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Meta-Analysis Summary of Broiler Chicken Trials with Dietary Actigen™ (2009-2012)

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Abstract: Statistical meta-analyses of results from broiler pen trials and a few field trials published during 2009-2012 using dietary Actigen were conducted. Actigen (Alltech, Inc., Nicholasville, Kentucky, USA) is a second-generation, yeast cell wall product considered to be a "growth permitter" through its roles in immune modulation and improved intestinal health. Parameters evaluated were dietary inclusion rates for Actigen, age of birds, body weight, Feed Conversion Ratio (FCR) or feed/gain ratio (F/G ratio) and mortality %. Eighteen reports were collected allowing 29 comparisons of negative control (nCON) diets and Actigen supplemented diets (200 to 800 g/tonne) fed during the entire trials. Similarly, 15 reports were collected allowing 20 comparisons of positive control (antibiotic supplemented) diets and Actigen supplemented diets (200 to 882 g/tonne). When added to basal diets continuously to an average broiler age of 41.72 days (n = 29), Actigen significantly and beneficially changed body weight by +0.0.80 kg (+3.34%), FCR or F/G ratio by -0.033 (-1.84%) and mortality % by -0.80 (-12.5% relative to nCON). Compared with positive control (antibiotic) results, dietary Actigen fed continuously to an average broiler age of 42.73 days (n = 20) gave results statistically equivalent with those of dietary antibiotics. Comparisons between this present meta-analysis and those done previously on another yeast cell wall compound (Bio-Mos) suggest that the second generation product Actigen may be more effective in terms of growth promotion.

Key words: Actigen, antibiotic, broiler chicken, mannan oligosaccharide, meta-analysis

INTRODUCTION

To keep coccidiosis and bacterial diseases such as necrotic enteritis under control when broiler chickens are produced on litter, dietary coccidistats or vaccines and various antibiotic growth promoters or alternative products are used. Bacitracin methylene disalicylate (BMD®, Alpharma, Inc., Fort Lee, New Jersey, USA) is selective in its action in that it affects only Gram-positive microbes such as streptococci, staphylococci and clostridia. Bacitracin suppresses synthesis and induces lysis of bacterial cell walls, interferes with synthesis of protoplastic proteins within the cells and reduces toxin production by certain bacteria resulting in less inflammation of the gut (International Minerals and Chemicals Corporation, ca. 1978). Virginiamycin (Stafac®, Phibro Animal Health, 2010) is a streptogramin antibiotic approved for broiler chickens at 5 g/ton (2, 000 lb) to improve feed conversion ratio, 5-15 g/ton to improve weight gain and 20 g/ton for prevention of necrotic enteritis caused by *Clostridium perfringens* susceptible to virginiamycin. The use of low-level antibiotics such as bacitracin and virginiamycin have come under pressure from consumers of chicken due to concern about antibiotic resistant bacteria and the potential diminished effectiveness of antibiotics used for humans.

Mannan oligosaccharide from yeast outer cell wall has been used as a dietary supplement in broiler feeds (Kumprecht *et al*., 1997; Waldroup *et al*., 2003; Rosen, 2007) since about 1993 when Alltech, Inc., Nicholasville, Kentucky, USA introduced the first generation commercial product (Bio-Mos). Oligosaccharides are carbohydrates which on hydrolysis yield about 2 to 10 monosaccharides. The idea to use yeast mannan oligosaccharide in poultry feeds evolved from the concept that certain sugars, particularly mannose, largely block the colonization of intestinal pathogens such as *Salmonella* species and *Escherichia coli* which contain type 1 fimbrae, from attaching to intestinal mannose, proliferating and producing toxins and damage.

Some of the demonstrated modes of action of dietary mannan oligosaccharide include:

1. Binding of enteric pathogens with Type 1 fimbrae (mannose seeking lectins) and thus blocking their adhesion to the gut lining (Eshdat *et al*., 1978; Spring *et al*., 2000)
2. Modifying microflora fermentation (less propionic acid and ammonia production) to conserve nutrients for the bird to utilize (Ferket *et al*., 2005)
3. Maintaining integrity of gut lining and improved gut health such as greater villi height (Iji, 2001), more goblet cells/mm villus height thus increasing the brush border mucin barrier and thinner muscularis layer (Ferket *et al*., 2005)

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4. Immune modulation enhancing immune responses (adjuvant effect and liver secretion of mannose-binding protein to bind bacteria and initiate the complement cascade of the bird's immune system) (Savage *et al*., 1996; Cotter *et al*., 2002; Shashidhara *et al*., 2003; Ferket *et al*., 2005).

The presence of dietary mannan oligosaccharide and pathogens together in the lumen of the intestine functions as an adjuvant and antigen system, allowing enhanced antigenicity and superior immune response (Shafey *et al*., 2001).

A second-generation yeast outer cell wall specific-compound derived product is Actigen (Alltech, Inc., Nicholasville, Kentucky, USA). This was developed using nutrigenomics technology (gene chips) which allows detection of changes in expression of genes in intestinal cells. Internal trials by Alltech confirmed this to be at least 2.5 more times more concentrated in biological activity than the first generation mannan product (Bio-Mos). The higher activity is clearly what makes this compound unique. Actigen is typically supplemented to broiler chicken feeds at 200 to 800 g/tonne which is about 40% of the original product's inclusion rate. Actigen is considered to be a "growth permitter" through its roles in immune modulation and improved intestinal health. The units of activity in the commercial product may be determined by rapid kit test developed by Alltech, Inc. and a separate in-feed assay is also available to confirm quantitatively and qualitatively the presence of the product.

Changes in gene expression in the gut mucosa of broiler chickens fed diets containing Actigen (400 g/tonne) and/or bacitracin methylene disalicylate (BMD® 50 g/ton) have been studied (Brennan *et al*., 2011; Xiao *et al*., 2011). Genes involved in protective functions and pathways were influenced by Actigen and/or BMD®. Microarray analysis revealed that when birds were supplemented with Actigen, 928 genes were significantly changed ($P \leq 0.05$, $FC \geq 1.2$; 456 down-regulated, 472 up-regulated) while BMD® supplementation resulted in 857 genes that significantly changed (408 down-regulated, 449 up-regulated). Surprisingly, 316 genes were commonly and significantly changed by Actigen and BMD® (146 down-regulated, 170 up-regulated).

When differentially affected genes (that is, up-regulated or down-regulated) were grouped by biologic function, it was found that Actigen and BMD® commonly altered genes involved in antimicrobial response, inflammatory response and infection mechanism, cell-to-cell signaling and interaction and cellular development. Gene ontology analysis showed that a broad range of biological functions were associated with the altered gene expressions. Pathway analysis suggested a strong connection between Actigen and up-regulation of signaling pathways directly involved in cellular immune response, inflammatory response and antimicrobial responses such as toll-like receptor signaling, interferon signaling and retinoic acid inducible protein-1 (R1G1) receptor mediated innate immunity. Significant upregulation of such genes as toll-like receptor 3 (TLR3), myxovirus resistance 1 (MX1), Interferon Regulatory Factor 7 (IRF7), suppressor of cytokine signaling 1 (SOCS1) and down-regulation of ADP-ribosyltransferase (CHAT2) further indicated that Actigen had modulatory effects on the intestinal immune system (Brennan *et al*., 2011; Xiao *et al*., 2011).

Brennan *et al*. (2010) compared the effects of supplementing Actigen or BMD® to the diet on mRNA levels of mucin and mucin-regulating genes in the jejunum of 42-day old broiler chickens. The mRNA levels of mucin 2 (cMUC2) tended to be 1.29-fold greater in Actigen- and BMD®-treated birds than controls ($p<0.10$). The mucin 2 gene encodes a protein component of the mucosal layer that protects the intestinal cell wall from bacterial translocation. Change in mucin 2 mRNA levels corresponded to changes in goblet cells and reflected a beneficial change in gut health. Analysis of tissue morphology indicated that supplementation with either Actigen or BMD® resulted in an increased villus height, goblet cell count and an increased villus height to crypt depth ratio in the jejunum (Collett *et al*., 2011). The mRNA levels of mucin-regulating genes interleukin 18 (IL18) and keratinocyte growth factor 7 (KGF7) were similar between Actigen- and BMD®-treated birds. The toll-like receptors 2 and 5 (TLR2 and TLR5), two key markers for pathogenic insult in the gut, had mRNA levels greater by 1.20-fold and 1.23-fold respectively in BMD®-treated birds than in controls (Brennan *et al*., 2010).

The objective of this meta-analysis summary article was to collect and statistically analyze by paired t-test [Statistix 8®, (2003) Analytical Software, Inc., Tallahassee, Florida, USA] broiler feeding trial results worldwide from 2009-2012 to compare negative control (basal diets) or positive control (antibiotic-supplemented) diets with Actigen-supplemented diets. The studies included pen trials and field trials.

MATERIALS AND METHODS

Worldwide broiler chicken pen trial reports (2009-2012) were analyzed statistically to determine effects of *Saccharomyces cerevisiae* var. *boulardii* yeast outer cell wall specific-compound derived product (Actigen, Alltech, Inc., Nicholasville, Kentucky, USA) on live performance. Actigen was developed using nutrigenomics technology which allows detecting changes in expression of genes in intestinal cells. Criteria for selecting studies were:

1. Written report
2. Antibiotic(s) or Actigen were fed for the entire trial
3. Age of birds (duration of trial)

4. Negative (basal) and/or positive (antibiotic) control
5. Antibiotic stated for positive control
6. Body weight and feed conversion ratio (FCR) or feed/gain ratio (F/G ratio) results were given (and mortality % was included when reported).

Results were analyzed by treatments using paired t-test in Statistix 8® software (Analytical Software, Inc., Tallahassee, Florida, USA).

RESULTS

Negative control (nCON) diets versus Actigen (ACT) diets: Presented in Table 1 is a summary of live performance results from broiler chicken trials with negative control (nCON) versus Actigen-supplemented (ACT) diets. There were 18 written reports providing 29 comparisons of results from these 2 treatments. The average age (and trial duration) was 41.72 days. Average inclusion rates for Actigen by phases varied from 800 to 200 g/tonne and it was fed during the entire trial in each case. Body weight was very highly significantly ($p<0.001$) greater for the ACT birds than for nCON birds (+0.080 kg; +3.34%). The feed conversion ratio (FCR) or feed/gain ratio (F/G ratio) was very highly significantly ($p<0.001$) decreased for ACT birds compared to nCON birds (-0.033; -1.84). Mortality % was significantly ($p = 0.031$) reduced for Actigen birds compared to nCON birds (-0.80%; -12.5% relative to nCON).

Table 1: Summary of live performance results from broiler trials with negative control (nCON) versus Actigen-supplemented (ACT) diets

		Body wt or gain, kg		FCR or F/G ratio		Mortality (%)		
Age, days[1]	Actigen g/tonne[2]	nCON	ACT	nCON	ACT	nCON	ACT	Reference (Yaer)
42	800/400/200	2.382	2.501	1.947	1.852	4.83	4.46	Mathis (2009)
42	400	2.370	2.516	1.740	1.660	13.9	12.5	Kill *et al.* (2010)
42	400/2003	2.370	2.552	1.740	1.660	13.9	11.5	Kill *et al.* (2010)
42	200	2.370	2.441	1.740	1.700	13.9	17.4	Kill *et al.* (2010)
40	800/400/2004	2.521	2.657	1.636	1.603	4.30	6.20	Nollet and Kay (2010)
42	200	2.066	2.065	2.020	2.010	6.25	6.25	Peric *et al.* (2010)
42	400	2.066	2.234	2.020	1.950	6.25	2.30	Peric *et al.* (2010)
42	800	2.066	2.151	2.020	1.960	6.25	4.93	Peric *et al.* (2010)
35	400/200[5]	1.600	1.650	1.890	1.870	5.00	5.00	Venkatesh (2010)
49	400	2.743	2.825	1.942	1.939	3.34	5.50	Corneille (2011)
42	400	2.469	2.478	1.790	1.750	8.51	4.07	Gernat (2011)
42	400/200	2.469	2.468	1.790	1.750	8.51	5.99	Gernat (2011)
42	200	2.469	2.451	1.790	1.770	8.51	4.46	Gernat (2011)
42	200	2.515	2.847	1.741	1.694	6.67	6.67	Lea *et al.* (2011)
42	400	2.515	2.677	1.741	1.729	6.67	3.33	Lea *et al.* (2011)
42	800	2.515	2.749	1.741	1.725	6.67	5.00	Lea *et al.* (2011)
34	800/500/300[6]	2.165	2.200	1.520	1.490	5.00	6.40	Lausten *et al.* (2011)
34	800/500/300[6]	2.118	2.135	1.610	1.560	3.90	3.30	Lausten *et al.* (2011)
42	800/400/200[7]	2.081	2.134	1.825	1.784	3.69	4.77	Mathis (2011a)
52	400	2.763	2.865	1.872	1.820	5.60	3.80	Mathis (2011b)
42	800/400/200	3.317	3.437	1.746	1.708	5.56	3.89	Munyaka *et al.* (2011)
32	400	1.877	1.901	1.658	1.654	4.00	4.00	Nollet (2011)
49	1800/400/200[5]	2.790	2.799	1.960	2.020	6.30	7.60	Sasou and Corneille (2011)
42	400	2.349	2.346	1.750	1.720	5.30	3.79	Guo *et al.* (2012)
42	800/400/200[8]	2.349	2.264	1.750	1.760	5.30	3.79	Guo *et al.* (2012)
42	200	2.397	2.383	1.830	1.830	4.39	3.72	Ivkovic *et al.* (2012)
42	400	2.397	2.392	1.830	1.790	4.39	2.70	Ivkovic *et al.* (2012)
52	800/200[8]	2.832	2.992	1.846	1.772	0.83	1.04	Mathis (2012)
35	800/400/200[9]	2.541	2.699	1.494	1.481	8.30	8.30	Swick *et al.* (2012)
Comparisons (n=)		29	29	29	29	29	29	
Mean		2.396[b]	2.476[a]	1.792[a]	1.759[b]	6.41[a]	5.61[b]	
P-value			<0.001		<0.001		0.031	
Difference			+0.080		-0.033		-0.80	
Diff. from nCON, %			+3.34		-1.84		-12.5	

[1]Average age was 41.72 days (number = 29).
[2]Actigen in starter 0-21 days, grower 21-35 days and finisher 35-42 days unless otherwise stated.
[3]Actigen at 400 g/tonne from 0-21 days and at 200 g/ton from 21-42 days.
[4]Actigen in starter 0-10 days, grower 10-25 days and finisher 25-40 days.
[5]Feed phase ages not given.
[6]Actigen in starter 0-7 days, grower 7-28 days and finisher 28-34 days.
[7]Actigen in starter 0-17 days, grower and finisher 17-52 days.
[8]Actigen in starter 0-7 days, grower 7-21 days and finisher 21-42 days.
[9]Actigen in starter 0-10 days, grower 10-24 days and finisher 24-35 days.

Table 2a: Summary of live performance results from broiler chicken trials with antibiotic growth promoter-supplemented positive control (AGP) versus Actigen-supplemented (ACT) diets

Age	Actigen	Body weight, kg		FCR or F/G ratio		Mortality (%)		
days[1]	g/tonne[2]	AGP	ACT	AGP	ACT	AGP	ACT	Reference (Year)
42	400/200[3]	1.831	2.037	1.840	1.840	21.0	16.3	Hitech Hatch (2009)
42	800/400/200	2.530	2.501	1.843	1.852	4.17	4.46	Mathis (2009)
35	400/200[4]	1.652	1.636	1.502	1.513	4.87	4.95	Philippines (2009)
42	400	2.551	2.516	1.690	1.660	9.70	12.5	Kill *et al.* (2010)
42	400/200	2.551	2.552	1.690	1.660	9.70	11.5	Kill *et al.* (2010)
42	200	2.551	2.441	1.690	1.700	9.70	17.4	Kill *et al.* (2010)
38	882/441/220[5]	1.857	1.955	1.681	1.680	2.92	3.01	U.S. Broiler Integrator (2010)
42	400	2.468	2.478	1.750	1.750	6.95	4.07	Gernat (2011)
42	400/200	2.468	2.468	1.750	1.750	6.95	5.99	Gernat (2011)
42	200	2.468	2.451	1.750	1.770	6.95	4.46	Gernat (2011)
42	800/400/200[6]	2.124	2.134	1.803	1.784	3.85	4.77	Mathis (2011a)
52	400	2.900	2.865	1.807	1.820	4.00	3.80	Mathis (2011b)
42	800/400/200	3.430	3.437	1.720	1.708	6.39	3.89	Munyaka *et al.* (2011)
61	400/200[7]	4.300	4.377	1.980	2.004	2.33	2.39	N.C. A and T Res. (2011)
40.5	800/400/200[8]	2.939	2.758	1.869	1.791	6.15	2.85	Baynton (2012)
42	400	2.406	2.346	1.730	1.720	5.30	3.79	Guo *et al.* (2012)
42	800/400/200[9]	2.406	2.264	1.730	1.760	5.30	3.79	Guo *et al.* (2012)
52	800/200[6]	2.976	2.992	1.805	1.772	0.83	1.04	Mathis (2012)
35	800/400/200[10]	2.597	2.699	1.413	1.481	3.30	8.30	Swick *et al.* (2012)
37	800/400/200[11]	2.502	2.486	1.566	1.614	2.23	2.27	Chrystal and Owens (2012)
Comparisons (n =)		20	20	20	20	20	20	
Mean		2.575	2.570	1.731	1.731	6.13	6.08	
P-value			0.771		0.889		0.935	
Difference			-0.005		0		0 -0.05	
Diff. from AGP (%)			-0.19		0		0 -0.82	

[1] Average age was 42.73 days (number = 20).
[2]Actigen in starter 0-21 days, grower 21-35 days and finisher 35-42 days unless otherwise stated.
[3]Actigen in starter and grower 0-24 days and finisher 24-42 days.
[4]Actigen in starter 0-21 days, grower and finisher 21-35 days.
[5]Actigen in starter 0-15 days, grower 15-28 days and finisher 28-38 days.
[6]Actigen in starter 0-17 days, grower 7-31 days and finisher 31-52 days.
[7]Actigen in starter 0-18 days, grower and finisher 18-61 days.
[8]Actigen in prestarter about 0 to 7-10 days, starter to day 18-19, grower to day 30, then finisher to 40-41 days.
[9]Actigen in starter 0-7 days, grower 7-21 days and finisher 21-42 days.
[10]Feed phase ages not given; mortality % from 0-32 days.
[11]Actigen in starter, grower and finisher 1 and 2 feeds (ages not given).

Table 2b: Antibiotics programs used in obtaining broiler trial results presented in Table 2a

Reference (year)	Antibiotic	Inclusion rate by days of age (feeding phases)[1]
Hitech Hatch Fresh (2009)	BMD®	0-42 days 350 g/tonne
Mathis (2009)	BMD®	0-21 days 50 g/ton, 21-42 days 25 g/ton
Philippines Field Trial (2009)	Surmax®	0-28 days (avilamycin, approved 2.5-15 g/tonne in Australia, for example)
Kill *et al.* (2010)	Avilamycin	0-42 days 100 g/tonne
U.S. Integrator (2010)	BMD®	0-28 days (dose not stated)
Gernat (2011)	ZnBacitracin	0-42 days (dose not stated)
Mathis (2011)	BMD®	0-21 days 50 g/ton, 21-42 days 25 g/ton
Mathis (2011a)	BMD®/Stafac®	0-31 days BMD® 50 g/ton, 31-52 days Stafac® 20 g/ton
Munyaka *et al.* (2011)	BMD®	0-42 days 100 g/ton
N.C. A and T Research (2011)	BMD®/Stafac®	0-18 days BMD® 50 g/ton, 18-35 days BMD® 25 g/ton; 35-61 days Stafac® 10 g/ton
Baynton (2012)	BMD® 0 to	18-19 days BMD® 110 g/tonne, then 55 g/tonne to 40-41 days
Chrystal and Owens (2012)	ZnBacitracin	0-35 days (adjusted to 37 days) 100 mg/kg
Guo *et al.* (2012)	CTC®	0-42 days 150 g/tonne
Mathis (2012)	BMD®/Stafac®	0-31 days BMD® 50 g/ton; 35-61 days Stafac® 20 g/ton
Swick *et al.* (2012)	ZnBacitracin	0-10 days 100 mg/kg; 10-35 days 50 mg/kg

[1]"Tonne" is metric ton (1, 000 kg or 2, 204.6 lb) and "ton" is U.S. ton (907.19 kg or 2, 000 lb).

Antibiotic growth promoter (AGP) diets versus Actigen (ACT) diets: Listed in Table 2a are the broiler chicken live performance results from 15 written reports providing 20 comparisons of antibiotic growth promoter supplemented (AGP) diets versus Actigen supplemented (ACT) diets. Average age (and trial duration) was 42.73 days. Average inclusion rates for Actigen by phases varied but ranged from 200 to 882

Table 3: Comparison of Hooge (2004 and 2009) unrelated trial meta-analyses and Rosen (2007) holo-analysis of broiler trial results using dietary Bio-Mos with the present Actigen meta-analysis results herein

			Difference due to Bio-Mos or Actigen vs. control		
Reference	Additive	Comparisons no.	Body weight or gain, kg (%)[1]	FCR or F/G (%)[1]	Mortality, % actual (% relative)[1]
Bio-Mos or Actigen diets vs. neg. control (Except Rosen 2007, not significant difference NS) were significant unless marked NS					
Hooge (2004)	Bio-Mos	44-26	+0.038 (+1.75)	-0.035 (-1.89)	-0.759 (-16.4)^{NS}
Rosen (2007)	Bio-Mos	82-44 from eq.	+0.0276 (+1.48)	-0.0391 (-2.11)	+0.0311 (+0.43)
Hooge (2009)	Bio-Mos	48-27	+0.050 (+2.43)	-0.033 (-1.76)	+0.12 (+1.44)^{NS}
Present report	Actigen	29-20	+0.080 (+3.34)	-0.033 (+1.84)	-0.80 (-12.5)
Bio-Mos or Actigen diets vs. antibiotic diets					
Hooge (2004)	Bio-Mos	26-20	-0.007 (-0.32)^{NS}	-0.008 (-0.11)^{NS}	-0.83 (18.1)
Present report	Actigen	29-20	-0.005 (-0.19)^{NS}	0 (0)^{NS}	-0.05 (-0.82)^{NS}

[1]Percent (%) difference relative to the respective negative control or antibiotic control.

g/tonne and it was included in the diets during the entire trial in each case. All of the live performance results for AGP and ACT were statistically equivalent (within the same statistical groupings) showing no significant differences and differences were quite small.

The antibiotic growth promoters and dietary inclusion rates pertaining to results in Table 2a are given in Table 2b. The antibiotic growth promoters used in the trials included Surmax® (Avilamy-cin), BMD®, BMD®/ Stafac® and zinc bacitracin.

DISCUSSION

Actigen is a second generation product containing Mannan Oligosaccharide (MOS), a specific compound derived from the cell wall of yeast (*Saccharomyces cerevisiae* var. *boulardii*). In-feed assays and product assays allow the confirmation of the active ingredient quantitatively and qualitatively (through ELISA technology). These are key points in differentiating Actigen from the MOS feed additive products which have gone before it.

Hooge (2004) conducted meta-analyses of broiler chicken pen trials evaluating dietary mannan oligosaccharide from 1993-2003 and all trials involved supplementation of feeds with the first generation product Bio-Mos (Alltech, Inc., Nicholasville, Kentucky, USA) from which Actigen was derived (see Table 3). Compared to broiler results using negative control diets, Bio-Mos diets significantly ($p = 0.020$) improved body weight by 0.038 kg or +1.75%, feed conversion ratio by -0.035 or -1.89% and mortality % by -0.759% actual or -16.4% relative to negative control. Nonsignificant ($p = 0.408$) changes using Bio-Mos diets compared to antibiotic growth promoter diets were -0.007 kg or -0.32% relative to antibiotic control in body weight and -0.008 or -0.11% in feed conversion ratio. The Bio-Mos diets highly significantly ($p = 0.007$) changed mortality % by -0.83% actual and -18.1% relative to the antibiotic growth promoter diets, indicating a strong beneficial effect.

Rosen (2007) reported a holo-analysis of broiler chicken trials from 1997-2003 evaluating dietary mannan oligosaccharide product Bio-Mos versus negative control (see Table 3). From multiple regression equations, body weight was 0.0276 kg (1.48%) greater, feed conversion ratio was 0.0391 (2.11%) lower and mortality was 0.0311% (actual) (0.43% relative to negative control) higher with Bio-Mos diets compared to negative control diets. Beneficial response frequencies with dietary Bio-Mos were 65, 70 and 52%, respectively, for these 3 parameters.

Hooge (2009) prepared a meta-analysis of 48 additional comparisons beyond those included in the Hooge (2004) article and found significant improvements with Bio-Mos diets compared to negative control diets of +0.050 kg (+2.43%) for broiler body weight and of -0.033 (-1.76%) for feed conversion ratio (Table 3). Mortality % was statistically equivalent for these 2 treatments (+0.12% actual mortality for Bio-Mos group, or +1.44% higher relative to negative control).

In the present summary reported herein, body weight was greater ($p<0.001$) for the Actigen (ACT) fed birds than for the negative control (nCON) fed birds (+0.080 kg; +3.34%), feed conversion ratio (FCR) or feed/gain ratio (F/G ratio) was lower ($p<0.001$) for ACT-fed birds than for nCON-fed birds (-0.033; -1.84) and mortality % was significantly ($p = 0.031$) reduced by dietary ACT. The ACT birds had 0.80% lower mortality which amounted to a 12.5% relative reduction in mortality % compared to nCON birds. There was a non significant ($p = 0.771$) and only slight difference of -0.005 kg (-0.19%) in body weight in favor of the AGP treatment compared to the ACT treatment. The Feed Conversion Ratio (FCR) or feed/gain ratio (F/G ratio) averages were identical for the ACT and AGP groups. Mortality % was not significantly different ($p = 0.935$) for ACT and AGP fed groups (-0.05% actual for ACT-fed birds, amounting to -0.82% decline relative to AGP mortality result). All of the live performance results for AGP and ACT were statistically equivalent (that is, within the same statistical groups).

Table 3 has a compilation of Bio-Mos meta-analysis results from Hooge (2004), Rosen (2007) and Hooge (2009) in comparison with Actigen meta-analysis results obtained from this current exercise.

Bozkurt *et al.* (2009) found significantly improved body weight and feed conversion ratio at 21 and 42 days in male broilers fed a mannan oligosaccharide product (Bio-Mos, 0.1%) compared to negative control broilers. De Oliveira *et al.* (2009) fed dietary mannan oligosaccharide at 0.1% from 0-21 days and 0.05% from 21-42 days and found that litter ammonia volatilization decreased when mannan oligosaccharide diets were fed versus unsupplemented diets.

Mathis (2011b) reported results of a pen trial conducted on 10.2 cm (4 in.) built-up litter top dressed with pine shavings and using straight-run Cobb chicks. Three dietary treatments were: (1) Negative control (2) Actigen at 800 g/tonne 0-7 days, 400 g/tonne 7-21 days and 200 g/tonne 21-42 days and (3) BMD® at 50 g/ton 0-21 days and 25 g/ton 21-42 days. Salinomycin at 50 g/ton (0-21 days) and 60 g/ton (21-35 days) was the coccidiostat. Intestinal villus height, villus height: Crypt depth ratio and goblet cell count were increased ($p<0.010$) and litter scores were improved ($p<0.001$), when birds were fed ACT or BMD® vs. nCON. Improved intestinal morphology of broilers fed dietary mannan oligosaccharide has been observed by several other researchers as well (for example: Iji, 2001; Yang *et al.*, 2008; de Oliveira *et al.*, 2009).

Conclusion: This meta-analysis summary of 18 reports with 29 comparisons of Actigen diets vs. negative control (basal) diets suggests that Actigen may be effective as a dietary growth promoter/ permitter for broilers due to the significant increases in average body weight (+0.080 kg) and decreases in average feed conversion ratio (-0.033) and mortality % (-0.80% actual) observed.

Statistically equivalent broiler live performance improvements were found in this meta-analysis for Actigen fed groups vs. antibiotic fed groups and results were quite close (15 reports, 20 comparisons). In conclusion, these results give indication of the broiler live performance benefits to be expected when using Actigen diets vs. basal diets or those supplemented with various antibiotic growth promoters.

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