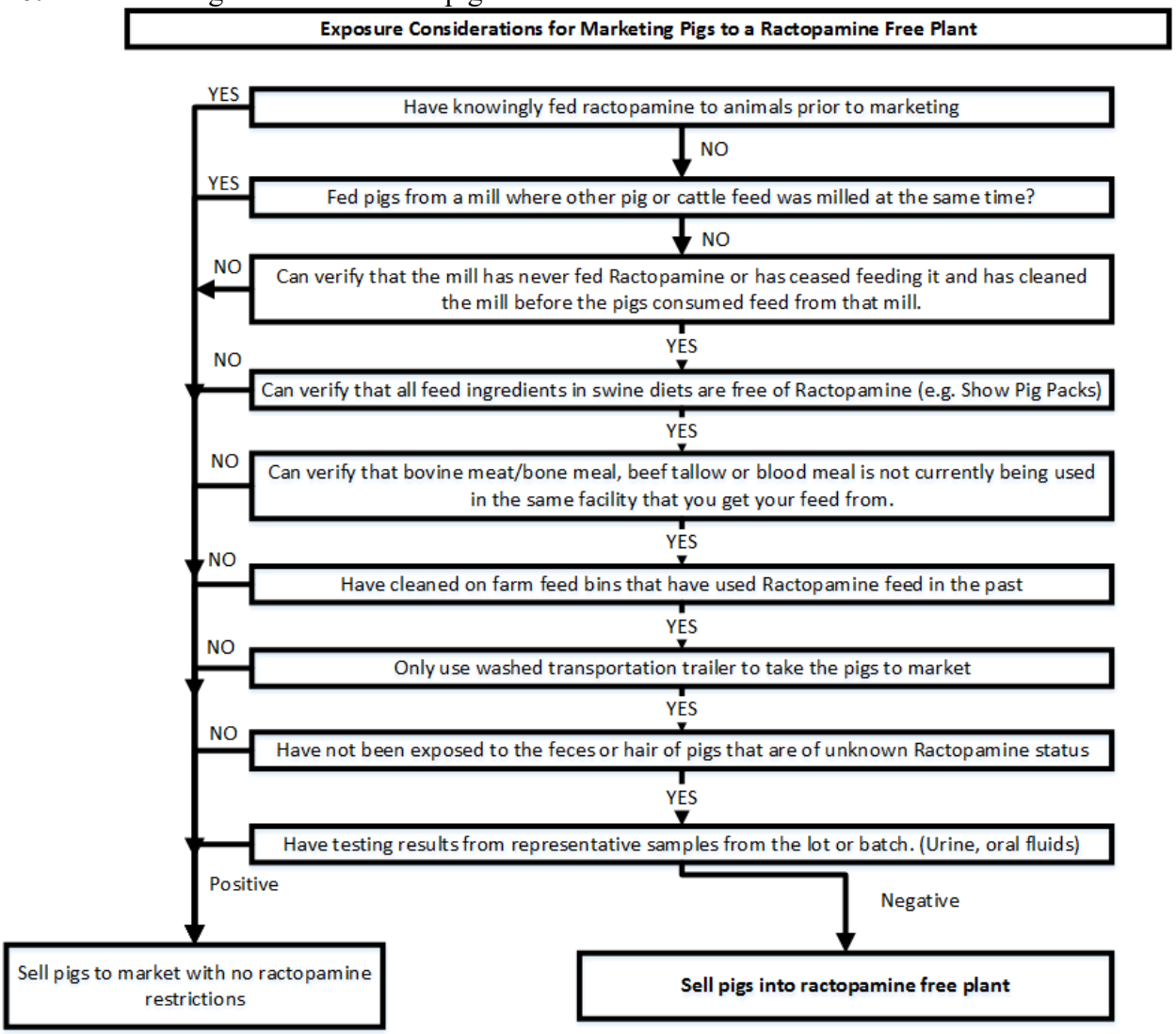
Q3: How much additional withdrawal time does it take to go from the FDA tolerance level (0.05 PPM) to a level that would test negative or free of ractopamine in most tests (0.25 PPB)?
A3: Unfortunately, there is not a study that directly measures this. At a minimum, ractopamine can be detected for 42 days after the end of feeding in pig hair. However, we do know that carcass changes induced by ractopamine are not permanent and begin to revert to the animal's baseline phenotype as soon as ractopamine is removed. So, it is likely that most or all benefit of feeding ractopamine would be lost by the time that the pig tested negative.

Q4: Given the extreme sensitivity of the tests available, can cross-contamination cause pigs that have never been fed feed treated with ractopamine to potentially test positive?
A4: There are a variety of reports that have identified cross-contamination between treated and untreated pigs as a likely problem. Contamination can happen directly through contaminated urine, feces, bedding and feed that untreated pigs have access to in pens or livestock trailers. Contamination has been anecdotally reported in swine and there are published examples in swine and other species. In one study, meat and bone meal was intentionally contaminated with 56 ppm of ractopamine and fed to pigs at a 7% inclusion rate. This led to pigs testing positive by urine testing. Further, in this study, one of the control diets was contaminated at the mill despite a plan for preventing ractopamine contamination. This was detected in the urine of pigs that were not fed the meat and bone meal and were part of the control group. A hospital based-prospective cohort study found that 8.1% of a human cohort of 370 patients tested positive for ractopamine in urine above a limit of detection of 0.026ppb. These levels were presumably obtained from the diet. Anecdotal reports from companies and feed mills that have eliminated ractopamine entirely indicate that detailed and repeated cleaning of all areas, even those that do not contact the feed directly, is necessary to achieve levels below current testing capabilities. Feed bins and feed lines on farms that have previously fed ractopamine must be cleaned as well to prevent contamination.

Q5: What happens if the processor finds a residue of ractopamine?
A5: If ractopamine levels are measured that exceed the FDA tolerance level by Food Safety and Inspection Service testing, FSIS will coordinate the appropriate follow-up, including notification to the Food and Drug Administration (FDA), AMS and FSIS District Enforcement Operations (DEO). FDA and FSIS/DEO will pursue regulatory action including criminal prosecution, where warranted. Each phase or ownership stage will independently have to demonstrate that their system requirements are adequate and are meeting standards. If the plant's own testing finds evidence of ractopamine, the plant will determine the response to the owner or producer. The producer is encouraged to contact the plant of interest directly to understand requirements and implications of positive tests.

Q6: Do you have a checklist of steps that need to be considered to market my pigs to a ractopamine free harvest facility?

A6: The following flowchart will help guide considerations:



Q7: If I need my pigs to be ractopamine free, what do I need to do in terms of cleaning my feeding equipment/barn at home?

A7: Everything that has come in contact with ractopamine treated feed, pigs that were fed ractopamine (urine, feces, hair, etc) or dust from feed treated with ractopamine will need to be cleaned with soap and water. Pay special attention to:

- Discontinue getting feed from a feed mill that uses ractopamine, and discontinue its use at your farm at harvest. None of this feed should carry over to the next groups.

    - This would include any mill that feeds any ractopamine based products (Optaflexx® or Actogain® for cattle as well)
- Bulk bins, augers and feeders should be thoroughly washed for the next group of pigs. Clean up efforts may take months and repeated efforts to totally clean up.
- Be aware that bovine products in diet ingredients such as bovine meat, bone and blood meal, and tallow can be contaminated with ractopamine.
- Ractopamine is eliminated mostly via urine, but a significant portion is eliminated in the feces as well. This means that proper cleaning of pens, pits and anything in contact with these waste products is necessary to avoid exposure to subsequent pigs.
- There are anecdotal reports of pigs that were raised with ractopamine free feed testing positive at processing after transport in livestock trailers that previously hauled ractopamine fed pigs. Controlled research testing the parameters around how this might occur is not available.
- Although Ractopamine is at safe levels within 12 hours as per US regulations, it is near impossible to eliminate the residue to a level below detection by tandem mass spectrometry The entire operation or farm should be cleaned thoroughly to avoid contamination of waste, fluids, and even dust from previously Ractopamine fed pigs.

Q8: Do I need to talk to my feed mill where I am purchasing feed to ensure that they have steps in place to prevent potential residual?
A8: Yes! A clean feed mill with strong quality control to prevent contamination is a vital part of ensuring a ractopamine-free feeding program. Given the very low detectable levels of ractopamine in pork, cross contamination from feed is a significant potential issue if your mill also makes feed for other species using ractopamine. It may be a good idea to ask your feed mill if they stock ractopamine for other clients to gauge your level of potential cross contamination risk.

Q9: Will I be able to show pigs that have been treated with ractopamine at county and state fairs?
A9: At this time, county and state fairs are making decisions about allowing ractopamine in competition animals. It will likely depend on the ability of each terminal show to find a processor for the pigs and what that processor's expectations regarding ractopamine are currently. Not all processors in the United States have banned ractopamine at this time. Given the ease with which contamination of ractopamine free pigs can occur, shows may need to ban ractopamine completely to find a buyer that will purchase the pigs from the show.

Q10: Is there a test which would allow checking pigs at a county fair with results before pigs are shipped?
A10: There are a variety of validated tests including liquid chromatography–mass spectrometry (LC-MS), gas chromatography–mass spectrometry (GC-MS), lateral flow devices (LFD) and ELISA (ELISA) tests. Both LFD and ELISA tests can be deployed in the field at pen side in nearly real-time but GC-MS and LC-MS are laboratory-based tests. In total, there are at least 11 tests that are validated, the lower limit of detection ranges from 250ppb to 0.25ppb and these tests have been validated in feed, urine, tissue, and

plasma. Testing has also been reported for hair using LC-MS, and the limited data on hair has found ractopamine for at least 42 days after the end of treatment. Since the study ended there, it is likely that hair would be positive longer. These testing options range in cost from $250 - $675 per sample. You should consult with your veterinarian or diagnostic laboratory to establish which test is most appropriate for a specific situation.

Q11: What do we do with county fair pigs if packers refuse to purchase them because of ractopamine use?
A11: Fairs may consider banning ractopamine or marketing to a buyer that is not ractopamine free. Cross-contamination at several levels makes it unlikely that ractopamine exposed and ractopamine free animals could be housed and shown at the same fair and any marketed as ractopamine free.

Q12: Can packers or counties have parents/exhibitors sign an addendum to the drug residue statement saying pigs have never been fed ractopamine?
A12: Discussions about solutions for exhibit and competition pigs will have to involve a variety of stakeholders to develop a fair and practical system that allows all parties to be successful.

Q13: If liver is the marker tissue for FDA and FSIS compliance, is liver the tissue that will be used by processor driven testing to confirm that a pig has never ever been fed ractopamine?
A13: Processor testing to confirm that pigs are free of ractopamine may use a variety of tissue, fluid and test combinations based on that processor's objectives, resources and abilities. Liver is not a gold standard for zero tolerance. In the US, drugs that have a tolerance, as defined by the US FDA, also specify a tissue for the measurement of that tolerance since different tissues can have different levels of drug and require different times to eliminate a drug. For ractopamine, the United States FDA has established two tolerance levels and producers must be below both levels to comply. In swine, a tolerance of 0.15 ppm is established for liver, and 0.05 ppm for muscle. There are tests validated for these tissues as well as other tissues such as urine and plasma. If a US processor has established a zero tolerance for the pigs they buy, they may, or may not specify which tissue they are testing. A zero tolerance implies that all tissues would need to be free of the ractopamine. Specific processor protocols have included collecting bladders at processing and testing urine, plasma testing and oral fluids collection in lairage for testing prior to euthanasia. Other protocols are possible and are not standardized between all plants.

Q14: If an exhibitor buys pigs from a sale in March, that were fed ractopamine for a week before the sale, but exhibitor does NOT feed ractopamine the entire summer for the state fair in August, will the urine be negative, but tissue positive?
A14: The label for feeding ractopamine stipulates it is to be fed for the last 45 to 90 pounds of gain, meaning that feeding it to feeder pigs pre-sale (feeder pigs in March) likely illegal. No scientific studies have been published investigating the effects of ractopamine for the length of time between a potential March sale and August slaughter date. Therefore, we do not know for certain how long ractopamine could potentially be found in any tissue. It is found in hair at least as long as 42 days and would likely be found in these potential situations.

Q15: If an exhibitor hauls their pig that has NOT been fed ractopamine in the same trailer as their heifer that has been fed Optaflexx® (a cattle product containing ractopamine), can their pig test positive ractopamine?
A15: Unless the trailer is well cleaned, there is a risk of cross contamination that would be detected by current testing in a variety of tissues. Ractopamine is water soluble so thorough washing using soap and warm water should substantially reduce this risk. Both cattle and pigs excrete a portion of ractopamine as intact molecule that could then be consumed by another animal and potentially result in a positive test at the sensitivity levels of current tests. This has not been confirmed by direct measurement or scientific study at this time.

Q16: If an exhibitor is feeding ractopamine to pigs for a non-terminal youth show (summer type conference) where ractopamine is not banned, will the pigs in the same barn NOT being fed ractopamine have trouble at the state fair?
A16: While every situation is different, given the extremely low levels at which ractopamine can be detected in tissues and urine, cross contamination (even through feed dust) could possibly result in ractopamine positive animals that have never been directly fed ractopamine. This has not been confirmed by direct measurement or scientific study at this time.

Q17: If ractopamine is banned from use at a fair or exhibition with zero tolerance, and the standard test is urine (only champion and reserve have tissue samples taken), will urine be a clear way of eliminating competitors that use it?
A17: Urine testing will confidently identify pigs to which ractopamine has been fed. However, given the sensitivity of the testing available, it may also identify some animals that have been contaminated accidentally. It should be noted that either scenario (intentional use or contamination) is problematic for processors that are marketing pork to countries where it has been banned. There is likely a useful difference in concentration of ractopamine that would discriminate direct feeding (at least within a window that would provide competitive benefits) versus contamination of untreated animals. However, research is needed to determine what those levels might be or how reliably direct use could be distinguished from contamination.

Q18: If the manufacturers of swine ractopamine products withdraw them from the market in the near future, but ractopamine products are still FDA approved for swine, can producers substitute cattle products such as Optaflexx® for use in pigs?
A18: Products that are approved for use in feed may not be used in a manner that does not follow the label instructions. If a product is not labeled with instructions for feeding pigs, it cannot be legally used for pigs. If FDA approval is withdrawn, it will no longer be permissible to use even from stockpiled stores that were purchased prior to the date it is pulled from the market. There is no allowance for extra-label use of feeds containing ractopamine. The label must be followed exactly. This means that ractopamine that is only labeled for other species (such as Optaflexx® in cattle) cannot be legally fed to swine.

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