# EA NEWS

ETHICAL AGENTS
VETERINARY MARKETING

August 2023

**Edited by:**
**Dennis Scott BVSc MACVSc**

**EA Veterinary Marketing Ltd**
**54 Hobill Ave Wiri**
**PO Box 97-110 Manukau City**
**Manukau 2241**

**Ph 09-262-1388 Fax 09-262-1411**
**Freephone 0800 800-624**
**email info@ethicalagents.co.nz**
**website www.eavm.nz**

## Ciprofloxacin-Not a Good Idea


Off label use of ciprofloxacin in small animals may seem a cheaper option to many clinicians but it is truly a very false economy.

There is a very good reason why enrofloxacin and marbofloxacin have been registered for use in cats and dogs and ciprofloxacin is not, and that reason is bioavailability.

While ciprofloxacin can be used in cats, bioavailability is low (most of the drug does not enter the cat's body effectively) and bioavailability is somewhat unpredictable in the dog which means higher doses must be used.

More consistent results are expected in quinolones approved for veterinary use.

Work by world renowned veterinary pharmacologist Mark Papich stated that

"One of the reasons why ciprofloxacin frequently is administered to dogs is to decrease the expense of treating large dogs, and larger tablets made for humans can be more convenient than multiple tablets of the veterinary formulations.

However, using the tablet formulated for humans may have an unintended consequence of less systemic exposure (AUC) for larger dogs compared to smaller dogs."

In short the extra dosage required totally negates the perceived economic benefits as much larger doses are required to achieve any benefit.

There is a concern that the frequent use of inexpensive generic ciprofloxacin tablets has been linked to increased antimicrobial resistance.

The kinetics of marbofloxacin and enrofloxacin are both much superior to ciprofloxacin in both cats and dogs.

If a clinician decides that a highly critical important antimicrobial such as a fluoroquinolone is required they are behoven to use the most efficacious one possible, as is actually the case for any other antimicrobial prescribing.

Neither convenience nor thrift are considered valid reasons for antimicrobial choice.

Therefore, not only is using ciprofloxacin not best practice, it actually qualifies as poor practice.

Reference: M. G. Papich, Ciprofloxacin Pharmacokinetics in Clinical Canine Patients, J Vet Intern Med 2017; 31: 1508–1513

**Inside this issue:**




**Special points of interest:**

- Product launch—Bimoxyl LA
- A couple of environmental issues from left field.
- Nanoemulsions—what exactly are they?

# Bimoxyl LA

New, to New Zealand but proven in Europe, is Bimoxyl LA, a long-acting injectable formulation of amoxicillin.

Amoxicillin is a broad-spectrum semisynthetic penicillin which is bactericidal against a wide range of Gram-positive and Gram-negative bacterial pathogens so is ideally indicated for general infections, respiratory tract infections, secondary bacterial infections associated with viral diseases such as bovine viral pneumonia along with local infections such as cystitis and also dermatitis, abscesses, infected wounds and ear infections.

So, what sets Bimoxyl LA apart from other amoxicillin generics in the marketplace?

First of all, Bimoxyl LA has very rapid absorption due to the patented penetration enhancer incorporated into the formulation and starts to work straight away, with prolonged activity for 48 hours.

Studies comparing Bimoxyl LA with the European market leader have shown that Bimoxyl LA produces a significantly higher initial peak of amoxicillin in plasma over the rival product. Bactericidal levels were reached within 15 minutes and the peak concentration of 3.5mcg/ml after one hour compared to 1.35 mcg/ml - more than 2 times greater.

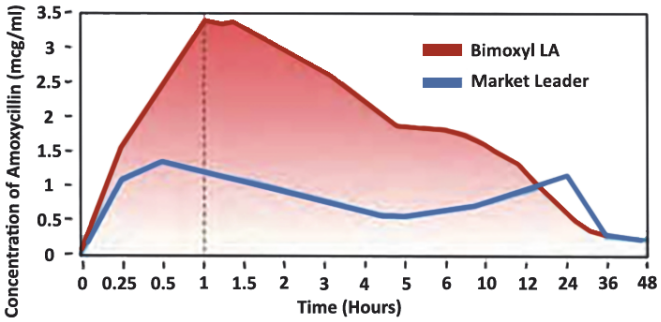
**"Not a problem with Bimoxyl LA which has good syringeability as a major feature."**

In the first 48 hours following injection, amoxicillin concentrations were 25% higher with Bimoxyl LA. With amoxicillin being a time dependent antibiotic levels above MIC for the time the drug is in the body is vitally important. Bimoxyl LA ensures that this is the case.

The other issue is syringeability, which can be a problem with some amoxicillin formulations. Not a problem with Bimoxyl LA which has good syringeability as a major feature.

In line with syringeability is the fact that several amoxicillin formulations seem to interfere with the rubber seals in plastic syringes making the syringes sticky and difficult to use, again not a problem with Bimoxyl LA.

Good syringeability, high blood levels and packed in sustainable packaging - Bimoxyl LA should be a welcome addition to the veterinary arsenal.




***Concentrations of amoxicillin in bovine plasma with time, after intra-muscular injection of two long acting amoxicillin injections (150mg/ml) at a dose rate of 15mg/kg.***

# The Atheist

An atheist was strolling along the cliffs by the sea when he slipped and wnet over the edge. He instinctively grabbed a small bush growing from a crevice.

It halted his fall, but as he looked down past his swaying legs at the jagged rocks below he wondered how long the frail bush could hold him.

He hung there terrified. Then he looked up at the edge of the cliff above him and called loudly, "Help. Is there anybody there?"

From somewhere above the clouds a deep thundering voice replied,

"Yes my son, I hear you. Trust in me, have faith. Let go of the shrub."

The atheist thought it over for a minute then looked up and shouted,

"Is anyone else there?"

# Plastic Greener Than Glass!

Ireland, the first country in the world to ban smoking in bars, also were world leaders in banning single use shopping bags in supermarkets, nearly 20 years before New Zealand. This focus on sustainability is a feature of Irish veterinary companies such as Bimeda and Chanelle meaning both fit well into the sustainability practices of Ethical Agents Veterinary Marketing.

When we look at some of the populism driven ideas for sustainability many fail scientific scrutiny. For example, planting forests on verdant farm land may appease urban voters but does little for sustainability. (See story overleaf). Similarly, the strong push for reusable glass containers instead of plastic may seem a great idea but it is not necessarily so.

So, when is plastic a better sustainability option than glass for containers? PET plastic can be. Polyethylene terephthalate, also called PET, is the name of a type of clear, strong, lightweight and 100% recyclable plastic.

Unlike other types of plastic, PET plastic is not single-use -- it is 100% recyclable, versatile, and made to be remade. PET is what's used to make bottles for soda, water and other drinks. It's also used to make cooking oil containers, plastic peanut butter jars and containers for other popular food items.

Many veterinarians and farmers prefer injectable products to be plastic rather than glass so there is less risk of breakage, but an unseen benefit is that it actually can be more environmentally friendly than glass, which does seem an oxymoron.

The reason for this is simply weight of product. PET injection bottles are 79% lighter than the comparable glass bottles hence they require much less energy for transport.

Considering the majority of our product comes from the other side of the globe this is a vitally important point.

Bimeda has a strong world-wide commitment to sustainability as exemplified by a food development program in Africa, a responsible electronics disposal in Mexico, sustainable waste management in Canada, rainwater collection in China, highway cleanup in USA etc… the list goes on – all listed at https://www.onebimeda.com/index.php/case-studies.

Bimeda's bolus manufacturing facility in the UK, manufacturers of Cosecure bolus, changed the material used for immediate packaging from a non-recyclable to a recyclable material. As a result 175,000 blister packs equating to over 3 tons of material per year can now be recycled, instead of going to landfill.

Part of this sustainability program was the switching of Bimoxyl from glass bottles to PET plastic, which is every bit as recyclable as glass but far less energy demanding in transport.


# Irish Philosophy

There are only two things to worry about

Either you are well or you are sick.

If you are well,

Then there is nothing to worry about.

If you are sick,

There are two things to worry about.

Either you will get well or you will die.

If you get well,

Then there is nothing to worry about

If you die,

There are two things to worry about.

Either you will go to heaven or to hell.

If you go to heaven,

Then there is nothing. to worry about.

But if you go to hell,

You'll be so damn busy shaking hands with your friends.

You won't have time to worry!

SO WHY WORRY?

# Monoculture Plantations

There is a lot of angst in the dairy world with the push to plant prime dairy land in pine forests, supposedly to satisfy green intentions. Such a process is known as afforestation. Afforestation is the establishment of forest through planting and/or deliberate seeding on land that, until then, was not classified as forest.

The hope with afforestation is to counteract the vast amount of deforestation taking place across the globe. There is a marked divide in the state of the world's forests. In most rich countries, across Europe, North America and East Asia, forest cover is increasing, whilst in many low-to-middle income countries it's decreasing.

However, it would be wrong to think that the only impact rich countries have on global forests is through changes in their domestic forests. They also contribute to global deforestation through the foods they import from poorer countries. Today, most deforestation occurs in the tropics. 71% of this is driven by demand in domestic markets, and the remaining 29% for the production of products that are traded. 40% of traded deforestation ends up in high-income countries, meaning they are responsible for 12% of deforestation. It is therefore true that rich countries are causing deforestation in poorer countries. (Source: Pendrill, F., Persson, U. M., Godar, J., & Kastner, T. (2019). Deforestation displaced: trade in forest-risk commodities and the prospects for a global forest transition. OurWorldInData.org/forests-and-deforestation).

Thus richer countries, and we fall into that category, hope to salve their conscience by techniques such as afforestation.

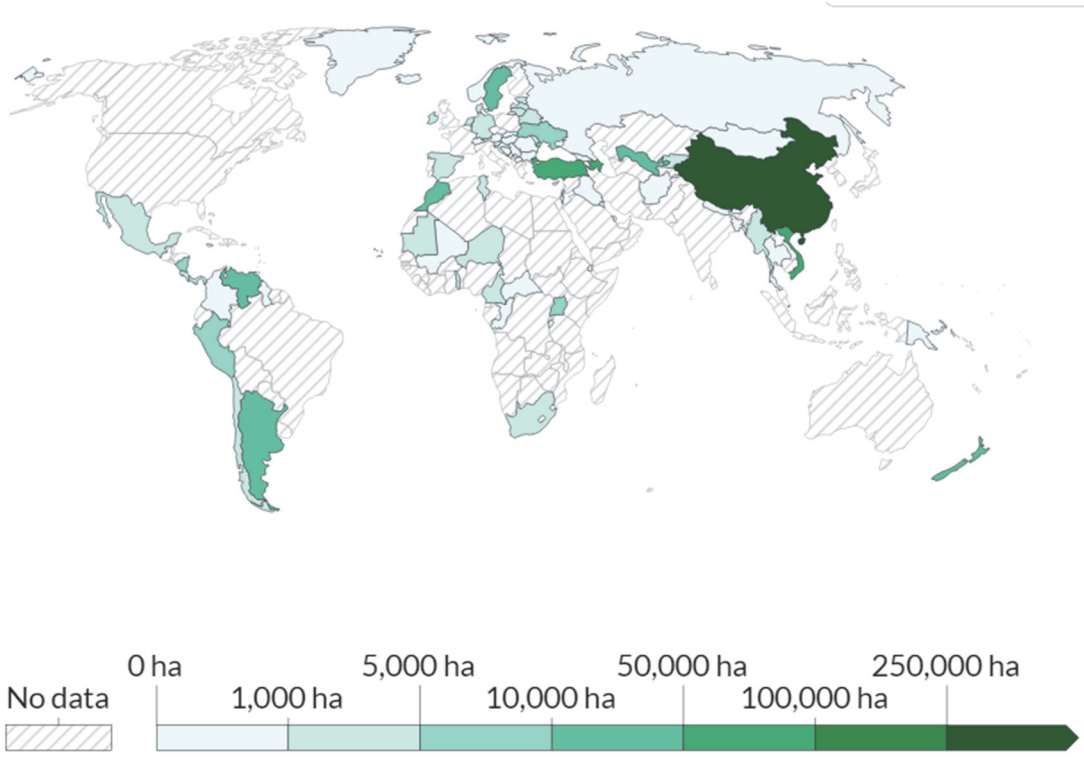
Data on net forest change, afforestation and deforestation is sourced from the UN Food and Agriculture Organization's Forest Resources Assessment. Since year-to-year changes in forest cover can be volatile, the UN FAO provide this annual data averaged over five -year periods. This of course means it is a little dated on line, with the latest available being 2015 figures, but trends are relevant and it is reasonable to assume that there will not be dramatic change over a five-year period.

**New Zealand is in there moderately green and saying, "look at me, look at me!"**

From such data we can see that many countries have not responded, leading one to assume they are hiding something. The accompanying map shows the areas that are positive, with the depth of colour being highly pertinent, i.e., the deeper the colour the greater the afforestation.

New Zealand is in there moderately green and saying, "look at me, look at me!" but are we really that good? The short answer is no, and the reason for that is New Zealand is planting predominantly monoculture forests.

For a few years these forests will soak up carbon dioxide but then they are cut down and release it all so there is no net benefit, except to self-aggrandising governments. If we really wanted to make a difference, we would be planting native bush rather than monoculture forests. One could argue that many farmers are already




*(Continued on page 5)*

# Monoculture Plantations

*(Continued from page 4)*
doing their bit in this space with all the riparian strips going in.

There is also an issue of a growing world population that needs feeding. Converting prime farmland into forest means less efficient farming so adding to global warming. It also gives an excuse to rabid right wingers, like Bolsonaro in Brazil with their destruction of the Amazon rain forests to open up land for farming. The world would be a far better place if that did not happen and prime New Zealand dairy land was utilised for the purpose for which it is intended rather than planted in ineffective monoculture forests to assuage populist trends.

For every action there is a reaction and also, for every theory there is a counter theory, i.e., there is, as always, another side to the story. According to Farm Forestry New Zealand, monocultures are natural forests. Mixtures rarely stay as mixtures as one species soon comes to dominate. Monocultures are at no greater risk than mixtures. Indeed, they may be at less risk.

This however is from the point of view of disease control in the forest itself, i.e., that is the risk assessed. Just as dairy farmers can be defensive about their farming systems, foresters are defensive about monoculture forests, although it is a rather spurious argument. Native New Zealand bush has, for centuries, maintained diversity and the idea that mixtures ultimately end up with one species dominating only refers to specific planting of tall species such as pine and redwood.

Even the far North kauri groves have a vibrant diverse undergrowth that soaks up a lot of carbon.

Most of the world agrees that climate is almost out of control and tree planting is one means of lowering the carbon footprint. However, ill thought populist plans to plant monoculture forests on prime producing land, although a possible vote winner, do not help the overall situation and may in fact hinder it. Using land effectively means farming the land most suitable for farming and planting carbon dioxide soaking bush in the appropriate places. Monoculture forests engender money but are relatively ineffective in carbon dioxide management.

They may well engender a 'feel good' factor but do little for climate change and do nothing to feed the world.

# Seagulls for Sale

Nagy was at the beach walking along with his wife, when he saw an apparent simpleton who had set up a sign on the beach saying, "Seagulls for sale."

Smirking a little Nagy said. "I think we should humour him and asked how much were the gulls.

"Five dollars each," the jolly hawker replied.

"Okay," said Nagy, handing over five dollars, "I'll take one."

The man took the note, pointed skywards and said, "That is your one up there!"


# One Liners From This Year's Edinburgh Festival

Olaf Falafel: Getting mythology wrong is my Hercules ankle.

Leila Navabi: I have an unconscious bias. I'm biased firmly towards being unconscious.

Sikisa: Cats are like strippers – they sit on your lap and make you think they love you.

Ginny Hogan: Everyone says your 20s are all about finding yourself. If that's true, your 30s are about wishing you'd found somebody else.

Alison Spittle: What does Kylie sing while counting sheep? I can't get ewe out of my head.

Kuan-Wen Huang: My relationship with my mum is like the evolution of payment technology – we went from physical contact to electronic only, then it was contactless.

Amos Gill: Last year, I had a great joke about inflation. But it's hardly worth it now.

# Nano and Micro Emulsions

The tinfoil hat brigade gained notoriety in the Parliament occupation indicating the salient fact that people who do not understand basic science can be fearful and subject to wild unsubstantiated rumours. From antivaxxers to fear of cell phone towers and wi-fi signals there seems to be no end to the list of preposterous theories that many believe implicitly, and that is not even starting on genetic modification!

Another word a few years ago that drummed up claims of uncontrolled chemical risk was the word nanotechnology, the fear being so persuasive that, at one stage, AVPMA, the Australian equivalent of our ACVM, refused outright to register any product with nanotechnology claims. Thankfully common sense has since prevailed over the ditch.

Just what is nanotechnology? It is all about emulsions. An emulsion is a temporarily stable mixture of immiscible fluids, such as oil and water, achieved by finely dividing one phase into very small droplets; they look like a simple solution to the naked eye and only at the microscopic level are the two phases differentiated. In an emulsion, one liquid is dispersed in the other, generally water in oil or oil in water. For example, milk is an oil in water emulsion and margarine is a water in oil emulsion.

Surfactants adsorb at the interface between oil and water, thereby decreasing the surface tension. Surfactants are amphiphilic, meaning that they contain hydrophilic (water-loving) head groups and hydrophobic (water-hating, or oil-loving) tails.

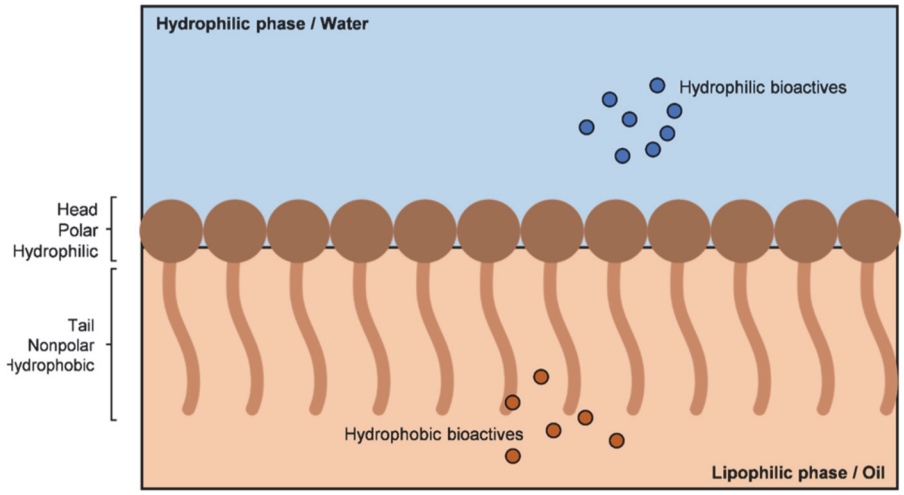
Emulsifiers stabilize emulsions by coating droplets within an emulsion so preventing them from coalescing or coming together to grow larger droplets.

Egg yolks, mustard, and honey are examples of emulsifiers. They help the two liquids get along better. The most common emulsions are salad dressings.

Simple dressings that are made from oil, water and seasonings are temporary emulsions, which is why they must be given a good shake before using so that the ingredients mix together.

Dressings that use eggs or dairy products as a base, such as ranch, Caesar or blue cheese, are permanent emulsions that do not need shaking before use.

As well as simple emulsions, we have nanoemulsions and microemulsions. Microemulsions offer greater stability than conventional macroemulsions. As the name suggests, microemulsions have smaller droplet sizes than regular emulsions, making them appear transparent rather than opaque. Given enough time, a macroemulsion will break down into water and oil phases, but time is not a factor in how long a microemulsion will remain in its current state. Compared to macroemulsions, microemulsions require more surfactant.




Microemulsions are considered thermodynamically stable dispersions of mean droplet size approximately 100–400 nm, whereas nanoemulsions are thermodynamically unstable dispersions of mean droplet size approximately 1 to 100 nm that usually require a cosurfactant for their stabilization due to the higher free energy.

Nanotechnology is therefore all about droplet size in the emulsion itself, and that is all it is!

A cosurfactant is a chemical used in combination with a surfactant to enrich the properties of the primary surfactant formulation. The surfactant decreases the interfacial tension and the cosurfactant holds the excess of aqueous phase by hydrogen bonding.

Nanoemulsions and microemulsions represent versatile options for the delivery of drugs through lipophilic barriers, and many synthetic and natural compounds have been formulated using these delivery systems, aiming to improve stability, delivery and bioactivity

While most of the micro/nanoemulsions on the market are held by the cosmetic industry to enhance the activity of drugs used in skincare products, research on the development of novel pharmaceutical formulations designed for the topical, dermal and transder-

*(Continued on page 7)*

# Nano and Micro Emulsions

*(Continued from page 6)*
mal administration of therapeutic drugs is well underway.

This is where the fear factor arises. Because, by definition, a nanoparticle is 1 to 100 nanometres in size the fear is that devious molecules can cross barriers unrestrained and do untold harm.

A water molecule is about 0.27 of a nanometre across, it is the smallest of all molecules but much smaller than any nanoparticle. Clearly a 1 nanometre particle in any emulsion will not have many molecules of any kind in it.

In actual fact, while some authors indicate that the droplet size in a nanoemulsion must be less than 100 nanometres most manufacturers would have difficulty in reaching droplets with dimensions within this range. So, even the most sophisticated nanoemulsions will be at the higher end of the definition, i.e. less than 100 nanometres, and so most are really more precisely designated as microemulsions.

In fact designing transdermal medication, although now possible, is still in its infancy and there is no possibility of chemicals so minute that they run all through the body uncontrolled.

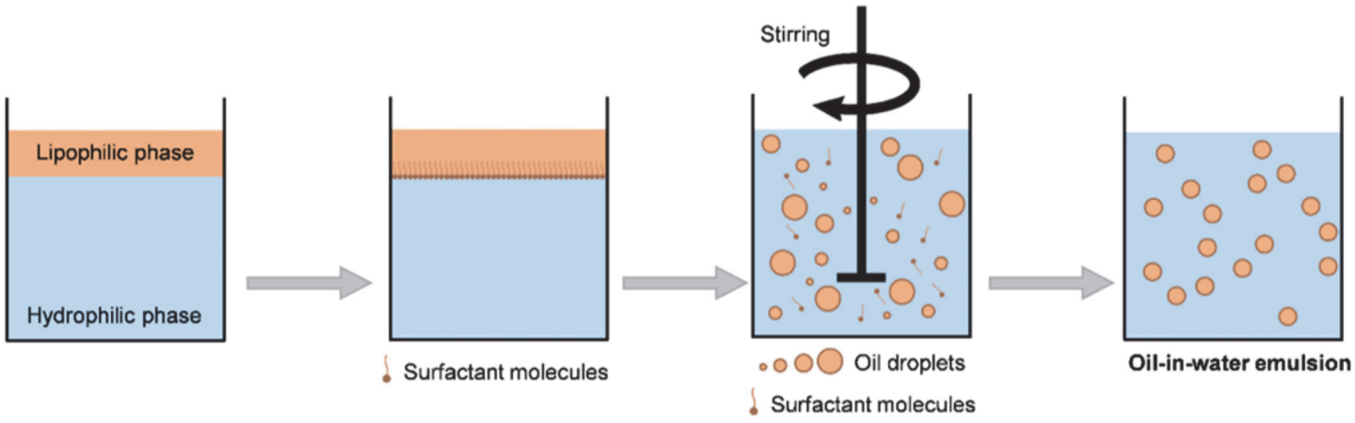
Probably the one upside from the irrational fear of nanotechnology is that it has prevented the pseudoscience of unscrupulous marketeers from adopting it ad nauseum for their products.

In the meantime, microemulsions themselves are proving extremely beneficial, particularly in the disinfection world.

For example, the microemulsion of SteriGENE allows much easier access to tiny cracks and crevices and higher dilutions, resulting in much less chemical actually being put into the environment.

This plus the fact that SteriGENE is totally biodegradable makes this highly efficacious product a really environmentally sustainable option.

Reference: Souto *et al*, Microemulsions and Nanoemulsions in Skin Drug Delivery, Bioengineering2022,9,158.https://doi.org/10.3390/bioengineering9040158




# Dog Maths

Nagy dragged a shaggy dog into a talent scout's office and announced, "This is the best dog act you're ever likely to see. This dog can count and I trained him myself."

The agent gave the pair a dubious stare.

"Okay, I'll prove it," said Nagy and, holding a commanding finger to the dog said, "Right Rover, what is two plus two."

The dog went, "woof, woof,"

Then there was a pause until Nagy said, "Come on Rover, you can do it."

There was another "woof"" then a long pause, followed by another "woof."

"Come on Rover," said Nagy, "Just one more!"

## Changing Ends

Farmer Jones had groomed the prize bull for the annual show and was confident of winning a blue ribbon, but on the eve of the very big event he was aghast to find the bull had gone cock-eyed.

He made a panicked call to the vet who was quickly on the scene and summed up the situation on a professional and composed manner. He simply picked up a length of plastic pipe, inserted one end into the bull's rectum and blew forcefully into the other. The bull's eyes popped straight ahead.

But the next day as Farmer Jones unloaded the bull into his stall at the show, he was distraught to find the cock-eyed affliction had returned. He shoved the pipe up the bull's rear end and blew for all he was worth, but to no avail. In desperation he made another panic call to the vet who once again arrived in his usual calm manner.

"Ï did what you did but it does not work," said Farmer Jones.

"Show me," said the vet.

Once again Farmer Jones shoved the pipe in and blew his best.

"No, no," said the vet. He pulled the pipe out, turned it around and plunged the opposite end into the beast. He gave one puff and the bull's eyes popped straight.

"Oh, so I was using the wrong end of the pipe?" said Farmer Jones.

"No," said the vet, "it makes no difference."

"Then why did you turn it around?"

"You don't think I would use the same end as you had in your mouth, do you?" said the vet.