Intermediate drug mixing

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MILL MANAGEMENT

The results of a premixing research project conducted at Kansas State University were reported at the Thirty-Seventh Annual Kansas Formula Feed Conference held in Manhattan, Kansas January 25-26, 1982. The stated purpose of this research was to determine if intermediate drug mixing, or premixing, and the pre-packaging of the premix in a final batch use size could consistently provide the proper drug levels in each package and, thus, provide the prescribed medication levels in final feeds.

Intermediate drug mixes were mixed in a laboratory model, horizontal, double ribbon mixer driven by a 1 H.P. motor at 60 R.P.M. Prior to the experiment, the mixer was tested by the Quantab®[1] chloride titrator method to determine optimum mixing time and to verify the ability of the mixer to mix efficiently. Based on the tests results, a 10 minute mixing time was selected. Table 1 describes the materials that were included in the intermediate mix.

After mixing the ingredients for 10 minutes, the 100# (45.359 kg) finished premix was packaged directly off the mixer discharge in 20—5 pound (2.27 kg) packages. Each of the individual packages was, then, assayed for levels of the drug by the drug manufacturer and for iron particle tracer counts by the tracer manufacturer[2] using the rotary detector method. The experiment was replicated to provide 40 packages for assay.

Assay results for the drug (Table 2) and for the iron particle tracers (Table 3) display a normal distribution curve. For example, 10% of the samples were assayed at less than 90% of the *average* drug level in all samples ($\bar{x}$); and 37.5% were assayed at less than 90% of the *expected* drug level. Tracer count results showed 22.5% of all samples at less than 90% of the *average* of all samples ($\bar{x}$); and 57.5% at less than 90% of the *expected* recovery level.

The particle sizes (Table 4) of the ingredients, apparently, affected dispersion and the analytical results obtained. The active drug with an average particle size of 381 microns and over 93,000 particles per gram was dispersed more thoroughly than the iron particle tracer which had an average particle size of 450 microns and 25,000 particles per gram. However, the coefficients of variation for both the drug (6.80%) and the iron particle tracers (9.52%) appear to be statistically acceptable.

The microbiological assay method for the drug calls for a "one-teaspoon" sample size. At 35# per cubic foot, a feed will weigh approximately .56 grams per cubic centimeter; and one teaspoon contains approximately 5 c.c. or 2.8 grams.[3] In the prepared premix, the level of active drug equals 5.447 particles per gram (247,080 particles ÷ 45,359 grams). One teaspoon of the premix would, therefore, contain an expected 15.25 particles (2.8 grams × 5.447 particles per gram). A 30 gram sample of the iron particle tracers should contain 33 particles, or counts. In either case, the number of particles per sample is too small to meet the 5 percent coefficient of variation suggested by Larrabee (1976) and other authors. Pfost (1966) stated "If there were an average of 100 particles per sample, then the coefficient of variation would be 10%. Hence, even if a mixer operated "perfectly," there would still be a coefficient of variation of 10% among samples . . . . the coefficient of variation of 5% selected by some authors appears to be conser-

[1]Trademark of the Ames Company, Elkhart, Indiana

[2]Microtracers, Inc., San Francisco, California

[3]Personal communication with Dr. Paul Seib, Dept. of Grain Science and Industry, Kansas State University. February 24, 1982

Table 1. Experimental premix formula

Ingredient	Weight per ingredient (Kg)
Microtracer F(1)	0.002 (2 grams)
Drug (60 grams/pound)(2)	.020 (20 grams)
Diluent (ground cereal grain)	45.337
Total	45.359 kilograms

(1)Microtracers®, Microtracers, Inc., San Francisco, California
(2)13.2278% active drug—each pound contains 60 grams (132.276 grams/kilogram) active drug.

Table 2. Drug assay results—experimental premix

	Expected		Mean ($\bar{x}$)	
% Found	No. obs.	%	No. obs.	%
80.1-85.0	5	12.5	0	0.0
85.1-90.0	10	25.0	4	10.0
90.1-95.0	11	27.5	8	20.0
95.1-100.0	8	20.0	7	17.5
100.1-105.0	4	10.0	12	30.0
105.1-110.0	2	5.0	4	10.0
110.1-115.0	0	0.0	4	10.0
115.1-120.0	0	0.0	1	2.5
Total	40	100.0	40	100.0
Range (%)	83.18 - 107.56		89.26 - 115.43	
Expected Mean	52.9 grams/ton		49.295 grams/ton	
Standard deviation			3.35	
Coefficient of variation (%)			6.80	

$$c.v. = \frac{s}{m} \times 100$$

Where:
c.v. = coefficient of variation in percent
s = standard deviation of the assay value
m = mean of the assay value or $\bar{x}$

Table 3. Tracer count[1] results—experimental premix

% Found	Expected No. obs.	Expected %	Mean ($\bar{x}$) No. obs.	Mean ($\bar{x}$) %
70.1-75.0	2	5.0	0	0.0
75.1-80.0	7	17.5	0	0.0
80.1-85.0	7	17.5	2	5.0
85.1-90.0	7	17.5	7	17.5
90.1-95.0	9	22.5	4	10.0
95.1-100.0	7	17.5	3	7.5
100.1-105.0	1	2.5	14	35.0
105.1-110.0	0	0.0	2	5.0
110.1-115.0	0	0.0	7	17.5
115.1-120.0	0	0.0	1	2.5
Total	40	100.0	40	100.0
Range (%)	72.73 - 103.03			
Expected	33 counts/30 grams			
Mean			28.873 counts/30 grams	
Standard deviation			2.75	
Coefficient of variation (%)			9.52	

C.V. = $\frac{s}{m} \times 100$ (See Table 2)

[1]Rotary detector method, Microtracers, Inc., San Francisco, Califorinia.

Table 4. Particle sizes[1]—experimental premix ingredients

Ingredient	Av. diameter	Average number of particles: Per gram of ingredients	Average number of particles: per 45.359 kg. premix
Microtracer F[2]	450 microns	2,500	50,000
Drug	381 microns	93,400	247,080
.3175 cm (⅛") ground corn[3]	574 microns	31,275	1,418,458,860
Total premix	n/a	33,000 (av)	1,418,743,430 (total)

[1]Pfost, Headley, Method of Determining and Expressing Particle Size. 1976
[2]Microtracers™, Microtracers, Inc., San Francisco, California
[3]Includes 17,3546 grams of diluent in the base drug premix, total diluent was 45.3544 kilograms in the finished premix.

vative."

McEllhiney, et al, (1981) found coefficient of variation ranging from 4.344% to 7.172% in final feed rations for the same drug used in these experiments when the drug was introduced into the final feed at varying premix dilution levels where the expected particle count was 61.78 particles per one teaspoon sample size and a range of 18.818% to 30.085% C.V. for the iron particle tracers where the expected recovery was only 12 particles per 50 gram sample.

Conclusion: Under carefully controlled laboratory weighing, mixing, and packaging conditions—with no conveying, elevating, spouting, and binning prior to packaging, it appeared in these results that the level of drug, or tracer, in the separable packages will display a normal distribution curve. A conclusion would, therefore, be that a package taken from the low end of the curve would be under-medicated and that the resultant final feed using that additive package would also be under-medicated to an even greater degree. By the same token, a package taken from the high end of the curve could result in a higher level of the drug than expected.

Users and manufacturers should be aware that intermediate mixes, particularly of drugs, could amplify the variation of drug assay results in final feeds. **FM**

References

Larrabee, W. L., 1976. A Guide to Mixing Microingredients in Feed. Merck and Company. Rahway, New Jersey. 44

McEllhiney, R. R., 1982. Premixing and "2nd Generation" Drugs. In: Proceedings, Thirty-Seventh Annual Kansas Formula Feed Conference, Kansas State University, Manhattan, Kansas. B1-22.

McEllhiney, R. R. and Tangprasertchai, P., 1981. The Effect of Dilution Levels in Premixes on Microingredient Dispersion in Animal Feeds. Contribution number 82-192-J, Grain Science and Industry, Kansas Agriculture Experiment Station. Unpublished. Kansas State University, Manhattan, Kansas

Pfost, H. B., 1966. Criteria for Evaluating Feed Mixer Performance. Feedstuffs, 38(43): 30.

Pfost, H., and Headley, V., 1976. Methods of Determining and Expressing Particle Size. In: H. B. Pfost, Editor, Feed Manufacturing Technology. American Feed Manufacturers Association, Arlington, Virginia. 512-517.