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Even safer feed:

Validating cross-contamination control

by David Eisenberg

Mr Eisenberg is the president of Micro-Tracers, Inc, based in San Francisco, USA, which specialises in technology to measure cross-contamination and mixing quality. See 'Cross Conta' in FEED INTERNATIONAL April 2006 for his previous comments on GMP+ feed safety and quality assurance. Contact on e-mail MICROTRACE@aol.com or website www.microtracers.com.

Why is it important to validate cross-contamination control procedures at feed mills and feed premix plants? The obvious answer is: Mad cow disease!

Bovine spongiform encephalopathy or BSE—with the possible risk of new-variant Creutzfeldt-Jakob disease or vCJD in humans—is the main motivating force for concern over cross-contamination of manufactured feeds and premixes. In North America, for example, a low incidence of BSE cases is undercutting the beef industries of the USA and Canada. The disease also undercuts the feed industries supplying beef cattle producers, especially if their business is oriented towards meat exports. Most mammalian protein feed ingredients are banned from ruminant feeds in the USA and Canada. The concern exists, however, that if such ingredients are formulated in feeds for non-ruminants, such as poultry or pigs, at the same feed mill where ruminant feeds are being produced, then cross-contamination between these feeds can occur and thus mad cow disease can be spread.

By contrast, in the European Union, all ruminant proteins—mainly meat-and-bone meal—are banned from all feed use. The North American restrictions are less severe in part because the incidence of BSE disease is far lower. However, even the cost of more limited controls in the USA and Canada is significant and may increase dramatically if more stringent regulations come into effect.

Less obvious: Drug residue risk

There also is a less obvious—but possibly more important—reason to validate cross-contamination control procedures at feed mills and feed premix plants: Many medicated feeds have required withdrawal times applicable to the target species and are not allowed for non-target species. This issue is critical in countries worldwide—even in European Union countries where growth promoting antibiotics are banned from most feeds but where medicated products may be incorporated in feeds under veterinary prescription.

When cross-contamination occurs at feed mills, even low levels of a drug in a non-medicated feed can sometimes lead to violative residues of the drug in the tissue of the animals or poultry consuming the contaminated feed.

For example, 20 years ago, Japan banned US pork exports because the Japanese government had found a high incidence of sulfamethazine residues. The price of pork in the USA dropped US$0.11 per kilogram and the National Pork Producers Association requested all its members to not use that form of medication. This was a disaster for the pharmaceutical manufacturers but also led to a significant economic loss to the swine industry.

Until recently, many major poultry integrators exporting to Japan would not use nicarbazin in their feeds, for fear that cross-contamination to finisher feeds could lead to violative tissue residues in exported chicken. At the time, Japan had a 'zero tolerance' for such drug residues. However, in the past two years, a minimum residue level has been established so the poultry integrators and other feed manufacturers can use the drug safely, if they can be sure that cross-contamination of the drug to finisher feeds is kept to very low levels.

Harmonised worldwide regulation

The EU has by its regulation of the feed industry recognised cross-contamination of feeds as a significant food safety issue and has required that feed manufacturers

validate cross-contamination controls at their feed mills. Japanese regulations are developing that are likely to be similar to those enacted in Europe. Countries such as Brazil, USA, and Canada, which export to these premium markets, appear to have little choice but to enact similar standards.

At the same time, attention on keeping export meat markets open leads to comparable standards for domestic meat production, also. For example, when Canada's Province of Quebec enacted mixer validation and cross-contamination testing requirements in 1987, the regulatory action was in response to the Japanese having condemned shipments of pork for sulfamethazine residues. While the impetus for the regulation came from a restriction on the Province's exports, the government required feed manufacturers producing only for domestic consumption to meet the same standards.

Determining cross-contamination

Determining cross-contamination of animal proteins or drug residues in feeds requires validation of the testing and control procedures. In the EU, regulations delegate responsibility for determining testing procedures to validate mixer performance and cross-contamination control to each member country. Procedures are not standardised, although information is being shared and joint research conducted. Certain procedures using coloured iron particles, coloured stainless steel particles, cobalt and manganese compounds, and methyl violet have now gained official status as GM P+ test methods and these can be used to achieve FamiQS status and to support ISO Accreditation.

Choice of a 'tracer' is important in validating both mixer performance and cross-contamination control. In general, a safe feed ingredient not normally found in the feed tested is added as a tracer at a relatively high level to an initial batch of feed and samples are taken from not only the initial batch but also from one or more following batches and sometimes from a preceding batch as well.

It is assumed the tracer behaves similarly to the meat-and-bone meal or the medicated products that are the primary regulatory concern in animal feeds. However, this is not always the case: Research at Tecaliman (national feed research institute in France) and at Kansas State University (which specialises in feed science in the USA) has established that powdered ingredients mix more quickly in feeds than granulated ingredients. Other research has indicated powdered ingredients cross-contaminate more than granulated ingredients.

In any case, it has been difficult to establish that tracers used to validate cross-contamination control procedures behave similarly to meat-and-bone meal and drugs in feeds. Analytical procedures for these ingredients of interest at low levels of cross-contamination often do not exist, or, if they exist, they are not very accurate. This situation makes it difficult to correlate results between the tracers and the ingredients of concern.

Tecaliman and TNO: Correlating results

Extensive data have been developed by Tecaliman and TNO (feed research centre in the Netherlands) correlating results for various tracers where good analytical procedures do exist at appropriate levels of interest for materials of concern.

TNO researchers compared coloured stainless steel particles versus cobalt (see table 'Tracer vs cobalt'). The average contamination was calculated by assigning a weight to each sample taken, as the first sample taken represented much less than 5% of the total feed. The level of cross-contamination was calculated as a percentage of the formulated tracers, not as a percentage of the tracers found by analysis in the study.

Data from a Tecaliman study provided

Tracer vs cobalt

Sample	Fine coloured stainless steel particles	Cobalt
1	31.59%	31.19%
2	1.00	0.51
3	0.08	0.41
4	0.46	0.00
5	0.54	0.30
8	0.15	0.15
12	0.08	0.05
16	0.38	0.00
Average (n=20)	**0.75%**	**0.65%**

Study of tracer versus coca: TNO research centre in the Netherlands.

Tracer vs oxytetracycline

	Coloured iron powder	Oxytetracycline
Trial 1		
Batch 2		
Sample 1	29.5%	2' .9%
Sample 2	3.6	3.3
Sample 3	3.7	2.3
Batch 3		
Sample 1	5.3	4.3
Sample 2	1.1	2 1
Sample 3	1.8	0.0
Trial 2		
Batch 2		
Sample 1	23.2%	14.0%
Sample 2	3.0	2.3
Sample 3	3.5	2.2
Batch 3		
Sample 1	3.7	3.0
Sample 2	0.9	2.4
Sample 3	1.8	0.0

Study of tracer versus oxytetracycline from Tecaliman in France, 2002.

results for coloured iron powder and oxytetracycline for several repeat trials (see table 'Tracer vs oxytetracycline'). Results for the TNO and Tecaliman studies were similar, evidencing a very high level of cross-contamination in the first sample taken from the first batch of feed following the batch where both tracers were formulated at high levels.

Testing the 'worst case scenario'

The highest levels of cross-contamination occur in the first sample of the batch immediately following the batch formulated with the ingredient of concern—for example, meat-and-bone meal, drug, or tracer. The level of cross-contamination also increases as the feed passes through the feed mill from the mixer, to the surge bin, to the bucket elevator, to holding bins above the pellet mill, through the pellet mill, through the pellet cooler and holding bins before loading onto trucks for delivery.

Data from a study using coloured iron particles as a tracer in duplicate tests shows how cross-contamination appears to be highly variable, but often much higher in the first sample taken from the batch following the batch formulated with tracer (see table 'Batch-to-batch').

For accurate analysis of cross-contamination, it is critical that samples be taken from feed taking the identical route through the feed mill as the actual product, with that feed isolated from all other production.

If feed from the study commingles with other feed, cross-contamination results may be much lower than a 'worst case scenario'. Yet, if cross-contamination is at an acceptable level under the worst case scenario, then it will be at a lower level under less rigorous conditions.

Levels of cross-contamination

What levels of cross-contamination are possible and what levels are acceptable in countries with active testing programmes?

In a study using coloured iron particles as ingredients in poultry coccidiostat premixes at three feed mills, tracer was found in retained samples of pellets which were not supposed to contain any tracer. The percentage of the total tracer found in retained samples supposed to contain no tracer was as follows:

- Feed mill 1—tracer formulated in salinomycin-4.8%;
- Feed mill 2—tracer formulated in nicarbazin-0.26%; and
- Feed mill 3—tracer formulated in nicarbazin-0.45%.

The amount of tracer formulated in nicarbazin reaching non-target feeds was far lower than for the tracer formulated in salinomycin. A major reason for this was that the nicarbazin was formulated in only 10% of the feed at the two feed mills studied. By contrast, salinomcyin was formulated in approximately 60% of the feed at the feed mill studied. This result demonstrates that the amount of cross-contamination of a drug—or other ingredient—can be reduced by simply using less of it!

In Germany, the IFF Feed Research Institute has suggested cross-contamination at commercial feed mills should be kept below 4% and at premix plants below 1%. In France, Tecaliman has set a 'passing' standard of not more than 1% cross-contamination of medicated feeds into non-medicated feeds and of 5% between one non-medicated feed and another. However, these are 'target levels', not yet subject to government regulatory enforcement.

Nonetheless, feed manufacturers are wont to follow good manufacturing practices and know the limits of their equipment and procedures in controlling cross-contamination. In 1992, a premix plant in England caused a multi-million dollar loss when a selenium premix in a mixer leaked into a race horse-polo pony feed. This cross-contamination from Batch 2 to Batch 1 occurred because the discharge gate of the mixer leaked. Other losses have occurred when feed containing nicarbazin leaked into broiler breeder feed with toxic consequences.

Batch-to-batch cross-contamination

	Contamination to second batch	
	Test 1	Test 2
Mixer probe sample	0.88%	0.56%
Mixer discharge		
Sample 1	5.31%	1.24%
Sample 2	0.00	0.34
Sample 3	0.00	1.35
Average	1.77%	0.98%
Surge bin		
Sample 1	1.10%	2.21%
Sample 2	0.92	0.60
Sample 3	1.68	1.82
Average	1.23%	1.54%
After elevator		
Sample 1	7.31%	6.15%
Sample 2	7.14	1.79
Sample 3	1.85	0.74
Average	5.43%	2.89%
Bin above pellet mill		
Sample 1	6.67%	6.20%
Sample 2	4.13	1.28
Average	5.40%	3.74%
After pelleting		
Sample 1	6.12%	7.43%
Sample 2	1.47	0.53
Sample 3	8.70	1.93
Average	5.43%	3.29%

Data from a study using coloured iron particles as a tracer in duplicate tests are illustrative: Cross-contamination appears to be highly variable, but is much higher in the first sample taken from the batch following the batch formulated with tracer.

Low-cost assurance

If the feed mill or premix plant only tests for coloured steel particles or coloured iron powder or, as in Europe, for methyl violet, then the analytical cost of studying cross-contamination is very low. However, if many batches are studied and expert consultation is required, then the

cost can rise to possibly US$5,000 or more. However, the cost of using cobalt or drugs as tracers is greater and the time required to obtain results is longer, although in some situations such assays may provide more meaningful results.

Following cross-contamination testing that uncovers problems, there is the cost of modifying feed manufacturing equipment and procedures which may be significant. However, the cost of doing nothing and simply banning or severely restricting the use of certain ingredients—such as all animal proteins or some of the most useful drugs—is most certainly much greater.

A safe, economical approach may be for those feed mills and premix plants which prove their capability—through study and validation of their cross-contamination control procedures—to be allowed to use controlled ingredients, such as non-ruminant meat-and-bone meal and nicarbazin. On the other hand, those feed mills which choose not to study and validate their procedures would not be allowed to use such ingredients. This approach somehow seems more fair and in favour of the public interest—and much less expensive—than banning ingredients of concern or building new feed mills dedicated to feed for only one species.

The issues of cross-contamination are major concerns in the European Union countries and Japan now and are likely to emerge in the USA, Brazil, China, and the rest of the world very soon. A pro-active precautionary approach—rather than a reactive response—would seem best at this juncture, or else at some time it will be imposed.