

# EFFECTS OF SOURCE AND LEVEL OF COPPER ON PERFORMANCE AND LIVER COPPER STORES IN WEANLING PIGS<sup>1</sup>

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## ABSTRACT

Five 28- to 33-d experiments involving 460 crossbred pigs weaned at  $28 \pm 2$  d of age (initial weight, 6.7 to 8.1 kg) were conducted to determine the effects of feeding high dietary levels of Cu sulfate ( $\text{CuSO}_4$ ) or Cu oxide ( $\text{CuO}$ ) on rate and efficiency of gain and liver Cu stores of weanling pigs. The pigs were housed in groups of five to six/pen and fed a fortified, unmedicated, corn-soybean meal-dried whey basal diet (1.1% lysine, 30 ppm Cu). In Exp. 1 and 2, pigs (eight replicates) were fed the basal or the basal plus 125 or 250 ppm Cu from  $\text{CuSO}_4$  or  $\text{CuO}$  for 28 d. In Exp. 3 and 4, four replications were fed the same diets as in Exp. 1 and 2 plus two additional diets (500 ppm Cu from  $\text{CuSO}_4$  or  $\text{CuO}$ ). In Exp. 5, dietary levels of 0, 125, 250, 375 or 500 ppm Cu from  $\text{CuSO}_4$  were evaluated using four replications. At the end of each experiment, the liver from one pig in each pen was collected for Cu analysis. Overall, rate and efficiency of gain were improved ( $P < .01$ ) by feeding 125 or 250 ppm Cu as  $\text{CuSO}_4$ , with the 125 ppm dietary level being about 75% as effective in stimulating growth as 250 ppm. Performance of pigs was not different from controls when the highest (500 ppm) level of Cu (from  $\text{CuSO}_4$ ) was fed. Liver Cu increased 10- to 70-fold when 250 to 550 ppm Cu from  $\text{CuSO}_4$  was included in the feed. Withdrawal of 500 ppm dietary Cu for 28 d decreased in liver Cu from 1,513 to 274 ppm of DM. All dietary levels of  $\text{CuO}$  failed to influence performance or liver Cu levels, suggesting that the Cu in  $\text{CuO}$  was largely unavailable and ineffective as a growth promotant for weanling pigs.

(Key Words: Pigs, Growth Promoters, Copper Sulfate, Cuprous Oxide, Availability.)

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## Introduction

Copper is a unique mineral element in that it acts as a growth stimulant in swine when fed at high dietary levels. The growth rate response from feeding 250 ppm Cu (as  $\text{CuSO}_4$ ) is well documented in the weanling pig (Wallace, 1967; Roof and Mahan, 1982; Edmonds et al., 1985; Burnell et al., 1988) and seems to be additive to that obtained from the feeding of antibiotics (Beames and Lloyd, 1965; Mahan, 1980; Stahly et al., 1980; Hagen

et al., 1987). The relative effects of feeding less or more than 250 ppm Cu are not well established.

The sulfate salt of Cu is the most common source used in feeds for growth promotion. In studies with growing-finishing swine (Bunch et al., 1961, 1963), the oxide form of Cu was reported to be nearly as effective as the sulfate form, yet liver Cu levels were not elevated in their pigs when  $\text{CuO}$  was fed. However, in studies at our station, the feeding of high levels of Cu in the sulfide form neither enhanced growth rate nor did it influence liver Cu stores (Cromwell et al., 1978).

The purpose of this research was to determine the efficacy of various levels of dietary Cu as a growth promotant for weanling pigs and to determine the relative effectiveness

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of the sulfate and oxide forms of Cu as growth promotants.

### Experimental Procedures

Five experiments involving 460 Hampshire-Yorkshire crossbred pigs were conducted. The pigs were weaned at  $28 \pm 2$  d of age and allotted at random to treatments from weight outcome groups. Sex was balanced in each treatment, and littermates were distributed across treatments insofar as possible. The average initial weights of the pigs ranged from 6.7 to 8.1 kg, and the length of experimental periods ranged from 28 (Exp. 1 to 4) to 33 d (Exp. 5).

The pigs were housed in groups of five to six pigs in flat-deck pens with expanded metal floors in a temperature-controlled nursery unit. They were fed corn-soybean meal-dried whey diets fortified with vitamins and minerals to meet or exceed NRC (1979) standards (Table 1). The basal diet was calculated to contain 1.1% lysine. Antibacterial agents were not included in the basal diet. The diets were fed in meal form, and the pigs were allowed ad libitum access to their diets and water.

Copper was added in the form of  $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$  or  $\text{CuO}$  at dietary levels of 125, 250, 375 or 500 ppm. These levels are in addition to 17.5 ppm Cu provided by the trace mineral mix and 12.5 ppm Cu supplied by the natural ingredients (i.e., total of 30 ppm Cu in basal diet). The  $\text{CuO}$  was predominantly cupric oxide (~94%) with some cuprous oxide (~3%) and metallic Cu (~5%) (personal communication, S. Klatt, American Chemet Corp.).

Dietary treatments in Exp. 1 and 2 were the basal, the basal plus 125 or 250 ppm Cu from  $\text{CuSO}_4$  and the basal plus 125 or 250 ppm Cu from  $\text{CuO}$ . These diets were fed to three (Exp. 1) and five (Exp. 2) replications of five to six pigs/pen. The pigs initially averaged 6.9 and 8.1 kg body weight, respectively. The trials lasted 28 d and the pigs averaged 15.6 and 17.8 kg, respectively, at the end of the two trials.

The treatments in Exp. 3 and 4 were the same as in Exp. 1 and 2 except there were two

TABLE 1. COMPOSITION OF BASAL DIET<sup>a</sup>

Ingredient	%
Ground corn	60.00
Dehulled soybean meal	27.00
Dried whole whey <sup>b</sup>	10.00
Dicalcium phosphate	1.65
Limestone, ground	.75
Iodized salt	.35
Vitamins <sup>c</sup>	.10
Trace minerals <sup>d</sup>	.15
Total	100.00

<sup>a</sup>Calculated to contain 1.1% lysine, .8% Ca, .7% P and 30 ppm Cu.

<sup>b</sup>Edible grade, spray-dried whey.

<sup>c</sup>Supplied per kg of diet: vitamin A, 6,600 IU; vitamin D<sub>3</sub>, 880 iCU; vitamin E, 22.0 IU; vitamin K, 4.4 mg; riboflavin, 8.8 mg; pantothenic acid, 22.0 mg; niacin, 44.0 mg; vitamin B<sub>12</sub> 22.0 µg.

<sup>d</sup>Supplied, mg/kg of diet: Fe, 175; Zn, 150; Mn, 60; Cu, 17.5; I, 2; Se, .1.

additional treatments consisting of 500 ppm Cu supplied by either  $\text{CuSO}_4$  or  $\text{CuO}$ . There were two replicates of five or six pigs/pen in each experiment. The length of the experimental period was 28 d. Average initial weights were 7.1 and 6.9 kg, and final weights were 12.2 and 13.2 kg for Exp. 3 and 4, respectively.

In Exp. 5, four replicate pens of five pigs/pen were fed the basal diet with 0, 125, 250, 375 or 500 ppm Cu (as  $\text{CuSO}_4$ ) for 33 d, from 6.7 to 18.0 kg. At the end of the test period, eight pigs that had been fed the 500 ppm diet (two pigs that were the closest to the pen average from each replication) were switched to the basal diet. Four of these pigs (one randomly selected pig/replication) were slaughtered 14 d after withdrawal of Cu and the remaining four pigs were slaughtered 28 d after withdrawal of dietary Cu to determine the depletion rate of Cu from the liver.

At the end of each experiment, one pig from each pen (the pig closest to the pen average weight) was slaughtered and the liver was removed for Cu analysis. In Exp. 5, the pig in each pen was chosen before the selection of the pigs for the Cu depletion study. The gall bladder and extraneous fat were removed, the entire liver was homogenized in a blender, and the homogenized samples were freeze-dried. After wet ashing, the liver was assayed for Cu according to the methods described by Kline et al. (1971) using

<sup>2</sup>Phelps Dodge Refining Co., New York.

<sup>3</sup>American Chemet Corp., Helena, MT.

TABLE 2. EFFECTS OF SOURCE AND LEVEL OF COPPER ON PERFORMANCE AND LIVER COPPER OF WEANLING PIGS (EXP. 1 AND 2)<sup>a</sup>

Item	Basal, 0 ppm <sup>b</sup>	CuSO <sub>4</sub>		CuO		CV
		125 ppm <sup>b</sup>	250 ppm	125 ppm	250 ppm	
Daily gain, g <sup>c</sup>	279	327	347	279	283	13.3
Daily feed, g	554	610	599	542	547	12.6
Feed/gain <sup>c</sup>	2.00	1.92	1.78	1.95	1.94	5.6
Liver Cu, ppm of DM <sup>de</sup>	23	33	246	28	25	183.0

<sup>a</sup>Eight replicate pens of five or six pigs/pen; 7.6 to 16.9 kg; 28-d test.

<sup>b</sup>Level of added Cu in addition to 30 ppm Cu in the basal diet.

<sup>c</sup>Basal vs 125 and 250 ppm Cu from CuSO<sub>4</sub> ( $P < .01$ ).

<sup>d</sup>Basal vs 250 ppm Cu from CuSO<sub>4</sub> ( $P < .01$ ).

<sup>e</sup>125 vs 250 ppm Cu from CuSO<sub>4</sub> ( $P < .01$ ).

an atomic absorption spectrophotometer<sup>4</sup>. Liver Cu is expressed on a tissue DM basis.

The data were subjected to analysis of variance procedures (Steel and Torrie, 1980). There was no evidence of an experiment  $\times$  treatment interaction ( $P > .3$ ) for any of the criteria in the combined analysis of the data from Exp. 1 and 2, so these data were pooled. The same was true for the data of Exp. 3 and 4. Also, the lack of an experiment  $\times$  treatment interaction allowed the pooling of the data of the 0, 125 and 250 ppm treatments of all five experiments. Orthogonal contrasts of basal vs added Cu, level of added Cu and source of Cu were made in Exp. 1 to 4. In nearly all cases, the Cu source  $\times$  Cu level interaction was significant ( $P < .01$ ); therefore, a second set of nonorthogonal contrasts of the basal vs certain treatment groups were made. These latter statistical comparisons are presented in the tables. In Exp. 5, orthogonal polynomials were used to make linear and nonlinear contrasts among treatment means. In all cases, the pen was considered the experimental unit.

### Results

*Experiments 1 and 2.* Pigs fed 125 or 250 ppm Cu from CuSO<sub>4</sub> gained faster ( $P < .01$ ) and required less feed per unit of gain ( $P < .01$ ) than those fed the unmedicated control diet (Table 2). Daily feed intake tended to be greater for the pigs fed 125 or 250 ppm Cu from CuSO<sub>4</sub>, but this difference was not significant ( $P > .20$ ). Liver Cu was elevated

approximately 10-fold in pigs fed 250 ppm Cu from CuSO<sub>4</sub>, but no increase occurred when the lower (125 ppm) level was fed. Rate and efficiency of gain and liver Cu levels in pigs were not influenced by the feeding of CuO at either level of inclusion.

*Experiments 3 and 4.* Daily feed intake and growth rate were improved ( $P < .01$ ) in pigs fed 125 or 250 ppm Cu as CuSO<sub>4</sub> compared with those fed the basal diet (Table 3). The 500 ppm Cu level did not result in improved gains over controls and resulted in higher ( $P < .05$ ) feed:gain ratios. As in Exp. 1 and 2, CuO at any level did not improve performance of the pigs. Liver Cu increased ( $P < .01$ ) in pigs fed 250 and 500 ppm Cu as CuSO<sub>4</sub>, compared with controls, but Cu content of the liver was not affected by any dietary level of Cu when added in the oxide form.

*Experiment 5.* Rate and efficiency of gain were influenced quadratically ( $P < .01$ ), as was daily feed intake ( $P < .10$ ), by level of added Cu (Table 4). Rate and efficiency of gain improved in a curvilinear fashion with the addition of 125 and 250 ppm Cu, after which further addition of Cu resulted in a decline in performance to equal that of the controls. Based on the inflection point (calculated from the second derivative) of the quadratic equation, growth rate was maximized when the level of added Cu was 242 ppm (Figure 1).

As in the previous trials, liver Cu was not affected by the 125 ppm dietary inclusion rate, but marked increases in liver Cu occurred when the higher dietary levels of Cu were fed, resulting in a quadratic ( $P < .05$ ) response pattern. The 250, 375 and 500 ppm dietary levels resulted in 17-, 41- and 72-fold increases in liver Cu, respectively. When the 500

<sup>4</sup>Model 560, Perkin Elmer Corp., Norwalk, CT.

TABLE 3. EFFECTS OF SOURCE AND LEVEL OF COPPER ON PERFORMANCE AND LIVER COPPER OF WEANLING PIGS (EXP. 3 AND 4)<sup>a</sup>

Item	Basal, 0 ppm <sup>b</sup>	CuSO <sub>4</sub>			CuO			CV
		125 ppm <sup>b</sup>	250 ppm	500 ppm	125 ppm	250 ppm	500 ppm	
Daily gain, g <sup>c</sup>	193	259	257	199	181	202	206	14.6
Daily feed, g <sup>c</sup>	406	474	486	434	397	428	441	10.4
Feed/gain <sup>d</sup>	2.13	1.92	1.90	2.49	2.31	2.12	2.15	14.7
Liver Cu, ppm of DM <sup>ef</sup>	23	15	137	327	19	16	21	73.5

<sup>a</sup>Four replicate pens of five or six pens/pigs; 7.0 to 12.7 kg; 28-d test.

<sup>b</sup>Level of added Cu in addition to 30 ppm Cu in the basal diet.

<sup>c</sup>Basal vs 125 and 250 ppm Cu from CuSO<sub>4</sub> ( $P < .01$ ).

<sup>d</sup>Basal vs 500 ppm Cu from CuSO<sub>4</sub> ( $P < .01$ ).

<sup>e</sup>Basal and 125 ppm Cu vs 250 and 500 Cu from CuSO<sub>4</sub> ( $P < .01$ ).

<sup>f</sup>250 vs 500 ppm Cu from CuSO<sub>4</sub> ( $P < .01$ ).

ppm level of Cu was withdrawn from the diet, liver Cu concentrations decreased from 1,513 ppm to 508 ppm within 14 d (Figure 2). A further decrease to 274 ppm occurred after 28 d of Cu withdrawal.

### Discussion

The growth rate response to high levels of dietary Cu in the form of CuSO<sub>4</sub> is well documented in the literature (Bunch et al., 1961, 1963; Braude, 1967, 1975; Wallace, 1967; Kline et al., 1971, 1973; Cromwell et al., 1978; Prince et al., 1979, 1984; Stahly et al., 1980; de Lima et al., 1981; Roof and Mahan, 1982; Edmonds et al., 1985; Hagen et

al., 1987; Burnell et al., 1988). In our current study, the dietary inclusion of 250 ppm level of Cu (as CuSO<sub>4</sub>) improved growth rate 24 to 39% and improved efficiency of feed utilization 11 to 21%. Feed intake also was increased by 8 to 17% in pigs fed this dietary level and source of Cu.

In a previous study involving weanling pigs at our station (Stahly et al., 1980), 125 ppm Cu (as CuSO<sub>4</sub>) was as effective as 250 ppm Cu in stimulating growth. In this experiment, the 125 ppm level of Cu (as CuSO<sub>4</sub>) was as effective as the 250 ppm level in Exp. 3 and 4 but tended to be less effective in Exp. 1, 2 and 5. Based on an analysis of the pooled data from 0, 125 and 250 ppm Cu from CuSO<sub>4</sub> for these

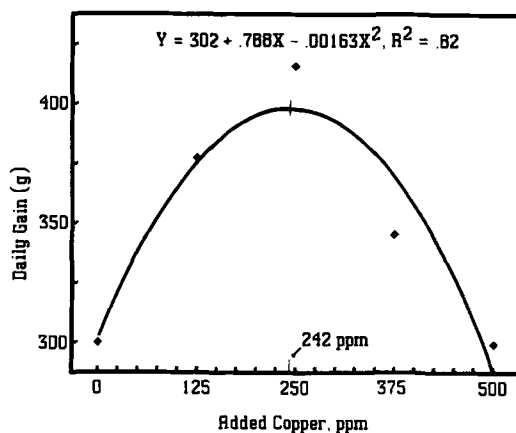


Figure 1. Influence of dietary Cu (as CuSO<sub>4</sub>) level on growth rate in weanling pigs (Exp. 5). Based on the maxima of the regression equation, growth rate was greatest at 242 ppm of supplemental Cu.

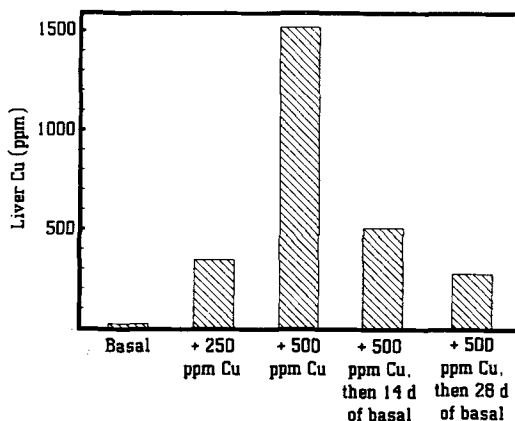


Figure 2. Liver Cu (ppm of DM) of pigs fed 0, 250 or 500 ppm Cu (as CuSO<sub>4</sub>) for 28 d or 500 ppm Cu for 28 d followed by a 14- or 28-d withdrawal of Cu from the diet (Exp. 5).

TABLE 4. EFFECTS OF LEVEL OF COPPER ON PERFORMANCE AND LIVER COPPER OF WEANLING PIGS (EXP. 5)<sup>a</sup>

Item	Cu (from CuSO <sub>4</sub> ) <sup>b</sup>					CV
	0 ppm	125 ppm	250 ppm	375 ppm	550 ppm	
Daily gain, g <sup>c</sup>	299	377	415	345	299	9.4
Daily feed, g <sup>d</sup>	678	740	730	624	590	12.0
Feed/gain <sup>c</sup>	2.29	1.97	1.82	1.89	2.00	7.2
Liver Cu, ppm of DM <sup>e</sup>	21	32	347	870	1,513	69.1

<sup>a</sup>Four replicate pens of five pigs/pen; 6.7 to 18.0 kg; 33-d test.

<sup>b</sup>Level of added Cu in addition to 30 ppm Cu in the basal diet.

<sup>c</sup>Quadratic ( $P < .01$ ) effect of Cu.

<sup>d</sup>Quadratic ( $P < .10$ ) effect of Cu.

<sup>e</sup>Linear ( $P < .001$ ) and quadratic ( $P < .05$ ) effect of Cu.

five experiments, the 250 ppm dietary level of Cu was more efficacious than the 125 ppm in stimulating growth rate (263 vs 323 vs 342 g/d for pigs fed 0, 125 and 250 ppm Cu, respectively;  $P < .15$ ) and efficiency of feed utilization (2.11 vs 1.93 vs 1.82;  $P < .05$ ). Based on these means, the 125 ppm dietary level of Cu was about 75% as effective in improving rate of gain and about 60% as effective in improving feed:gain as the 250 ppm dietary level of Cu. In studies with growing-finishing pigs, 250 ppm Cu also has been shown to be more effective than 125 ppm Cu (Braude, 1975; Cromwell, 1983).

The magnitude of the improvement in growth rate and feed:gain ratio was diminished when Cu (as CuSO<sub>4</sub>) was increased to 375 ppm and was completely lost when the diet was increased to 500 ppm Cu. Longer-term studies with growing-finishing pigs have shown that the feeding of 500 ppm Cu as CuSO<sub>4</sub> depressed performance in pigs (Kline et al., 1971, 1973; Prince et al., 1984), and in certain instances, toxicities have been reported (Wallace et al., 1960; NRC, 1980). However, our results indicate that with young pigs fed for a 4- to 5-wk period, 500 ppm Cu does not depress growth rate compared with pigs fed a low-Cu control diet, although it did reduce efficiency of feed utilization in some instances (Table 3).

Liver tissue of control pigs averaged 22 ppm Cu on a DM basis. Liver Cu was not increased by feeding 125 Cu as CuSO<sub>4</sub>, but liver Cu concentration was elevated 6- to 17-fold when 250 ppm Cu was provided. A further marked accumulation of Cu in liver tissue occurred when 375 and 500 ppm Cu as CuSO<sub>4</sub> was fed. The accumulation in liver Cu in pigs fed 500 ppm dietary Cu was greater in

Exp. 5 than in Exp. 3 and 4, perhaps because pigs were on test slightly longer (33 vs 28 d) and because pigs in Exp. 5 consumed more feed (590 vs 434 g/d; 19.47 vs 12.15 kg total feed) and hence consumed more total Cu than did pigs in Exp. 3 and 4. Accumulation of Cu in liver tissue in weanling pigs fed high Cu was similar to that reported in growing-finishing pigs (Kline et al., 1971, 1973; Prince et al., 1979; Williams et al., 1980; Cromwell, 1983). According to the results of Exp. 5, this Cu is rapidly depleted from the liver after pigs are returned to a low-Cu diet. Similar results were found in finishing pigs when they were fed a high-Cu diet followed by a low-Cu depletion diet (Prince et al., 1979).

The sulfate, carbonate, chloride and oxide salts of Cu and several organic chelates of Cu have been reported to be effective growth promotants in swine (Wallace, 1967; Stansbury et al., 1990). Bunch et al. (1961, 1963) concluded that CuO was as effective as CuSO<sub>4</sub> in improving growth rate in growing-finishing pigs. Based on studies with Cu<sup>65</sup>-labeled CuO and CuSO<sub>4</sub>, Buescher et al. (1961) concluded that Cu was equally available from these two forms. In studies with ruminants, Cu in the form of CuO needles has been reported to be an acceptable source of supplemental Cu for cattle and sheep (Judson et al., 1985a,b; Richards et al., 1985), although a study by Lassiter and Bell (1960) showed that the Cu from CuO powder was more available than the Cu from CuO needles. Conflicting results reported by Ledoux et al. (1987), who found that the Cu in CuO was not available to the chick.

In the studies of Bunch et al. (1961, 1963), liver Cu was not elevated nearly so much in

pigs fed CuO as in those fed CuSO<sub>4</sub>. If one assumes that liver Cu uptake reflects Cu availability, then one would predict that the CuO would have limited availability to the animal. In studies at our station, the sulfide salt of Cu did not result in increased liver Cu, and it was ineffective as a growth promotant. This suggests that solubility of Cu is needed for its growth-promotant effects, presumably within the gut. Because solubility also is needed for bioavailability of Cu, bioavailability and growth promotion are correlated.

The reason for the differences in response to high dietary levels of CuO in the studies of Bunch et al. (1961, 1963) and in our studies may have been due to the source of CuO used. They used CuO<sup>5</sup> that was produced by an ammoniacal leach process in which metallic Cu is converted to Cu ammonium carbonate, then to Cu carbonate and finally to cupric oxide (personal communication, S. Klatt, American Chemet Corp.). This process results in a highly soluble form of Cu. The CuO in our study was produced by heating metallic Cu and milling the CuO from the surface. Temperature is controlled to minimize sintering. Although both processes yield products that are largely cupric oxide (98 vs 94% for the two processes, respectively; personal communication, S. Klatt, American Chemet Corp.), the CuO used in the Bunch et al. (1961, 1963) studies may have been more soluble, resulting in a greater biological availability of Cu compared with the CuO used in our studies.

The results of the current study with weanling pigs indicate that CuO was ineffective as a growth promotant at the levels tested. Even a 500 ppm level of Cu as CuO did not increase liver Cu above control levels (Table 4). These results do not support the results of Bunch et al. (1961, 1963) or the conclusions of Wallace (1967) that CuO is an effective growth promotant. In fact, the liver Cu data strongly suggest that CuO is very poorly available, which is in contrast to the data reported by Buescher et al. (1961) for pigs and by Lassiter and Bell (1960), Judson et al. (1985a,b) and Richards et al. (1985) for ruminants, but is in agreement with the findings of Ledoux et al. (1987) for the chick.

### Implications

The results of these studies clearly indicate that the feeding of 250 ppm Cu as CuSO<sub>4</sub> markedly improves rate and efficiency of gain in weanling pigs. Exposure of young pigs to a high level (500 ppm) of Cu for 4 to 5 wk, as might occur if a producer were to add 250 ppm Cu to a commercial feed that already contained 250 ppm Cu, seems not to be detrimental, but this level does not stimulate growth. Although CuO is a more concentrated form of Cu (75% Cu) than CuSO<sub>4</sub> (25% Cu), Cu in the oxide form is ineffective as a growth promotant. Based on liver Cu stores, the bioavailability of Cu in CuO seems to be quite low; hence, the oxide form of Cu, due to its insolubility, is not useful as a major source of supplemental Cu in mineral mixes or as a growth promotant for swine.

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<sup>5</sup>Calumet and Hecla, Inc., Calumet, MI.

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