



**ETHICAL AGENTS**  
**VETERINARY MARKETING**

# EA NEWS

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**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](mailto:info@ethicalagents.co.nz)  
website [www.eavm.nz](http://www.eavm.nz)

## *Merry Christmas*

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*To all our clients*  
*From the sales team at EA*

## Penicillin - The Enigmatic Molecule

The mystique of penicillin is due to the fact that it is the oldest antibiotic. It is staggering to realise that the age of the antibiotic is less than 100 years old. There are people alive today who were alive before the discovery of penicillin.

In that time we have seen the rise and disappearance of video recorders, floppy discs, compact discs, fax machines and various other huge technological advances. The Holden car and the polaroid camera have also come and gone. Yet the enigmatic penicillin is still there and, in situations where the particular microbes are susceptible, it is still regarded as antibiotic of choice.

**"It may seem oxymoronic to say it but this is due to it being such an old drug coupled with the fact that it is a very young drug."**

Much of the confusion concerning penicillin is due to these three factors, i.e. it being the first antibiotic discovered, the dramatic advance in technology in its relatively short life time, and its position as drug of choice in certain situations.

Taking the latter point first, penicillin is regarded by WHO as the most effective antibiotic in cases of syphilis in humans and also in streptococcal throat infection, hence its listing by WHO as critical.

## Christmas Turkeys

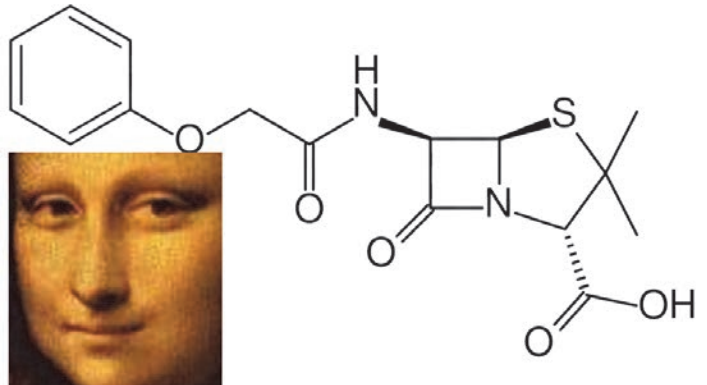
It was Christmas Eve in at the meat counter and a woman was anxiously picking over the last few remaining turkeys in the hope of finding a large one. Her search was in vain as early shoppers had taken the pick.

It is also listed as very important by OIE as it is drug of choice in many situations, especially *Streptococcus mastitidis* infections, which are numerous in pastoral raised dairy cattle in the transition period.

Therefore, despite WHO listing penicillin as critical, industry guidelines such as the NZCV guidelines list it as a green light antimicrobial in the traffic light system. This is because of the high use required in these situations and the requirement to use the most effective antimicrobial where applicable.

Most of the mysteriousness around penicillin is around dose rates and withholding times. It may seem oxymoronic to say it, but this is due to it being such an old drug coupled with the fact that it is a very young drug.

The fact that it was the first antibiotic discovered meant that dose rates were formulated in the early-mid 20<sup>th</sup> Century so they are very old. However the pharmacology around antibiotic therapy is still relatively young and research is happening all the time.



As we have seen in other fields, technology advances at a dramatic rate, and what seemed like appropriate dosing some decades ago is now regarded as insufficient. Most authorities now agree that penicillin dose rates should be twice that of label recommendations in large animals in particular.

Dramatically increasing the dose rate will naturally affect withholding times and so these should be revised but there is a Catch 22. Since the first penicillins for animals were registered many generics have come on the market. The original registrant would have had to provide residue data and naturally enough would have had patent protection for many years. Once patent expired the market is wide open for generics who have to provide bioequivalence to get registration.

With bioequivalence registration authorities grant all formulations

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In desperation she called over a shop assistant and said, "Excuse me. Do these turkeys get any bigger?"

"No, madam, 'he replied, "they're all dead."



## Vetnex Goat Milk Powder



Goat milk is rich in nutrients including a high level of bioavailable proteins, vitamins, minerals, electrolytes, enzymes and fatty acids.

It is easily digested and has a low risk of causing dairy allergy due to its low content of lactose, making it an ideal product for animals with sensitive stomachs or those allergic to other dairy products.

Vetnex Goat Milk Powder for Dogs and Cats 250g (Australian/NZ Origin) is a premium quality, freshly produced, local Australian/NZ goat milk powder made from fresh goat milk sourced from local Australian and New Zealand goat farms. It is high quality and naturally tasty with a great flavour.

Vetnex Goat Milk Powder is natural and gentle on the stomach. It is a premium nutritional choice for animals that require a high quality and low allergy risk product, e.g. puppies and kittens needing extra protein and calcium to develop and grow, sick or elderly animals needing gentle and quality nutrients to help build up strength, or animals in situations of weaning, malnutrition or upset stomachs.

Vetnex Goat Milk Powder is tasty with natural milk flavour which can be easily added daily to a pet's dry or wet foods or mixed in drinking water, providing premium quality nutrients for dogs or cats.

## Penicillin - The Enigmatic Molecule (Cont.)

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the identical withholding times, which is common sense, but that is the problem. Residue testing is very expensive and no company is prepared to establish withholding times at the higher dose rate for their competitors to immediately benefit.

In some jurisdictions this is a massive problem as "off label" usage is not allowed. The veterinarian legally must comply to the approved label dose rate even though modern pharmacology deems it insufficient. It is permitted in New Zealand but leaves the onus for resi-

dues squarely on the shoulders of the prescribing veterinarian.

A rule of thumb is that doubling the dose rate of a drug extends its duration in the body by one half life. This does not take into account excipients and dosage form.

The most accepted practical recommendation for clinicians is to simply increase the withholding period by one full day if doubling the dose rate.

To complicate matters further there is a recommended withholding period for procaine penicillin in racing horses although this is due

to the procaine presence and not the penicillin itself. Moreover doubling the dose has little effect on the race withholding period as it is a default period, not worked out on actual amount of procaine but to its mere presence. Thus this is a mere oddity and not really part of the penicillin ambiguity.

Nevertheless, although not quite fulfilling the Churchillian phrase of being "a riddle wrapped up in mystery inside an enigma", penicillin still has a few unknowns to its credit, leaving an air of mystery.

## Reward

A woman lost her handbag in the hustle and bustle of Christmas shopping in Sylvia Park. A small boy found it and returned it to her.

Looking in her purse, she reasoned, "Hmmm.... that's strange. When I lost my bag there was a

\$20 note in it. Now there are four \$5 notes."

The boy quickly replied with a charming smile, "That's right, madam. The last time I found a lady's purse, she didn't have any change for a reward."





## Belt and/or Braces?

Human behaviour has been shown to be one of the biggest allies any disease can have in its propagation. The Covid app for example is an extremely useful tool in the fight against the pandemic, but only if it is widely used. Clearly it is underutilized as many people are in too much of a hurry or too blasé.

Despite the mixed messages early in the piece about mask use, experts now all agree that masks are a great help in limiting spread.

Elimination did seem a good course to follow but, while it was fine for a considerable time, everywhere in the world where elimination was the primary tool vaccination lagged well behind, so that when the Delta variant arose it could rapidly



gain ground. Only now are we seeing vaccination reaching acceptable rates that will allow easing of restrictions. Elimination has basically failed but would have been a great success if the vaccine rollout had been concurrent.

What was taken on board in the very early stages was the need for hygiene. The Covid virus is an enveloped virus, which means that it is readily killed by soap or by cationic disinfectants, the mainstay of routine chemical antisepsis and disinfection. Sanitizer sales went through the roof in 2020 but have declined dramatically in more recent times.

With the latest scare, although far from perfect, people are masking and using the app in a better fashion and vaccination targets are getting much closer. However it seems that the focus on vaccination has diverted attention away from the requirement for personal hygiene. Those that do use the tracer app seem to bypass the hand sanitizer in the rush to enter premises, and gloves as part of PPE are non-existent.

One of the first rules of vaccination is that it is not a replacement for sanitation. Although this principle has been hijacked by that small but extremely vocal group, the antivax mob, some of whom propose disinfection instead of vaccination, the overriding principle is still extremely sound. In short it is not an 'either or' situation but a case of best practice utilizing all the tools in the armoury.

And that is what both vaccination and disinfection are, simple tools in the fight against a raging pandemic. The principle applies to any disease process, not just the Covid pandemic. In outbreaks of Parvo virus in dogs, apart from treating

clinical cases the 'go to' responses in virtually every clinic are to insist on a high level of clinic disinfection and also to vaccinate at risk animals. It is a belts and braces approach that really is veterinary science 101, and it works!

**"Apart from the lazy, the entitled and the naysayers, most follow the rules"**

The same applies to human health measures. In 2020 the message was "wash your hands," "wash your hands," at that stage no vaccine was available. Now the message from upon high is all about vaccination targets, so much so that handwashing is not being mentioned at all. This does not mean that it is off the agenda; it is still all important but being out of the public eye is being forgotten.

This is just human nature, especially to the public at large. Messaging needs to be constant and consistent. The overriding push for vaccination is totally understandable but it is a fight and, if nothing else fails, it can be likened to a game of chess.

For many amateur or part time chess players their major weakness is concentrating so hard on attack that they neglect defence and are not aware of their opponent's strategy until it is almost too late. Chess is often likened to battle tactics and such habits are like a general so obsessed with an attacking sortie that his flanks are exposed to an enemy counterattack. He, and the chess player need to be awake to all possibilities.

The point with a war on a pandemic is that it is a defensive war and

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## Belt and/or Braces?

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very few citadels throughout history did not fall eventually.

Early successes with elimination by lockdown were akin to the queen dominating the centre of the chess board with the painfully slow vaccine rollout being like the queen



not noticing those pesky knights sidling up into positions of threat, just like our general driving forward and ignoring his flanks.

As powerful as she is the queen alone cannot generate success without the help of the other pieces at her dispos-

al nor can the general make an attack without reserve troops and weapons such as artillery.

It is the same with the pandemic. Lockdown was a tool but always a temporary one and required both high level hygiene (antiseptic techniques and mask wearing) and the heavy artillery of vaccination to ensure success. In warfare, as much as the ground troops rely on artillery the artillery also needs the support of the other troops.

It is the same fighting a disease, hygiene and vaccination seem like a belt and braces approach but they work hand in glove. It is a symbiotic partnership each being more effective in the presence of the other.

While it is not difficult for the amateur chess player to ignore support or miss threats, such an action is unthinkable for a general. Unfortu-

nately the public at large and its Covid response seem to more accurately mimic our chess player, especially when there is more than one message to absorb.

Apart from the lazy, the entitled and the naysayers, most follow the rules and the rules have been use the app, wash hands, wear masks, vaccinate.

That is four messages to take heed of, and most marketers stress that a talk should have a maximum of three messages. It does seem the hygiene message is falling off the radar despite being such an effective means of control.

So vaccinate - yes, wear a mask - yes, socially distance - yes; and wash hands, wash hands, wash hands!

It is not rocket science - but it is science.

## Grace

A seven-year-old boy, was asked to say thanks for the Christmas dinner. The family members bowed their heads in expectation.

The little boy began his prayer, thanking God for his Mummy, Daddy, brothers, sister, Grandma,

and all his aunts and uncles.

Then he began to thank God for the food.

He gave thanks for the turkey, the stuffing, the Christmas pudding, even the cranberry sauce.

Then he paused, and everyone waited ... and waited.

After a long silence, the young fellow looked up at his mother and asked, "If I thank God for the Brussels sprouts, won't he know that I'm lying?"

## Payment

In the week before Christmas a pretty 18 year old girl sauntered up to the curtain counter, and was trying to decide which of the many types of tinsel she would buy.

Finally, she made her choice and asked the spotty youth who was manning the fabric section. "How much is this gold tinsel garland".

The spotty youth pointed to the Christmas mistletoe above the counter and said,

"This week we have a special offer, just one kiss per metre."

"Wow, that's great", she said, "I'll take 12 metres".

With expectation and anticipation

written all over his face, the boy measured out the tinsel, wrapped up the garland, and gave it to her.

She then called to an old man who had been browsing through the Christmas trees and said, "My Grandpa will settle the bill."

## Animal Research in mRNA COVID-19 Vaccine Development

Recently, the U.S. National Institutes of Allergy and Infectious Diseases published an excellent blog that summarized the importance of animal research in COVID-19 vaccine development. In less than a year, almost 5.3 billion doses of vaccine have been administered globally – resulting in one-third of the entire human population being fully vaccinated against the SARS-CoV-2 virus.

### “The Important Role of Animal Research in mRNA COVID-19 Vaccine Development

As the global COVID-19 pandemic continues, safe and effective vaccines are playing a pivotal role in preventing severe disease and death and limiting the spread of SARS-CoV-2, the virus that causes COVID-19.

The urgency of the COVID-19 pandemic necessitated rapid vaccine development and testing. Fortunately, NIAID’s decades-long support and conduct of coronavirus and vaccine research laid the groundwork for helping to develop a safe and effective COVID-19 vaccine in record speed.

### COVID-19 Animal Models

Animal research plays a key role in developing successful vaccines for humans. Before promising vaccine candidates can be tested in humans, they must first be tested for safety and effectiveness in animals as required by the U.S. Food and Drug Administration. To do this, scientists first determine whether a vaccine candidate can stimulate an adequate and safe immune response.

This important step is often conducted using small and then, potentially, larger animal models of disease. Mice are frequently used because they reproduce rapidly, have a well-characterized immune

system and a defined genome. Some labs turned to mouse models of infection early in the COVID-19 pandemic only to find that mice don’t get infected with SARS-CoV-2.

In order to infect cells, SARS-CoV-2 must bind to a human protein called ACE2. The human and mouse ACE2 proteins are different, and SARS-CoV-2 does not bind to mouse cells. Scientists overcame this problem by generating mice that can express the human version of ACE2 and can therefore be infected with SARS-CoV-2.

“Animal research plays a key role in developing successful vaccines for humans.”

When these genetically modified mice are infected by the virus, they lose weight and become sick in ways that are similar to what happens when people are infected with the virus. Mouse models provided vital information about COVID-19 symptoms and its disease course and continues to be used by researchers to understand COVID-19 disease.

Syrian hamsters are another important animal model for COVID-19 because disease in those animals closely resembles the disease in humans. Additionally, older male hamsters develop more severe disease than young female hamsters, which reflects some of the differences seen in humans infected by SARS-CoV-2. Hamster models have contributed to the evaluation of investigational COVID-19 vaccine candidates, immunotherapies, and antiviral drugs.

Vaccine development for COVID-19 also benefitted from nonhuman

primate studies. In assessing immunogenicity and protection of vaccines in pre-clinical animal models, nonhuman primates provide several advantages for clinical translation.

They are outbred, have greater similarity to humans than rodents in innate immune responses and B- and T-cell repertoires, and allow use of clinically-relevant vaccine doses. Recent studies in nonhuman primates show that SARS-CoV-2 targets similar replication sites and recapitulates some aspects of COVID-19 disease.

Nonhuman primates are used during the later stages of vaccine development and typically build upon the knowledge accumulated in earlier small animal studies.

### A New Type of Vaccine

The biopharmaceutical companies Moderna, Inc., based in Cambridge, Mass., and Pfizer, Inc., based in New York City, developed a new type of nucleic acid vaccine called an mRNA vaccine that when tested in clinical trials, proved to be more than 90 percent effective at preventing COVID-19. Animal studies contributed to the scientific understanding of how these new types of mRNA vaccines work.

For example, when the 2016 Zika virus outbreak occurred, researchers developed a nucleic acid vaccine that protected against Zika virus infection in mice and nonhuman primates.

The Moderna and Pfizer COVID-19 vaccines use the nucleic acid, messenger RNA (mRNA) to produce the viral spike protein found on the surface of SARS-CoV-2. Because mRNA is unstable, it is enclosed in lipid nanoparticles to prevent it from degrading following injection. Cells then produce the viral spike

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# Animal Research in mRNA COVID-19 Vaccine Development

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protein and display it on their surfaces. In this form, the viral spike protein is recognized by the body and triggers an immune response.

This response includes the production of antiviral antibodies and T-cell responses that allow the body to remember how to fight off SARS-CoV-2 if infected in the future.

Preclinical data with Moderna’s mRNA vaccine produced promising results in animal models. Mouse experiments demonstrated that a low dose of the vaccine induced a robust neutralizing antibody response and a high-level protection against SARS-CoV-2.

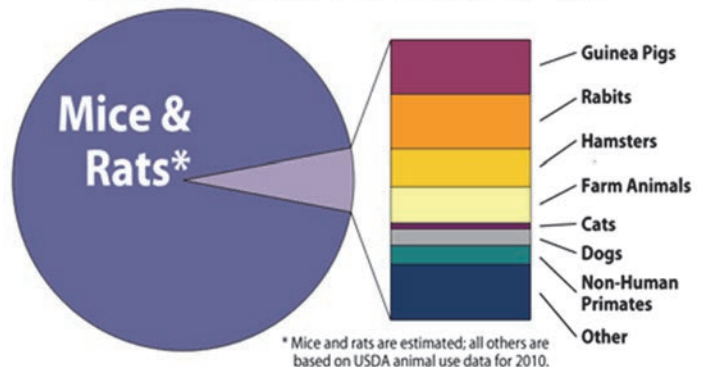
Moreover, vaccination of non-human primates with the mRNA vaccine induced robust SARS-CoV-2 neutralizing activity and notably, rapid protection in the upper and lower airways, similar to safety

and immunogenicity results subsequently observed in a phase I human clinical study.

## Looking to the Future

Biomedical studies involving animal models have greatly contributed to the public health response to SARS-CoV-2 by assisting in the development of COVID-19 vaccines and treatments. Animal studies will continue to provide vital information as new SARS-CoV-2 variants emerge and new questions arise as to the transmissibility of these variants, whether they are more harmful to people, and if they remain sensitive to available vaccines.

## Mammals in Research



Animal models play a critical role in pandemic response efforts as they are necessary for evaluating the safety and effectiveness of new vaccines and therapeutics.

Scientists will continue building on the lessons learned from COVID to develop animal models as part of our pandemic preparedness efforts to target other emerging or re-emerging infectious diseases.”

## Amazing Pig

The visitor was admiring the family’s pet pig.

“Yes, he’s an amazing animal,” said the farmer.

“Once he raised the alarm and stopped the house from burning down.

Another time he saved young John-

ny from drowning and pulled him out of the dam...”

“That’s incredible,” said the visitor, “but tell me, why does he have one leg missing?

“Well,” said the proud farmer, “a pig like that, you don’t eat him all at once!”

## Lining Up

The tough sergeant major knew that he was unpopular with the ranks and was carpeting a soldier who was due for discharge.

The sergeant major shouted, “I’ve heard it said that when I die some of you blokes are coming back to

urinate on my grave. I suppose you will be among them?”

“Not me sarge,” said the soldier.

“Once I get out of the army, I’ve promised myself I will never stand in long queues again.”





Animal Welfare is Our Business



## Inspiration

A young woman went to her mother and told her about her life and how things were so hard for her. She did not know how she was going to make it and wanted to give up. She was tired of fighting and struggling. It seemed as one problem was solved, a new one arose.

Her mother took her to the kitchen. She filled three pots with water and placed each on a high fire. Soon the pots came to boil.

In the first she placed carrots, in the second she placed eggs, and in the last she placed ground coffee beans. She let them sit and boil; without saying a word.

In about twenty minutes she turned off the burners. She fished the carrots out and placed them in a bowl. She pulled the eggs out and placed them in a bowl. Then she

ladled the coffee out and placed it in a bowl. Turning to her daughter, she asked, "Tell me what you see."

"Carrots, eggs, and coffee," she replied.

Her mother brought her closer and asked her to feel the carrots. She did and noted that they were soft. The mother then asked the daughter to take an egg and break it. After pulling off the shell, she observed the hard boiled egg.

Finally, the mother asked the daughter to sip the coffee.

The daughter smiled as she tasted its rich aroma. The daughter then asked, "What does it mean, mother?"

Her mother explained that each of these objects had faced the same adversity: boiling water. Each reacted differently. The carrot went

in strong, hard, and unrelenting. However, after being subjected to the boiling water, it softened and became weak. The egg had been fragile. Its thin outer shell had protected its liquid interior, but after sitting through the boiling water, its inside became hardened. The ground coffee beans were unique, however. After they were in the boiling water, they had changed the water.

So said her mother, "Will you become soft and weak, will you be stiff and unyielding, or will you change the situation for the better?"

