Review of the draft *Guidelines on compounding of medicines*

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**BACKGROUND**

The use of compounded veterinary medicines has become a critical and necessary part of modern veterinary practice in all areas other than food animal practice (where compounding has a very limited role, for example, compounding of antidotes for various intoxications encountered in grazing animals). Today it is not possible to provide the standard of care expected by animal owners without the use of compounded veterinary medicines.

Why is this the case?

There are a number of factors that contribute to this important role of compounded medicines.

LARGE NUMBER OF NON-FOOD ANIMAL SPECIES

Across the veterinary profession in Australia there is a need to examine and potentially treat more than 500 species of animal. The diversity of species presented for veterinary examination include domesticated, native, exotic and zoo vertebrate species which comprise mammals, birds, reptiles, amphibians and fish as well as a growing list of invertebrate species.

SMALL MARKET FOR VETERINARY MEDICINE DEVELOPMENT

The breadth of species of veterinary importance necessarily means that the vast majority are minor species and can never expect to enjoy the benefit of medicines developed and approved specifically for them. This is because the absolute number of each species will be small and the likely return on investing in product development will be unattractive to any pharmaceutical company.

LIMITED NUMBER OF PRODUCTS APPROVED BY THE APVMA

The cost of registration of a veterinary medicine can be very high, in the order of tens of millions of dollars for a pioneer product and tens of thousands of dollars for a generic product. Because of the need to recover the costs of development and registration only the most widely used products are generally developed and submitted to the APVMA for approval.

Currently (30 June 2014) the APVMA database of registered products contains 3,422 products for veterinary use. Of these products, there are 1,013 that are scheduled PRESCRIPTION ANIMAL REMEDY (S4). Amongst the S4 veterinary medicines there are 559 products registered for use in dogs, 311 in cats and 333 in horses.

While this may seem a large number of products, they are all prepared from a total of only 176 active pharmaceutical ingredients (APIs) (see APPENDIX).

There are 148 prescription only (S4) active pharmaceutical ingredients (APIs) contained in products approved by the APVMA for use in dogs. The top twenty most common classes of S4 product approved by APVMA for use in dogs include antibacterials (12 actives, 191 products), NSAIDs (3 actives, 54 products), corticosteroids (3 actives, 41 products), local anaesthetics (1 active, 9 products), ACEIs (1 active, 8 products).

For cats there are 105 prescription only (S4) active pharmaceutical ingredients (APIs) contained in products approved by the APVMA

For horses there are 96 prescription only (S4) active pharmaceutical ingredients (APIs) contained in products approved by the APVMA.

This number of APIs should be considered in the context of how many APIs are considered necessary for the practice of veterinary medicine. The report entitled VETERINARY PHARMACOLOGY CURRICULUM RENEWAL TO IMPROVE GRADUATE OUTCOMES AND PUBLIC SAFETY was published in 2011 by the Australian Government Office for Leaning & Teaching.

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| Australian Government Office for Leaning & Teaching<http://www.olt.gov.au/resource-library?text=veterinary%20clinical%20pharmacology><http://www.olt.gov.au/system/files/resources/PP9_1340_Mills_Report_2011.pdf>Veterinary pharmacology curriculum renewal to improve graduate outcomes and public safetyAuthor/s: Paul Mills, Stephen Page, Amanda CraigLead Institution: The University of QueenslandPartner Institutions Australian Veterinary Association, Chapter of Veterinary Pharmacology, Charles Sturt University, James Cook University, Massey University (NZ), Murdoch University, The University of Melbourne, The University of SydneyPublished: 2011 |

The curriculum included a formulary that was compiled from a consolidation of important medicines in veterinary textbooks and veterinary undergraduate teaching at Australian universities. The formulary (which is presented in the project report) identified 1,425 substances, each of which could be included in a variety of formulations. Approximately 1,100 of the substances would be scheduled as Prescription Animal Remedies. Clearly there is a major mismatch between what products are approved by the APVMA for use in veterinary practice and the products that are needed to practice veterinary medicine according to current standards. It is this mismatch, this vast chasm between approved medicines and the unmet need, that presents a significant role for compounded medicines.

To meet the standard of veterinary practice compounded veterinary medicines must be of high quality and for this reason the veterinary profession has a considerable interest in the guidelines on compounding practice and professional practice profile.

There has not been time to prepare a comprehensive response to the two consultations, but a summary of key points is set out below.

**RESPONSES TO CONSULTATION QUESTIONS ON THE DRAFT GUIDELINES ON COMPOUNDING OF MEDICINES**

Do the draft guidelines clearly differentiate between simple compounding and complex compounding?

YES

Do the draft guidelines clearly outline which requirements apply to pharmacists who undertake either or both types of compounding (simple and/or complex compounding), and which requirements apply only to pharmacists who undertake complex compounding?

YES

Is the content of the draft guidelines helpful?

YES

Is there any content that needs to be changed, added or deleted in the draft guidelines?

YES

Do you have any suggestions for questions to be answered in Frequently Asked Questions developed by the Board to support the guidelines?

YES

Is the purpose of the practice profile clearly explained in the draft guidelines?

YES

Do you have any other comments on the draft guidelines?

Regulatory Status

It is not clearly stated at present in the guidelines that compounded veterinary medicines prepared on instructions from a veterinarian are not subject to the AgVetCode Act as they are not included in the definition of a veterinary chemical product:

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| --- |
| **Agricultural and Veterinary Chemicals Code Act 1994**Act No. 47 of 1994 as amended**Section 5 Definition of *veterinary chemical product***Subsection (4) A veterinary chemical product does not include:(a) a substance or mixture of substances that is:(i) prepared by a pharmacist in accordance with the instructions of a veterinary surgeon |

Therefore compounded veterinary products are not subject to regulation by either the TGA or APVMA.

Veterinary Compounding Guidance

The **Australian pharmaceutical formulary and handbook** is solely focused on human medicines and does not address the special requirements of compounding for non-human species of veterinary interest. It would be invaluable to include in future editions sections specifically on veterinary compounding. The Chapter of Veterinary Pharmacology of the Australia New Zealand College of Veterinary Scientists could assist in this initiative.

Competence to undertake veterinary compounding

Pharmacists need to obtain competence in veterinary compounding from an accredited source relevant to Australian veterinary practice.

Suppliers of training on veterinary compounding and experts and mentors on this subject need also to have met a standard that currently is not described but needs to be co-developed by the pharmacy and veterinary professions.

Unique aspects of formulation in veterinary compounding

Inter- and intra-species differences in pharmacokinetics, pharmacodynamics and toxicology need to be understood by the veterinary prescribed and the compounding pharmacist.

Reputable references

A database of reputable references to support decision making in the appropriateness of compounding needs to be developed.

Counselling of patients

It is unlikely that pharmacists will have the skills or experience to counsel owners of animals to be treated with veterinary medicines. It is preferable in almost all cases that the prescribing veterinarian retains the responsibility for counselling and ensuring that the medicine can be readily administered.

Raw Materials

It is likely that many substances not approved for human use will be included in compounded veterinary medicines.

Quality Standards

The quality standards set out in the Therapeutics Goods Act 1989 may not be applicable to veterinary medicines. Nonetheless, a quality standard is necessary.

Adverse Reactions

For compounded veterinary medicines there is no regulatory agency with an interest to receive and investigate adverse reactions. How this can be best resolved is something that the pharmacy and veterinary professions could discuss.

Reference Texts

A list of recommended reference texts that address the issues of compounded veterinary medicines needs to be developed. Again, the Chapter of Veterinary Pharmacology could assist in developing such a list.

Batch production

The needs of the veterinarian are substantially different from his medical counterpart. In many case veterinarians have patients who may need daily treatment for long periods of time. For example, to treat cardiovascular or endocrine disorders. This may necessitate the provision of sufficient medication for some months, or at least the period of time between reexaminations. This will require the compounding of sufficient medicine for an identified patient, but the medication may be administered over a period of months.

Public consultation on the draft *Professional practice profile for pharmacists undertaking complex compounding*

Responses to consultation questions on the draft *Professional practice profile for pharmacists undertaking complex compounding*

Does the draft practice profile clearly explain its purpose, and how it should be used in relation to complex compounding?

YES

Is there any content that needs to be changed, added or deleted in the draft practice profile in relation to complex compounding?

YES

Do you have any suggestions for questions to be answered in Frequently Asked Questions developed by the Board, to assist pharmacists in using the practice profile for complex compounding?

YES

Do you have any other comments on the draft practice profile?

YES

Because of the importance of the compounded veterinary medicines in veterinary practice and the issues identified above, it is recommended that specific guidance on professional practice be directed at:

Standard 1.5 Maintain and extend professional competence

Standard 4.1 Undertake initial prescription assessment

Standard 4.2 Consider appropriateness of prescribed medicines

Standard 4.3 Dispense prescribed medicines

**APPENDIX**

| **PRESCRIPTION ANIMAL REMEDY ACTIVE PHARMACEUTICAL INGREDIENTS IN PRODUCTS APPROVED BY THE APVMA\*FOR USE IN CATS, HORSES AND DOGS** |
| --- |
| **105** | **96** | **148** | **176 ACTIVE PHARMACEUTICAL INGREGIENTS** |
| FEL |  | CAN | 4-AMINO PYRIDINE |
| FEL | EQU | CAN | ACEPROMAZINE MALEATE |
| FEL | EQU | CAN | ADRENALINE TARTRATE |
|  |  | CAN | AGLEPRISTONE |
| FEL |  | CAN | ALPHAXALONE |
|  | EQU |  | ALTRENOGEST |
|  | EQU | CAN | AMBROXOL HYDROCHLORIDE |
| FEL |  | CAN | AMINOPHYLLINE |
| FEL | EQU | CAN | AMOXYCILLIN |
|  |  | CAN | APOMORPHINE HYDROCHLORIDE |
| FEL |  | CAN | ATIPAMEZOLE HYDROCHLORIDE |
| FEL | EQU | CAN | ATROPINE SULFATE |
| FEL | EQU | CAN | BACITRACIN ZINC |
| FEL |  | CAN | BENAZEPRIL HYDROCHLORIDE |
| FEL | EQU | CAN | BENZATHINE PENICILLIN |
| FEL |  | CAN | BETAMETHASONE VALERATE |
|  | EQU |  | BOLDENONE UNDECYLENATE |
| FEL | EQU | CAN | BROMHEXINE HYDROCHLORIDE |
|  | EQU |  | BUSERELIN ACETATE |
| FEL |  |  | CARBIMAZOLE |
| FEL | EQU | CAN | CARPROFEN |
| FEL |  | CAN | CEFOVECIN AS SODIUM SALT |
|  | EQU | CAN | CEFTIOFUR AS CEFTIOFUR SODIUM |
| FEL |  | CAN | CEPHALEXIN AS THE SODIUM SALT |
|  |  | CAN | CEPHALONIUM DIHYDRATE |
| FEL |  | CAN | CHLORAMPHENICOL |
| FEL | EQU | CAN | CHLORPHENIRAMINE MALEATE |
| FEL |  | CAN | CHLORTETRACYCLINE HYDROCHLORIDE |
| FEL | EQU | CAN | CLAVULANIC ACID AS POTASSIUM CLAVULANATE |
|  | EQU |  | CLENBUTEROL AS CLENBUTEROL HYDROCHLORIDE |
| FEL |  | CAN | CLINDAMYCIN AS CLINDAMYCIN HYDROCHLORIDE |
| FEL |  | CAN | CLOMIPRAMINE HYDROCHLORIDE |
|  | EQU |  | CLOPROSTENOL AS SODIUM |
|  |  | CAN | CLOTRIMAZOLE |
| FEL | EQU | CAN | CLOXACILLIN AS THE BENZATHINE SALT |
|  | EQU | CAN | COPPER INDOMETHACIN |
| FEL |  | CAN | CYCLOSPORIN A |
|  |  | CAN | DELMADINONE ACETATE |
| FEL | EQU | CAN | DEOXYCORTONE PIVALATE |
|  |  | CAN | DERACOXIB |
|  | EQU | CAN | DESLORELIN AS DESLORELIN ACETATE |
|  | EQU |  | DETOMIDINE HYDROCHLORIDE |
| FEL | EQU | CAN | DEXAMETHASONE TRIMETHYLACETATE |
|  |  | CAN | DEXMEDETOMIDINE HYDROCHLORIDE |
| FEL |  | CAN | DEXTROMETHORPHAN HYDROBROMIDE |
|  | EQU | CAN | DIAZEPAM |
| FEL | EQU | CAN | DI-ISOPROPYLAMINE DICHLOROACETATE |
|  | EQU | CAN | DIMETHYL SULFOXIDE |
|  | EQU |  | DINOPROST |
|  | EQU | CAN | DIPYRONE |
|  |  | CAN | DIRLOTAPIDE |
| FEL |  | CAN | DISOPHENOL |
|  | EQU |  | DOMPERIDONE |
| FEL | EQU | CAN | DOXAPRAM HYDROCHLORIDE MONOHYDRATE |
| FEL |  | CAN | DOXYCYCLINE AS DOXYCYCLINE MONOHYDRATE |
|  | EQU |  | ELTENAC |
|  |  | CAN | ENALAPRIL MALEATE |
| FEL |  | CAN | ENROFLOXACIN |
| FEL |  | CAN | EPHEDRINE HYDROCHLORIDE |
| FEL | EQU | CAN | ETHYLESTRENOL |
|  |  | CAN | FIROCOXIB |
| FEL | EQU | CAN | FLUMETHASONE |
|  | EQU | CAN | FLUNIXIN MEGLUMINE |
| FEL |  | CAN | FLUOCINOLONE ACETONIDE |
|  |  | CAN | FLUOXETINE HYDROCHLORIDE |
| FEL | EQU | CAN | FRAMYCETIN SULFATE |
| FEL | EQU | CAN | FRUSEMIDE |
| FEL |  | CAN | FUSIDIC ACID |
| FEL | EQU | CAN | GENTAMICIN SULFATE |
| FEL | EQU | CAN | GLYCOPYRROLATE |
|  | EQU |  | GLYCOSAMINOGLYCAN POLYSULFATE |
|  | EQU |  | GNRF - PROTEIN CONJUGATE |
|  | EQU | CAN | GONADOTROPHIN-CHORIONIC |
|  |  | CAN | GONADOTROPHIN-SERUM |
|  | EQU |  | GUAIPHENESIN |
| FEL | EQU | CAN | HALOTHANE |
| FEL | EQU | CAN | HYDROCORTISONE AS THE ACETATE |
|  | EQU | CAN | HYDROXY PROGESTERONE HEXANOATE |
| FEL | EQU | CAN | HYOSCINE-N-BUTYLBROMIDE |
| FEL |  | CAN | IBAFLOXACIN |
|  |  | CAN | IMIDAPRIL HYDROCHLORIDE |
| FEL |  | CAN | INSULIN |
| FEL | EQU | CAN | ISOFLURANE |
|  | EQU |  | ISOXSUPRINE HYDROCHLORIDE |
|  | EQU | CAN | KETOPROFEN |
|  |  | CAN | LEVOTHYROXINE SODIUM (AS MULTIHYDRATE) |
| FEL | EQU | CAN | LIGNOCAINE HYDROCHLORIDE |
| FEL |  | CAN | LINCOMYCIN AS LINCOMYCIN HYDROCHLORIDE |
| FEL |  | CAN | MARBOFLOXACIN |
| FEL |  | CAN | MAROPITANT AS MAROPITANT CITRATE |
|  |  | CAN | MAVACOXIB |
| FEL |  | CAN | MEDETOMIDINE HYDROCHLORIDE |
| FEL |  | CAN | MEDROXYPROGESTERONE ACETATE |
| FEL |  | CAN | MEGESTROL ACETATE |
|  |  | CAN | MELARSOMINE DIHYDROCHLORIDE |
| FEL | EQU | CAN | MELOXICAM |
|  | EQU |  | MEPIVACAINE HYDROCHLORIDE |
| FEL | EQU | CAN | METHANDRIOL DIPROPIONATE |
| FEL |  | CAN | METHOCARBAMOL |
| FEL | EQU | CAN | METHYLPREDNISOLONE ACETATE |
| FEL |  | CAN | METOCLOPRAMIDE HYDROCHLORIDE |
| FEL | EQU | CAN | METRONIDAZOLE |
| FEL | EQU | CAN | MICONAZOLE PRESENT AS MICONAZOLE NITRATE |
|  |  | CAN | MOMETASONE FUROATE MONOHYDRATE |
|  |  | CAN | MOXIDECTIN MICROSPHERES |
| FEL | EQU | CAN | NANDROLONE LAURATE |
| FEL | EQU | CAN | NEOMYCIN SULFATE |
| FEL | EQU | CAN | NITROFURAZONE |
| FEL |  | CAN | NORETHANDROLONE |
| FEL |  | CAN | NYSTATIN |
|  | EQU | CAN | OESTRADIOL DIPROPIONATE |
|  |  | CAN | OESTRIOL |
|  | EQU |  | OMEPRAZOLE |
| FEL |  | CAN | ORBIFLOXACIN |
| FEL | EQU | CAN | OXYTETRACYCLINE HYDROCHLORIDE |
| FEL | EQU | CAN | OXYTOCIN |
|  | EQU |  | PENETHAMATE HYDRIODIDE |
| FEL | EQU | CAN | PENTOBARBITONE SODIUM |
|  | EQU | CAN | PENTOSAN POLYSULFATE SODIUM |
|  | EQU |  | PERGOLIDE MESYLATE |
|  |  | CAN | PHENOBARBITONE |
|  | EQU | CAN | PHENYLBUTAZONE |
|  |  | CAN | PHENYLPROPANOLAMINE HYDROCHLORIDE |
| FEL |  | CAN | PHTHALYLSULFATHIAZOLE |
|  |  | CAN | PIMOBENDAN |
| FEL | EQU | CAN | POLYMYXIN B SULFATE |
|  |  | CAN | POTASSIUM BROMIDE |
| FEL | EQU | CAN | PREDNISOLONE SODIUM SUCCINATE |
| FEL | EQU | CAN | PRILOCAINE HYDROCHLORIDE |
| FEL | EQU | CAN | PROCAINE HYDROCHLORIDE |
| FEL | EQU | CAN | PROCAINE PENICILLIN |
| FEL | EQU | CAN | PROGESTERONE |
| FEL |  | CAN | PROLIGESTONE |
|  | EQU |  | PROPANTHELINE BROMIDE |
|  |  | CAN | PROPENTOFYLLINE |
| FEL |  | CAN | PROPOFOL |
|  | EQU |  | RAMIFENAZONE |
| FEL |  | CAN | RAMIPRIL |
|  | EQU |  | RANITIDINE HYDROCHLORIDE |
| FEL |  | CAN | RECOMBINANT OMEGA INTERFERON OF FELINE ORIGIN |
|  | EQU |  | RESERPINE |
| FEL |  | CAN | ROBENACOXIB |
| FEL | EQU | CAN | ROMIFIDINE HYDROCHLORIDE |
|  |  | CAN | SEVOFLURANE 100% |
|  |  | CAN | SILVER SULFADIAZINE |
|  | EQU |  | SODIUM HYALURONATE |
|  | EQU | CAN | SODIUM SALICYLATE |
| FEL |  | CAN | SPECTINOMYCIN AS SPECTINOMYCIN SULFATE |
| FEL |  | CAN | SPIRAMYCIN |
| FEL | EQU | CAN | STANOZOLOL |
|  |  | CAN | STILBOESTROL |
| FEL | EQU | CAN | STREPTOMYCIN AS STREPTOMYCIN SULFATE |
| FEL | EQU | CAN | SULFACETAMIDE SODIUM |
| FEL | EQU | CAN | SULFADIAZINE |
| FEL | EQU | CAN | SULFADIMIDINE AS SODIUM ETHANE SULPHONATE SALT |
| FEL | EQU | CAN | SULFADOXINE |
|  |  | CAN | TEPOXALIN |
| FEL | EQU | CAN | TESTOSTERONE PROPIONATE |
|  | F |  | THIAMAZOLE |
| FEL |  |  | THIAMAZOLE |
| FEL | EQU | CAN | THIOPENTONE SODIUM |
| FEL |  | CAN | THIOSTREPTON |
| FEL |  | CAN | THYROXINE SODIUM |
| FEL |  | CAN | TILETAMINE HYDROCHLORIDE |
|  | EQU |  | TILUDRONIC ACID AS DISODIUM TILUDRONATE |
|  |  | CAN | TOCERANIB |
|  | EQU |  | TOLAZOLINE AS TOLAZOLINE HYDROCHLORIDE |
| FEL |  | CAN | TOLFENAMIC ACID |
|  | EQU |  | TRANEXAMIC ACID |
| FEL | EQU | CAN | TRIAMCINOLONE ACETONIDE |
|  |  | CAN | TRILOSTANE |
| FEL | EQU | CAN | TRIMETHOPRIM |
| FEL | EQU | CAN | TRIPELENNAMINE HYDROCHLORIDE |
| FEL | EQU | CAN | XYLAZINE AS THE HYDROCHLORIDE |
| FEL |  | CAN | YOHIMBINE HYDROCHLORIDE |
| FEL |  | CAN | ZOLAZEPAM HYDROCHLORIDE |
| \* Approvals obtained from Pubcris 30 June 2014 |