

# Can Subtherapeutic Levels of Antibiotics be Eliminated from Swine Diets?

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## ■ The Banning of Antibiotic Growth Promoters

### The Issues

The issue concerning the use of subtherapeutic levels of antibiotics in animal production to enhance growth and performance (i.e., antibiotic growth promoter, AGP), and the perceived risk associated with the emergence of antibiotic-resistant bacterial strains has developed into a global issue. The use of AGP's in animal agriculture and the potential link to the development of antibiotic-resistant bacterial strains which could potentially affect human health has become a topic of discussion for conversations originating from coffee shops to the White House. The issue has also turned into a media feeding frenzy which has fueled the general public's demand for the elimination of AGP's from animal agriculture. However, the public's outcry for the ban on AGP's and the possible link to the development of antibiotic-resistant bacterial strains has not been scientifically substantiated. Experts world-wide have served on numerous scientific and non-scientific committees to review and report on the possible link between AGP's and the evolution of antibiotic-resistant bacterial strains, yet no conclusive evidence has substantiated this possible link. Unfortunately, the lack of scientific evidence has not abated public concerns, and has not prevented the effort to ban the use of AGP's in animal agriculture. Fortunately, while the future of AGP use in animal agriculture hangs in the balance, efforts have been underway for years to identify non-antibiotic alternatives to AGP's.

### The Options

It has been suggested, and generally agreed upon, that the beneficial growth and performance responses associated with feeding subtherapeutic levels of

antibiotics stems from their preventative action on sub-clinical infections or competitive bacteria in the intestine (Doyle, 2001). It is also thought that by preventing sub-clinical infections, nutrients which would normally be utilized for immune function may be spared and diverted towards growth (Stahly, 1996; Williams et al., 1997). Therefore, it would seem logical that a viable alternative to AGP's would need to provide similar immunological protection from sub-clinical infection in order to achieve similar growth and performance benefits.

But which non-antibiotic alternatives truly provide a viable and scientifically proven alternative to AGP's? Should producers move towards the use of acidifiers, enzymes, probiotics, botanicals or competitive exclusion products to replace AGP's? And will these alternative compounds provide the beneficial growth and performance advantages which have become a necessity for profitability in animal production? The available propaganda on the use of various compounds to prevent disease and infection, or to stimulate immune function grows on a daily basis. Additionally, many of the claims associated with the beneficial effects of some of these compounds, especially with the various botanicals, have not been scientifically documented, and are often based on anecdotal data or testimonials.

One particular class of compounds, immune system modulators, has received considerable attention in recent years, and has been the subject of many scientific studies, especially in the area of animal agriculture. The primary immunologically active compounds which have been investigated in the arena of animal agriculture include antibodies, cytokines and various nutritional supplements such as spray-dried plasma (SDP) and fish oil. While scientific studies on each of these have provided promising results, the focus of the remainder of this report will be on the use of SDP in swine production.

## ■ **Spray-Dried Plasma**

### **Introduction**

Over the past 20 yr, weaning age has been reduced from 28 to 21 days (or less) in U.S. swine production systems. As a result, pigs are smaller and have less mature immune and digestive systems at weaning, making them more susceptible to problems in the early postweaning period. During the early 1990's, in an effort to enhance postweaning growth and performance, SDP was being added to the first diet after weaning. Data from initial studies indicated that the addition of SDP to the first diet after weaning could dramatically improve feed intake and growth (Hansen et al., 1993; Cain, 1995; Coffey and Cromwell, 1995; de Rodas et al., 1995).

## Mode of Action

While the exact mechanism by which SDP improved postweaning growth and performance has not been identified, several possible modes of action have been suggested, ranging from improved palatability (Ermer et al., 1994) to providing immune protection either from the beneficial affects of the immunoglobulin fraction of SDP (Coffey and Cromwell, 1995) or from the ability of SDP to prevent pathogen adhesion to the intestinal mucosa (Nollet et al., 1999).

Currently, the majority of available research data would support an immunologically protective effect of SDP. In fact, mounting evidence does suggest that the fraction of SDP that contains immunoglobulins yields similar performance to feeding whole SDP (Cain, 1995; Gatnau et al., 2001). Research trials have demonstrated that the response to SDP was greater in a conventional on-site environment versus an off-site environment that is managed to reduce the potential pathogen exposure to the weaned pig (**Table 1**; Coffey and Cromwell, 1995). Additionally, recent studies using *Escherichia coli* (*E. coli*) challenges in cattle and pigs have demonstrated decreased mortality with the feeding of SDP (Quigley and Drew, 2000; Bosi et al., 2001).

Similarly, recent research in our laboratory would suggest that the enhanced performance of pigs consuming SDP may be the result of the pigs being more immunologically naïve than pigs consuming diets with no SDP (Carroll et al., 2002). Thus allowing more nutrients to be diverted to growth rather than utilized for immune functions. In support of this theory are our results which demonstrate that pigs fed SDP exhibit greater immune stimulation when challenged with an endotoxin from the cell wall of *E. coli* (i.e., lipopolysaccharide; LPS) as demonstrated by increased serum cytokine responses associated with the acute phase immune response (**Figure 1**; Touchette et al., 2002), and a greater activation of the stress axis (**Figure 2**; Carroll et al., 2002). We speculate that the increased immune and stress responses noted in pigs fed SDP is related to the lack of immunological priming. As noted previously, feeding SDP is thought to have a protective effect in the pig, such that the immunoglobulins present in SDP are thought to bind to and prevent attachment of pathogens to the intestine, although other mechanisms may also be involved (Nollet et al., 1999). Preventing pathogen attachment in the intestine would limit activation of the immune system, thus resulting in an animal which would not be fully immunocompetent, and would therefore have a greater immune response to an immune challenge such as LPS which bypassed the intestinal mucosa. This theory is also consistent with the previously noted reports that the beneficial effects of SDP on growth and performance are more pronounced in conventional on-site production systems where the endemic pathogen load would be greater compared to an off-site environment.

**Table 1. Effect of protein source and environment on performance of early weaned pigs <sup>1,a</sup>**

Protein Source <sup>b</sup>	Experimental Nursery		Conventional Nursery		CV
	DSM	SDPP	DSM	SDPP	
<b>Days 0 to 14</b>					
Gain, g/d <sup>cd</sup>	263	277	214	300	8.9
Feed intake, g/d <sup>efg</sup>	402	470	251	399	10.7
Feed/gain <sup>hi</sup>	1.53	1.70	1.18	1.34	9.9
<b>Days 14 to 28</b>					
Gain, g/d <sup>i</sup>	510	514	439	447	7.8
Feed intake, g/d <sup>i</sup>	894	874	758	715	8.0
Feed/gain	1.76	1.71	1.72	1.60	6.5
<b>Days 0 to 28</b>					
Gain, g/d <sup>hi</sup>	386	396	327	373	6.6
Feed intake, g/d <sup>ij</sup>	648	672	504	557	6.6
Feed/gain <sup>i</sup>	1.68	1.70	1.54	1.50	3.5

<sup>1</sup>Recreated from Coffey and Cromwell, 1995

<sup>a</sup> Five replicate pens of four pigs per pen; 5.3 to 15.7 kg; 28-day test

<sup>b</sup> DSM – dried skim milk; SDPP – spray-dried porcine plasma

<sup>c</sup> Protein source x nursery environment interaction (P<0.005)

<sup>d</sup> DSM vs SDPP within the conventional nursery (P<0.001)

<sup>e</sup> Protein source x nursery environment interaction (P<0.05)

<sup>f</sup> DSM vs SDPP within the experimental nursery (P<0.04)

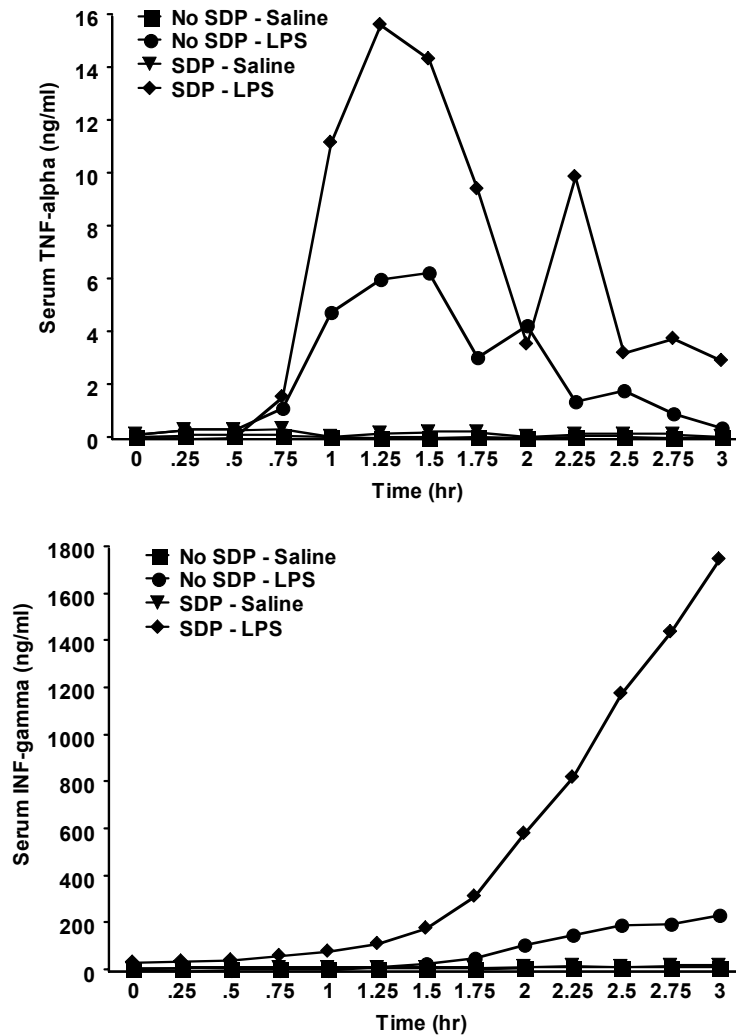
<sup>g</sup> DSM vs SDPP within the conventional nursery (P<0.001)

<sup>h</sup> DSM vs SDPP averaged across nursery environment (P<0.04)

<sup>i</sup> Experimental vs conventional nursery environment averaged across protein sources (P<0.001)

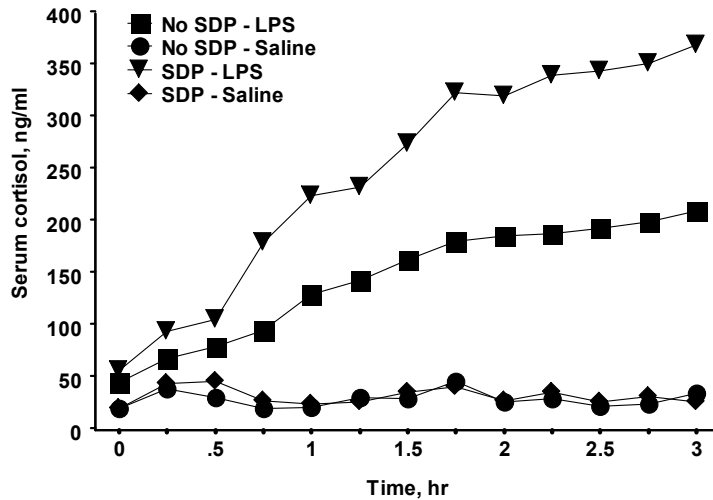
<sup>j</sup> DSM vs SDPP averaged across nursery environment (P<0.06)

**Figure 1.** The effect of spray-dried plasma (SDP) and lipopolysaccharide (LPS) treatment on serum tumor necrosis factor –alpha (TNF- $\alpha$ , top panel) and interferon gamma (IFN- $\gamma$ , bottom panel).



There was a significant diet by LPS treatment interaction ( $P < 0.05$ ) for serum TNF- $\alpha$  and IFN- $\gamma$  such that pigs fed the diet with SDP responded greater than pigs fed the diet without SDP. Error bars omitted for presentation purposes. Pooled SEM for serum TNF- $\alpha$  and IFN- $\gamma$  were 0.283 ng/ml and 29 ng/ml, respectively. Data from Touchette et al., 2002.

**Figure 2. The effect of spray-dried plasma (SDP) and lipopolysaccharide (LPS) treatment on serum concentration of cortisol.**



There was a diet by LPS treatment interaction ( $P < 0.007$ ) such that serum concentration of cortisol following the LPS challenge was greater for pigs fed a diet with 7% SDP compared to pigs fed a diet without SDP. There was no diet effect ( $P = 0.24$ ) on serum concentration of cortisol within the saline treated pigs. Error bars omitted for presentation purposes. Pooled SEM was 8.0 ng/ml. Data from Carroll et al., 2002.

## Summary

In summary, the inclusion of spray-dried plasma in the weaned pig's diet for the first two weeks postweaning has been scientifically demonstrated in numerous research publications to enhance growth and performance. While the exact mode of action still remains unresolved, the majority of research data would suggest that spray-dried plasma provides immunological protection to the pig, which may prevent immune system activation associated with sub-clinical disease or infection, thus allowing nutrients to be diverted towards growth. However, one should keep in mind that the magnitude of the growth response to spray-dried plasma will most likely be dependent upon the endemic pathogen load within the pig's environment. Finally, the intent of this report is neither to support nor oppose the use of subtherapeutic levels of antibiotics as AGP's in swine diets, but rather to provide sound scientific data on a possible alternative feed additive which has repeatedly been demonstrated to enhance growth and performance in weaned pigs.

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