ADVISORY COMMITTEE ON ANIMAL FEEDINGSTUFFS

ACAF Meeting 22nd September 2010

COPPER SUPPLEMENTATION IN FEED FOR CATTLE

DISCUSSION PAPER

Action required:

The Committee is invited to:

a. note the possible issue surrounding over-supplementation of copper in animal diets; and

b. agree on the core procedures to follow to ensure that supplementation is used appropriately to reduce the number of incidences of copper toxicity.

Veterinary Laboratories Agency
September 2010

COPPER SUPPLEMENTATION IN FEED FOR CATTLE

Purpose

1. The aim of this paper is to inform the Committee of Veterinary Laboratories Agency (VLA) and industry concerns regarding what appears to be excessive copper supplementation to dairy cattle. It is proposed that a code of practice is prepared for the feed industry providing advice as to the best practice for copper supplementation of feeds. It is also proposed that advice is subsequently developed for veterinarians and farmers.

Background

2. Copper is an essential trace element.

3. Many forages in Britain, such as grass, hay and silage, are low in copper, so the probability of copper deficiency in British cattle on unsupplemented diets is high.

4. However, cattle being fed manufactured feed rarely suffer copper deficiency and are at risk of copper toxicity because levels of copper in concentrate feeds are usually high relative to their requirement for copper. Absorbability (uptake from the gastrointestinal tract) of copper from relatively high concentrate rations is also higher than for copper in forage-based rations.

5. Soil ingestion is known to reduce copper absorption. Copper absorbability is especially reduced by the presence of molybdenum, sulphur and iron. In most of England and Wales, forage molybdenum depresses copper absorption slightly. This effect is only likely to cause copper deficiency disease if the copper status of the diet is already marginal. However, there are some localised areas in England and Wales, for example the 'teart pastures' in central Somerset, which have sufficiently high concentrations of molybdenum in the herbage to cause clinical copper deficiency even in diets that appear to have adequate copper.

6. The VLA continues to diagnose copper toxicity especially in dairy cattle and more recently in fattening calves originating from the dairy sector.

7. Copper toxicity can be caused by extremely high levels of copper fed over a short period, but it is most often caused by more moderate (but still excessive) levels fed over a longer term. Copper absorbed in excess of requirements is stored in the liver. Excessive accumulation of copper in the liver can ultimately cause liver degeneration, with the release of stored copper from the liver into the blood. This liver degeneration may initially be mild, but can increase: the copper released causes red blood cells to break up (haemolyse) causing death.

8. Commission Regulation (EC) 1334/2003 of 25 July 2003 provides controls on the use of copper–based additives in animal feed. For ruminating cattle the maximum content of copper in mg/kg of the complete feedstuff is 35 mg/kg (88% dry matter), which equates to 40 mg/kg of total diet dry matter (DM).

9. If the content of a complete feedstuff is above 35 mg/kg, a written veterinary medicated feedingstuff prescription is required for every 31 days supply of the product. When a prescription is issued it is the responsibility of the veterinary surgeon to be sure that it is necessary for the cattle to have the high levels of supplementation.

10. In copper poisoning incidents investigated by the VLA, the estimated concentrations of copper in the complete feedstuffs are frequently found to be in excess of the limit above which a veterinary prescription should be required. Also noteworthy is that in some investigations where concentrations of molybdenum, sulphur and iron have been measured in the forage there has frequently been no justification for supplementing the diet with high concentrations of copper.

Explanation of the problem

11. Copper toxicosis can occur as a result of trying to prevent or correct copper deficiency. The industry regards cattle as tolerant to moderate excess levels of copper, in contrast to sheep. The balance of risk has been regarded as favouring a precautionary approach over supplementation to help avoid copper deficiency and associated economic loss, because the risk of toxicity was thought to be low.

Copper deficiency

12. There are many copper dependent enzymes involved in multiple functions such as energy metabolism, coat pigmentation, immunity, iron metabolism, bone growth and development. Signs of deficiency can therefore be highly variable but are perhaps most commonly recognised as coat colour changes (red to yellow; black to brown), ill thrift, infertility and skeletal abnormalities in young stock. Most copper deficiency in ruminants in the UK is associated with the presence of copper antagonists, e.g. molybdenum, sulphur and iron in the diet that bind to copper in the rumen thus preventing the absorption of copper.

Beef cattle

13. Copper deficiency occurs most commonly in unsupplemented grazing cattle due to a combination of marginal copper supply in the forage based diets and moderate exposure to antagonists in forage and the soil.

14. VLA diagnoses copper deficiency relatively commonly in beef suckler cattle. Diagnosis is usually based on the total copper concentration in plasma (not whole blood or serum). The VLA reference range is 9- 19 µmol/l. Diagnosis is confirmed if there are clinical signs consistent with copper deficiency and a blood copper concentration < 5 µmol/l. Plasma copper concentrations only fall below the reference range when liver copper reserves have been depleted. Alternatively, liver tissue copper concentrations <300 µmol/kg DM accompanied by clinical signs consistent with copper deficiency is a sound basis for diagnosis.

15. Clinical response to supplementation together with monitoring of plasma and liver copper should be carried out to provide reassurance that supplementation was necessary and that the level of supplementation was adequate.

Dairy cattle

16. The risk of copper deficiency in lactating dairy cattle is extremely low due to the use of copper-supplemented concentrates and minerals. There may be a few exceptions in the 'teart areas' with high molybdenum, that require additional supplementation. Replacement heifers are at a similar risk to beef cattle if they are reared predominantly on forage and kept at pasture.

17. Infertility is a recognised problem in dairy cattle. The causes are multifactorial and include copper deficiency. However, copper deficiency is frequently blamed for infertility without any scientific evidence and this has led to indiscriminate supplementation of copper.

18. Varying terminologies have been used when describing conditions associated with copper deficiency, including secondary deficiency, copper responsive disease and molybdenum toxicosis (molybdenumosis) and this has created confusion amongst veterinarians, nutritionists and farmers.

19. The diagnosis of copper deficiency especially in relation to infertility is difficult. A number of blood analyses such as ceruloplasmin: copper ratio, trichloroacetic acid (TCA)-soluble and TCA-insoluble copper and specific enzyme tests have been used to assist with the diagnosis. However, none of the tests currently available in the UK are sufficiently robust for field use, and the results can even be misleading. Veterinary literature on this subject is also confusing. Much of the recent literature is not peer-reviewed. Many of the hypotheses used to determine whether to supplement were derived from experimentation in sheep and then extrapolated to cattle.

20. The same tests used in beef cattle are the most reliable for use in dairy cows. The gold standard to assess total body reserves of copper is to measure liver copper concentration but this is not a test that can be easily carried out in live cattle. Liver biopsies are at times carried out by veterinary practitioners. The alternative is to monitor liver tissue from cull cows. This can be done as a routine measure where copper deficiency is suspected, or to measure the impact of supplementation.

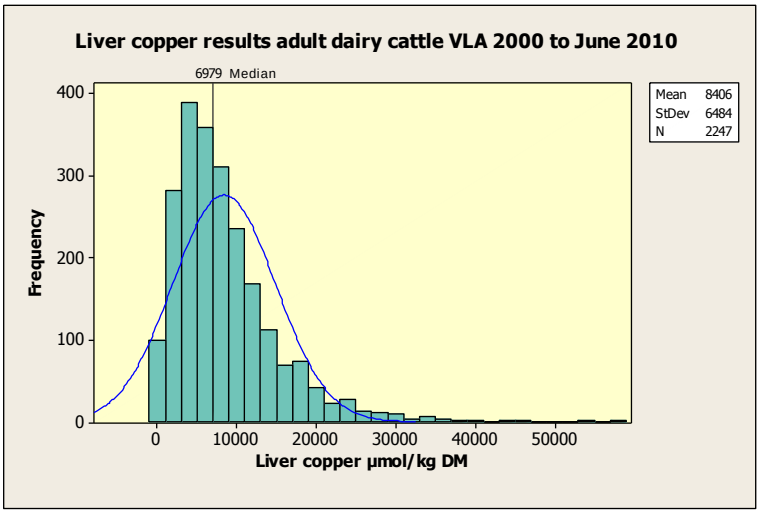
Case evidence and available data

VLA data

21. The graph on the next page shows liver copper concentrations from 2,247 adult dairy cows sampled over the last ten years. Samples are taken from both diagnostic and monitoring submissions. The sampled population is biased as many of the samples were collected in the post-mortem room and so will not describe the general population, but the results are of concern.

22. The graph shows that nearly 50% of adult dairy cattle sampled have liver copper close to the upper limit or in excess of VLA's reference range which is

300-8,000 µmol/kg DM. The reference range was determined many years ago and describes the expected distribution in the normal cattle population.



VLA Copper toxicity incidents

To reach a diagnosis of copper toxicity the following criteria must be met:

- **Appropriate clinical history**
- **Typical gross pathology or histopathology**
- **Supportive clinical chemistry (blood copper > 70 µmol/l or liver > 10,000 µmol/kg DM or kidney > 1,000 µmol/kg DM).**

23. Between 1 January 2005 and 31 July 2010 VLA diagnosed 143 incidents of copper toxicity in cattle; 114 of these were in milking cattle. Vets and farmers are not required to report suspected copper poisoning to VLA, so many cases of copper toxicity will not be reported. The VLA data should not be regarded as representing national incidence, which may be higher.

24. There do not appear to be any geographical trends in the VLA data. The number of incidents occurring appears to reflect the density of the cattle population in England and Wales.

Food safety copper toxicity incidents

A report of elevated copper levels incident is regarded as a food safety incident when liver copper concentration exceeds 500 ppm wet weight (WW) (approximately > 25,000 µmol/kg DM).

Year	Cattle copper incidents E&W
2010 (to end July)	2
2009	2
2008	1
2007	4
2006	2
2005	1
2004	0

25. In general, most diagnoses of copper toxicity are reached following examination of dead cows. Prior to death, liver copper is released into the blood stream. Therefore, in fatal clinical cases the liver copper concentration rarely exceeds 500 mg/kg WW and so do not trigger a food safety incident.

26. Many of the reports of very high liver copper concentrations arise from the monitoring by liver biopsy from what appear to be clinically normal dairy cows.

27. Concern has been expressed by the Food Standards Agency that, following relaxation of OTMS Regulations, cull cows can enter the food chain, and their livers used in manufactured food products.

Summary of concerns

- Copper toxicity is avoidable. Poor diagnosis and monitoring resulting in misplaced copper supplementation obscures the actual cause of infertility and other syndromes on farms.
- Unnecessary copper supplementation is an increased cost to farmers.
- Excess copper supplementation causes very high tissue liver copper residues and affected livers may enter the food chain.
- Unnecessary copper supplementation increases the excretion of copper in slurry and accumulation of soluble copper in soil, which has potential environmental impact.
- Copper toxicity in sheep was sometimes associated with grazing pastures treated with pig slurries. In the future could there be a problem with pastures treated with dairy cow slurry?

Action required:

28. The Committee is invited to:

a) note the possible issue surrounding over-supplementation of copper in animal diets; and

b) agree on the core procedures to follow to ensure that supplementation is used appropriately to reduce the number of incidences of copper toxicity.

Veterinary Laboratories Agency
September 2010

APPENDIX 1

Proposed Code of Practice for Supplementing Copper to Bovines

FOREWARD

This leaflet aims to outline some practical advice for the use of copper in feed, particularly in the dairy industry, on GB farms. It is supported by the following stakeholders: (example only at this stage)

Food Standards Agency (FSA), British Veterinary Association (BVA), British Cattle Veterinary association (BCVA), National Farmers Union (NFU), Agricultural Industries Confederation (AIC), Department for Environment, Food and Rural Affairs (DEFRA), Veterinary Medicines Directorate (VMD), Veterinary Laboratories Agency (VLA), British Association of Feed Supplement Manufacturers (BAFSAM), Royal Association of British Dairy Farmers (RABDF), Dairy Science Forum (DSF)

INTRODUCTION

Background

Copper is an essential trace element and copper deficiency is the most common trace element deficiency diagnosed in the UK. Copper toxicity has been common in sheep for sometime but has become a more common condition in cattle, especially dairy cows. This has prompted an industry-led working group to investigate the causes.

In the overwhelming majority of copper toxicity cases investigated there has been excessive supplementation of copper. The over-supply of copper is usually associated with the provision of multiple copper sources, none in themselves in excess of maximum levels, but sufficient, when added together, to cause copper poisoning.

It is likely that the sensitivity of black and white cattle to copper has increased over the past 20-30 years. In America, the National Research Council has reduced recommended limits for copper in cattle diets from 100 ppm in 1980 to 40 ppm in 2005. Decreased tolerance to copper exacerbates the effects of over-supplementation and explains why supplementation practices followed 30 years ago might not be appropriate today.

Regulatory MPL

The maximum level of elemental copper permitted under domestic and EU legislation without veterinary prescription is 35 mg/kg (88% dry matter) which equates to 40 mg/kg of total diet dry matter (DM).

COPPER REQUIREMENT

Nutritional requirements

To satisfy nutritional requirements the formulation level in normal situations should be based on 18 mg/kg DM

Copper antagonists

The "availability" of copper ingested by adult ruminants is variable, but under optimum conditions it is in the region of 5%.

It is well known that soil ingestion and especially antagonists such as sulphur, iron and molybdenum reduce copper availability to varying degrees.

Estimating copper availability

Estimating the variation in copper availability in the presence of antagonists has largely relied on mathematical equations derived from sheep experiments and extrapolated to predict copper availability to the dairy cow. It is proposed that this prediction be removed from all feedstuff mineral analysis reports to avoid confusion and to reduce the inadvertent risk of over-supply.

Copper deficiency and suspected deficiency has to be dealt with on a case by case basis, assessing copper status, increasing supplementation and monitoring the effects of increased supplementation.

Calves and dry Cows

Young calves are more susceptible to copper poisoning than adult cows. Pregnant females preferentially divert copper to the foetus. This means that we need to be careful with copper supplies to the late pregnancy cow if we are to avoid the calf being born with unnecessarily high copper loading.

ACHIEVING OUR OBJECTIVES?

It is proposed that a non-commercial standard protocol be adopted using a calculation supported by all of the industry stake-holders.

It is proposed that an example standard copper assessment format will be posted on stakeholder websites for use by all interested parties. As an example please refer to excel spreadsheet.

RECOMMENDATIONS

The Code of Practice on Farm for Supplementing Copper

- It is incumbent on all contributing agencies to fully consider the need for copper supplementation before advising a level of input.

- It is incumbent on all contributing agencies to fully investigate and calculate total copper inputs from all applicable sources e.g. grass, forages, compounds, straights, mineral powders, mineral blocks, mineral buckets, boluses, injections and water supply and ensure that in combination they are not excessive.

- If significant doubt exists as to the dietary copper contribution, feedingstuffs (including pasture / forage) should be analysed for copper content.

- Feedingstuff analysis reports should not report estimated copper "availability" levels.

- Records of copper supply changes and protocols should be kept and included into herd health plans.

- Copper concentration in total diet dry matter should "normally" be formulated to achieve 18 mg/kg DM.

- When it is deemed necessary to exceed the 18 mg/kg DM level, but not exceed the statutory limit, the situation should be fully reviewed by all participating parties and the course of action agreed for a specified period of time. Outcome monitoring, including copper status, should also be part of the process.

- An assessment of the residual copper status of the livestock should be undertaken prior to and following copper supplementation (to confirm efficacy even when not necessary for avoiding toxicity).

- In situations where the total copper supply is deemed to require a level exceeding 40 mg/kg DM, a full risk assessment should be employed before a prescription is written. Outcome monitoring, including copper status, should also be part of the process.