THE NATIONAL ACADEMIES
REPORT IN BRIEF

Safety of Dietary Supplements for Horses, Dogs, and Cats

Growing numbers of pet owners are giving their pets dietary supplements in hopes of supporting their health. This increased use of animal dietary supplements has raised concerns regarding the safety of specific supplements and the guidelines for determining safety of dietary supplements for horses, dogs, and cats. This report examines issues in determining safety of animal dietary supplements in general, and the safety of three animal dietary supplements; lutein, evening primrose oil, and garlic, in particular.

Like many people who take multivitamins and other supplements to support a healthy lifestyle, growing numbers of pet owners are also giving supplements to their pets for similar reasons. It is estimated that between 10 to 33 percent of dogs and cats in the United States are fed an animal dietary supplement, with some of the same supplements being fed to horses. But are these supplements safe for pets?

The increased use of animal dietary supplements has raised several concerns. Among the issues involved are the safety of specific dietary supplements, the general approaches taken to determine the safety of animal dietary supplements, the monitoring of adverse effects, and the state of the regulation of animal dietary supplements.

To assist in making decisions about the safety of dietary supplements for horses, dogs, and cats, the Food and Drug Administration (FDA) asked the Natural Research Council to produce a report on the safety of supplements in general and to review three specific supplements (lutein, evening primrose oil, and garlic) offered for horses, dogs, and cats. A committee of experts, consisting of animal nutritionist, veterinarians, clinical pharmacologists, and toxicologists, was established for this purpose. The committee addressed safety only; utility or efficacy of animal dietary supplements was not part of its task.

The committee found that there was a lack of quality safety data available for the supplements lutein, evening primrose oil, and garlic, that would be required to determine safety in drugs and animal food additives. Therefore, the committee could only report

BOX 1:
Definition: Animal Dietary Supplement

Animal dietary supplements are defined as any substance for oral consumption by horses, dogs, or cats, whether in/on feed or offered separately, intended for specific benefit to the animal by means other than provision of nutrients recognized as essential or for provision of essential nutrients for intended effect on the animal beyond normal nutritional needs, but not including legally defined drugs.

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on historical safe intakes (HSI) and estimate a presumed safe intake (PSI) for the three animal dietary supplements (see opposite page). The presumed safe intake (PSI) was estimated by reviewing evidence to determine a level at which the animal health or production efficiency were not impaired. While the historical safe intake (HSI) was based on the known levels consumed by wild or domestic animals over long periods of time with no apparent ill effects.

Despite these limitations, the committee took this opportunity to review the general issues of animal dietary supplement safety. They identified a number of data elements for consideration when constructing any framework for assessing animal dietary supplement safety that may be different from those routinely considered for prescription drugs.

REGULATION OF DIETARY SUPPLEMENTS IN THE UNITED STATES

Dietary supplements for both humans and animals are subject to regulation under the Federal Food, Drug, and Cosmetic Act (FFDCA). The way in which human dietary supplements are regulated was amended by the passage of the Dietary Supplement Health and Education Act (DSHEA) in 1994, but the Food and Drug Administration concluded that the Act does not apply to dietary supplements for animals. Thus, dietary supplements for humans and dietary supplements, despite often being the same substance, given in the same manner, and for the same purpose. Currently the FDA and other regulatory bodies are under pressure to resolve the public's desire to provide some of the same supplements available to humans to their animals.

BOX 2:
Definition: Adverse Events

As defined by the International Harmonization Conference (IHC), an adverse event is any untoward medical occurrence that may present during treatment with a (pharmaceutical) product, but which does not necessarily have a causal relationship with this treatment.

ASSESSING SAFETY OF ANIMAL DIETARY SUPPLEMENTS

The safety of a supplement, additive, or drug is generally assessed in two ways. Controlled studies, such as a study looking at the toxicity of a compound, usually done prior to the compound hitting the market, with the intent of identifying potential adverse events (box 2) associated with the administration of the compound. And surveillance studies, generally post market, done to monitor anticipated or unanticipated adverse events associated with general use of the compound.

The committee found that in addition to there being limited safety studies there are many other factors that further challenge the assessment of animal supplements safety, including the lack of standardization among active ingredients in the animal supplement market and the lack of a comprehensive adverse event reporting system. Because of these challenges, other types of evidence, found

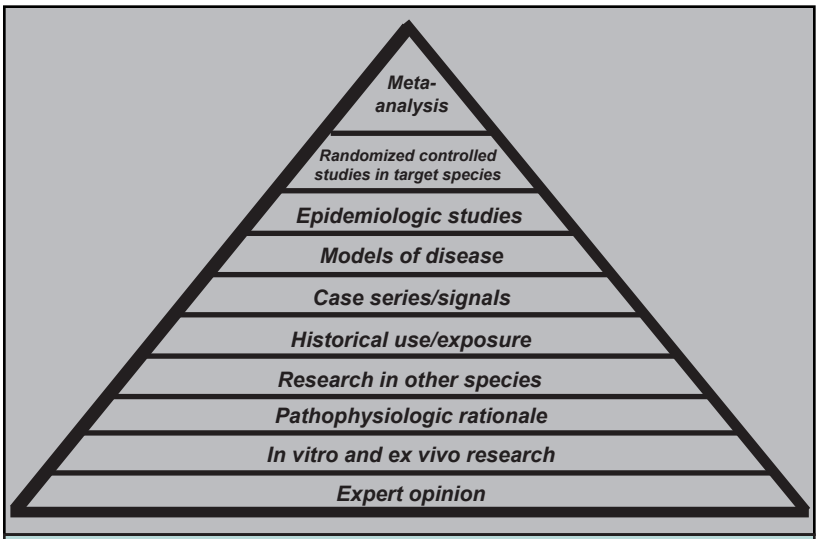

Figure 1 Evidence pyramid
The strength of evidence increases in progression from bottom to top. The guidelines for ranking strength of evidence should be considered when evaluating supplement safety.

in the evidence pyramid (figure 1), were reviewed and should be reviewed when determining safety of animal supplements such as lutein, evening primrose oil, and garlic.

FINDINGS AND RECOMMENDATIONS

In assessing animal dietary supplement safety, elements such as the relevance of the study to safety, dosage, contaminants in the supplements, and size of the study, all need to be considered when designing and assessing animal dietary supplements. Although the use of animal dietary supplements is potentially greater than the use of drugs or food additives, minimal safety data were available. Ideally, the committee would have liked to have adequate data to determine a no observed adverse effect level (NOAEL) for or a safe upper limit (SUL) for each of the three supplements. With the limited data currently available, the committee could only report historical safe intakes (HIS) and estimate presumed safe intake (PSI) for garlic (except for cats), evening primrose oil, and lutein.

The use of other species (i.e. non-target species) is important in assessing safety of supplements but is limited. Because of limited amounts of data about supplements in the animals of intended use (i.e. target species), research using other species can provide important safety signals. Although non-target species provide important evidence about safety they do not guarantee safety in the target animals. An example is garlic, although considered safe in humans when taken as a supplement, there is a concern that excess garlic supplement can cause hemolytic anemia in horses, dogs, and cats. The committee has identified several factors that should be considered when selecting appropriate substitute animals. Factors to be considered include the metabolic and natural dietary pattern similarities between surrogate and target animals and whether the supplement is naturally occurring in both animals' diet.

DIETARY SUPPLEMENTS FOR HORSES, DOGS, AND CATS

Presumed safe intake (PSI) and historical safe intake (HSI) are given in milligrams per kilogram of body weight (mg/kg BW)

LUTEIN

Lutein is abundant in green and yellow fruits and vegetables. The purported benefits of lutein supplements in humans include:

- Treatment or prevention of age-related macular degeneration
- Anti-oxidant and anti-cancer effect
- Protection against UV radiation
- Anti-aging effect

ANIMAL	PSI (mg/kg BW)	HSI (mg/kg BW)	Note
Horses	8.3*	8.3*	*When eaten as forage or natural sources; no data exist for supplements
Dogs	1.8	0.45	
Cats	7.2	0.85	

EVENING PRIMROSE OIL

Evening primrose oil (EPO) is an oil found in the evening primrose plant. EPO is made up of fatty acids. Two of the fatty acids found in EPO are recognized for their contributions to the maintenance of normal health and metabolism.

ANIMAL	PSI (mg/kg BW)	HSI (mg/kg BW)	Note
Horses	400*	25-80	*Assumes that total fat will not exceed 23 percent of diet
Dogs	424*	42-424	*Which is the upper limit used in trials
Cats	391*	20-391	*It is likely that cats could tolerate higher levels

GARLIC

Garlic has been used in the diet of humans for centuries. Ancient medical text from Egypt, Greece, Rome, China, and India include prescribed medical applications of garlic. Today garlic is thought to have numerous health benefits including reducing the risk of cardiovascular disease and cancer, stimulating immune function, and restoring physical strength

ANIMAL	PSI (mg/kg BW)	HSI (mg/kg BW)	Note
Horses	90	15	
Dogs	56	22*	*There is a long history of safe use.
Cats	n/a*	17	*The committee was unable to estimate a PSI for garlic.

There is a clear need for a comprehensive adverse event reporting system. Existing systems are deficient and limited by the difficulty of defining dosages, active ingredients, or consistent adverse signals. Some systems require payment to access (e.g., the poison control center of the American Society for the Prevention of Cruelty to Animals) or are limited by membership (e.g., the National Animal Supplement Council). Any system should be easily accessible for reporting and retrieving purposes, generate accurate data with a high level of confidence, and build upon the experience embedded in existing systems. The committee's analysis of these supplements has not uncovered a system for adverse reporting that is similar to those in place for drugs. The committee believes that lack of adverse events being reported to a manufacturer is weak evidence for a lack of adverse effects having actually occurred.

Current regulations addressing animal dietary supplements are in disarray. Clarification is required to clearly differentiate between an animal dietary supplement and a food additive or animal drug, as well as factors that differentiate regulation of human and animal supplements. Any future animal dietary supplement regulations should take into account existing standards set by the American Association of Feed Control Officials (AAFCO), Codex, and U.S. Pharmacopeia (USP).

CONCLUSION

Many people presume that supplements are safer than drugs, but the reality is that there is very limited safety data on dietary supplements for horses, dogs, and cats to determine safe use. The committee was unable to determine an upper limit of safe use for the three supplements, lutein, evening primrose oil, and garlic. This shortage of data resulted in trying to estimate existing intake levels as those presumed to be safe. The committee believes these levels are conservative for lutein and evening primrose oil, but probably more on target for garlic because of known reports of adverse events.

Many challenges stand in the way of determining whether or not animal dietary supplements are safe and at what dosage. Supplements considered safe in humans and other cross-species are not always safe in horses, dogs, and cats. An adverse event reporting system is badly needed. And finally, regulations dealing with animal dietary supplements are in disarray. Clear and precise regulations are needed to allow only safe dietary supplements on the market.

Committee on Examining the Safety of Dietary Supplements for Horses, Dogs, and Cats: Jim E. Riviere, (Chair), North Carolina State University; **Dawn M. Boothe**, Auburn University; **Gail L. Czarnecki-Maulden**, Nestle Purina PetCare PTC; **David A. Dzanis**, Dzanis Consulting & Collaborations; **Patricia A. Harris**, WALTHAM Centre for Pet Nutrition; **Wouter H. Hendriks,** Wageningen University; **Claudia A. Kirk**, University of Tennessee; **Lori K. Warren**, Univeristy of Florida; **Austin J. Lewis** (*Study Director*); **Ruth S. Arieti** (*Senior Project Assistant*).

This report brief was prepared by the National Research Council based on the committee's report. For more information or copies, contact the Board on Agriculture and Natural Resources at (202) 334-3062 or visit http://dels.nas.edu/banr. Copies of *Safety of Dietary Supplements for Horses, Dogs, and Cats* are available from the National Academies Press, 500 Fifth Street, NW, Washington, D.C. 20001; (800) 624-6242; www.nap.edu.

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