Preface

The purpose of this document is to create a base to examine the need for the compounding of veterinary medicines in South Africa.

South Africa’s animal population and wildlife are a strategic asset needing our protection for now and future generations. The Biodiversity Act seeks (amongst other things) to provide for the management and conservation of biological diversity within our country and the components of biodiversity. This goal requires integrated and coordinated planning and monitoring and the efficient use of limited resources including species-specific veterinary medicines.

The legal issues at play are complex. Local and accepted international regulators are struggling with solutions, yet South Africa holds the key due to a wide range of animal species it treats from wildlife such as elephants and crocodiles to companion animals and food-producing livestock.

The reason for the complexity lies in the conflict of laws at the interface between the control of subjects (people) that work with these objects (drugs, medicines and animals) used by humans to treat the animals. Subjects and objects are governed by different laws, including the common law, statutes (Professional Acts (people) and the Medicines Act (objects), the Biodiversity Act (environment)) and the Constitution (rights and obligations).

Here lies the solution, making these laws talk to each other by correct interpretation and respect for each statutes’ aims and objectives within the value base of the Constitution and the associated principles of openness, responsiveness and accountability. This proposal attempts this difficult task.

This work is one small piece in caring for our animals.

This for our animals and those that serve them.
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POLICY PROPOSAL
VETERINARY MEDICINES COMPOUNDING

A. PURPOSE

1. The purpose of this policy1 proposal is to provide:

   1.1. Background material on the compounding and manufacturing of veterinary medicines2 in South Africa;

   1.2. A policy framework to help distinguish between compounding and manufacturing activities for veterinary medicines; and

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1 A policy is a fixed system of principles to guide decisions and achieve rational outcomes. A policy is to state intent and is implemented as a procedure or protocol. Policies are adopted by the Board of or senior governance body within an organisation, but procedures or protocols would be developed and adopted by senior executive officers. Policies can aid in both subjective and objective decision making. Policies to help in subjective decision making would support senior management with decisions that must consider the relative merits of several factors before deciding and as a result are often hard to objectively test e.g. work-life balance policy. In contrast, policies to aid in objective decision making are operational and can be objectively tested. The term may apply to government, private sector organisations and groups, and individuals. Policy differs from rules or law. While the law can compel or prohibit behaviours, policy guides actions toward those that are most likely to achieve the desired outcome. Policy. (2016, May 5). In Wikipedia, The Free Encyclopedia. Retrieved 10:26, July 16, 2016, from https://en.wikipedia.org/w/index.php?title=Policy&oldid=718820057

2 Medicines Act Section 1: “veterinary medicine” means any substance or mixture of substances, other than a stock remedy or farm feed to be registered in terms of the Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act No. 36 of 1947), used or purporting to be suitable for use or manufactured or sold for use in connection with vertebrates, for the treatment, diagnosis, prevention or cure of any disease, infection or other unhealthy condition, or for the maintenance or improvement of health, growth, production or working capacity, or for curing, correcting or modifying any somatic or organic function, or for correcting or modifying behaviour.
1.3. Clarify the current thinking concerning the veterinary compounding of medicines.

B. SCOPE

2. This policy proposal framework’s scope covers medicinal products for veterinary or animal treatment and refers to veterinary medicines and Scheduled substances regulated under the Medicines and Related Substances Act No 101 of 1965 (Medicines Act).³

3. This policy directive is not applicable to medicines for human use.⁴

³ Medicines Act Section 1: “veterinary medicine” means any substance or mixture of substances, other than a stock remedy or farm feed to be registered in terms of the Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act, 1947 (Act No. 36 of 1947), used or purporting to be suitable for use or manufactured or sold for use in connection with vertebrates, for the treatment, diagnosis, prevention or cure of any disease, infection or other unhealthy condition, or for the maintenance or improvement of health, growth, production or working capacity, or for curing, correcting or modifying any somatic or organic function, or for correcting or modifying behaviour.

⁴ Medicines Act GNR.510 of 10 April 2003: General Regulations: 25. Categories and classification of medicines. - (1) The following are the basic categories of medicines—

a) **Category A** = Medicines which are intended for use in humans and which are, without manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine;

b) **Category B** = Medicines which cannot normally be administered without further manipulation;

c) **Category C** = Medicines intended for veterinary use which are, without further manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine; and

d) **Category D** = Complementary medicines intended for use in humans and animals which are, without further manipulation, ready for administration, including packaged preparations where only a vehicle is added to the effective medicine.

(3) Medicines in categories C and D (veterinary complementary medicines) are subdivided into the following pharmacological classifications...
4. Policy documents are meant to give help on how to meet the policies and governing statutes and regulations. They serve to offer review and compliance guidance to government employees, by that assuring mandates are implemented in a fair, consistent and efficient way.

5. Policy directives are administrative instruments that allow for flexibility in approach. Alternate methods to the principles and practices described in this document may be acceptable provided adequate justification supports them. Alternate methods should be discussed beforehand with the relevant officials to make sure that applicable statutory or regulatory obligations have been met.

6. It is equally important to note that the regulator and the inspectorate retain the right to ask information or material, or define conditions not explicitly outlined in this directive, to allow for the adequate assessment of the safety, effectiveness or quality of a compounded veterinary medicine.

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5. Wade (Administrative Law (5th ed.) says that “there is only a hazy borderline between legislation and administration, and the assumption that they are two fundamentally different forms of power is misleading.

6. Administrative guidance is non-binding advice given by an administrative agency to the public regarding how best to comply with a particular law or regulation. It may also be referred to by terms such as “advice” or “recommendation.” Guidance is often used to explain the objective or interpretation of a vague or nonspecific law or requirement. Administrative guidance. (2016, April 25). In Wikipedia, The Free Encyclopedia. Retrieved 06:04, July 17, 2016, from https://en.wikipedia.org/w/index.php?title=Administrative_guidance&oldid=717012334
7. This directive should be read with relevant sections of other applicable MCC, Pharmacy Council and Veterinary Council guidelines and regulations.\textsuperscript{7}

8. Policies are dynamic in nature, reflect current thinking and are given without prejudice to future measures which the regulator and the inspectorate may take in this area. Anyone applying the information in this document do so at their risk and responsibility.

\textsuperscript{7} Medicines Act Section 38. \textit{Operation of Act in relation to other laws.} - The provisions of this Act shall be in addition to and not in substitution for any other law which is not in conflict with or inconsistent with this Act.
C. POLICY GUIDING PRINCIPLES

- **Compounding must be a legitimate part of the practice of the pharmacist and veterinarian and must not be used as a means to bypass (circumvent) the Medicines Act and its medicines review and approval system or that of the Stock Remedies Act;**

- **All veterinary medicines compounding activities performed are regulated and fall under the Medicines Act, Pharmacy Act and Veterinary and Para-Veterinary Professions Act read together;**

- **In case of a dispute, deciding between compounding and manufacturing activities is handled on a case-by-case basis; and**

- **Pharmacovigilance monitoring of extemporaneously prepared compounded veterinary medicines is desirable in the public interest.**
D. SUBSTANTIATION

9. Compounding is both needed and necessary to treat individual veterinary patients and patient groups such as a herd of elephants.\(^8\) In contrast, the potential exists for causing harm\(^9\) to animals and the public when medicines are compounded without adherence to the precepts of contemporary pharmaceutics\(^10\) and current good compounding practices,\(^11\) as described in norms of practice for compounding by pharmacists and

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\(^8\) In the savannah subspecies, each family unit usually contains about 10 individuals, although several family units may join together to form a 'clan' consisting of up to 70 members led by a female. Forest elephants live in smaller family units.

\(^9\) Uppsala - Glossary of terms used in Pharmacovigilance: **Harm** - The nature and extent of actual damage that could be caused by a drug. Not to be confused with risk. **Risk** - The probability of harm being caused; the probability (chance, odds) of an occurrence. **Odds** - Probability of an occurrence \(p\) divided by the probability of its non-occurrence \((1 - p)\).

\(^10\) Pharmaceutics is the discipline of pharmacy that deals with the process of turning a new chemical entity (NCE) or old drugs into a medication to be used safely and effectively by patients. It is also called the science of dosage form design.

\(^11\) BN 129 of 17 December 2004: Rules relating to Good Pharmacy Practice (Government Gazette No. 27112)

1. INTRODUCTION

The keeping, compounding, dispensing or supply of any medicine or scheduled substance by a pharmacist, pharmacist intern or pharmacist's assistant or the provision of services which form part of the scope of practice of a pharmacist, may only take place in or from a pharmacy if the pharmacy complies with minimum standards relating to premises, facilities and equipment and is duly licensed by the Department of Health and recorded in terms of the Pharmacy Act.

In adhering to minimum standards of good pharmacy practice it must also be taken into consideration that pharmacists are obliged to exercise proper and/or reasonable care in respect of and control over—

a) the acquisition, storage, manufacture, dispensing, sale, supply or disposal of medicines, or of raw materials for the manufacture of medicines, for human or veterinary use;

b) chemical and hazardous substances;

c) access of the public to medicines and scheduled substances;

d) the hygiene, cleanliness and neatness of a pharmacy;

e) the appearance of a pharmacy.

Each section sets out minimum standards for premises, facilities and equipment for community, institutional, and mobile pharmacies as well as primary health care facilities, which must be met. Failure to meet the standards could form the basis of a complaint of misconduct and in some instances even the withdrawal of a licence to own a pharmacy in terms of the Pharmacy Act.
veterinarians. Without adequate safety, potency, and efficacy\textsuperscript{12} data for a compounded veterinary medicines in animals, the potential exists for treatment failures and adverse reactions,\textsuperscript{13} including death. Also, because the pharmacokinetics\textsuperscript{14} and residual depletion times for a compounded veterinary medicines are not known, assigning an empirical or practical withdrawal time may lead to residues of concern being in food acquired from treated animals. Inactive ingredients in a compounded veterinary medicines, such as excipients\textsuperscript{15} and vehicles may present added risk. These added ingredients can affect the effectiveness/risk\textsuperscript{16} of the therapy.

10. In South Africa, compounding of veterinary medicines is practised by pharmacists as an indispensable part of their profession and conducted under the Pharmacy Act No 53 of 1974 by the South African Pharmacy Council while compounding veterinarians are

Manufacturing pharmacies, wholesale pharmacies and distributors must comply with standards as prescribed in the Guidance Document: Good Manufacturing Practice published by the Medicines Control Council (MCC) (GNR.7659 of 2 May 2003) and Good Wholesale Practice for Wholesalers, Distributors and Bonded Warehouses (MCC 6 June 2003).

\textsuperscript{12} Uppsala: Efficacy - The ability of a drug to produce the intended effect as determined by scientific methods, for example in pre-clinical research conditions.

\textsuperscript{13} Uppsala: Adverse (Drug) Reaction (ADR) - A response which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. (WHO, 1972). An adverse drug reaction, contrary to an adverse event, is characterized by the suspicion of a causal relationship between the drug and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

\textsuperscript{14} WordWeb: The study of the action of drugs in the body: method and rate of excretion; duration of effect; etc.

\textsuperscript{15} Uppsala: Excipients: All materials included to make a pharmaceutical formulation (e.g. a tablet) except the active drug substance(s).

\textsuperscript{16} Uppsala Effectiveness/risk: The balance between the rate of effectiveness of a medicine versus the risk of harm is a quantitative assessment of the merit of a medicine used in routine clinical practice. Comparative information between therapies is most useful. This is more useful than the efficacy and hazard predictions from pre-marketing information that is limited and based on selected subjects.

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regulated under the Veterinary and Para-Veterinary Professions Act No. 19 of 1982 by the South African Veterinary Council.

11. No individual other than a pharmacist in a community pharmacy setting\textsuperscript{17} or veterinarian\textsuperscript{18} may compound or dispense drugs or medicines for administration to animals. Veterinarians preferring to prescribe or use a compounded medicine may either compound the medicine themselves or write a prescription or order for a pharmacist to compound the veterinary medicine on their behalf for administration to patients or a group of patients under their care. The latter practice is desirable when compounding high risk level medicines such as injectables because of microbial contamination, exceedingly potent harmful drugs such as opioids used in game

\textsuperscript{17} Pharmacy Act Regulation \textbf{18. Community or institutional pharmacy}. - Except as provided for in the Medicines Act, the following services pertaining to the scope of practice of a pharmacist may be provided in a community or institutional pharmacy –

... (c)

the provision of animal health care services which includes:

i. the compounding and dispensing of prescriptions written by veterinarians and ensuring the optimal use of veterinary medicines;

ii. the immunisation of animals;

iii. the handling of minor and/or self-limiting ailments in animals; and

iv. the provision of information and education regarding the promotion of animal health.

\textsuperscript{18} Veterinary Act Section \textbf{34. Dispensing of medicine}. - (1) A person who is registered or deemed to be registered in terms of this Act to practise a veterinary profession, may personally compound or dispense any medicine which is prescribed by himself or by any other person with whom he or she is in partnership or with whom he or she is associated as a principal or an assistant or a \textit{locum tenens}, for use in the treatment of an animal which is under his or her professional care; Provided that he or she shall not be entitled to keep an open shop or pharmacy.

(2) A person referred to in subsection (1) shall not accept or obtain any commission or other reward from a pharmacist or other supplier in connection with medicine which is compounded or dispensed by virtue of a prescription.
immobilization, materials hazardous to the health of the compounder or making complex preparations demanding specialized training, environmental control, facilities, equipment and procedures to secure proper therapeutic results.

12. Compounded veterinary medicines are not approved by the Medicines Control Council (MCC) and are distinct from those commercially available registered veterinary medicines which have completed the stringent evaluation and government licencing process.

13. Prescribing a compounded veterinary medicine requires the veterinarian to accept full responsibility for the quality, stability, safety, efficacy and potency of the compounded veterinary medicine. Besides, veterinarians should only use compounded veterinary medicines where there is a legitimate therapeutic need that offsets the risks involved.

19 Medicine Act Section 22A (17) For the purposes of this section -
  a) ... and
  b) “medicinal purpose” means for the purposes of the treatment or prevention of a disease or some other definite curative or therapeutic purpose, but does not include the satisfaction or relief of a habit or craving for the substance used or for any other such substance, except where the substance is administered or used in a hospital or similar institution maintained wholly or partly by the Government or a provincial government or approved for such purpose by the Minister.

20 Veterinary Rule 10. Use of veterinary medicine
(1) Whenever a veterinary professional, administers medicine to an animal or prescribes the administering thereof, he/she must satisfy himself that the administering thereof is justified with due allowance for the benefits and risks which that medicine may hold for –
  a) The animal to which it is administered, including withdrawal times of residues where relevant in the animal and/or the effect on the environment;
  b) The person by whom it is administered; and
14. Medicines manufacturing including veterinary medicinal products for commercial sale where no patient is involved, on the other hand, is regulated by the Medicines Control Council and the Department of Health\textsuperscript{21} under the Medicines Act.

15. Since the maintenance and enhancement of health and safety is a shared duty between government (various national departments and organs of state)\textsuperscript{22} industry, consumers, healthcare specialists and their respective professional regulatory authorities, it is vital that the foundations for compounding and manufacturing be distinctly recognised so the various parties and regulatory authorities can fulfil their obligations in a coordinated and efficient manner.

16. As a result, there is a need for transparency and harmony across roles and jurisdictions\textsuperscript{23} between the MCC, Pharmacy Council and South African Veterinary Council (who is

\begin{itemize}
  \item c) The consumer of the products of that animal if residues of the medicine concerned should be present in those products.
\end{itemize}

\textsuperscript{21} Medicines Act 34A. Delegation of powers. - (1) The Minister may in writing authorise the Director-General or any officer of the Department of Health to exercise any of the powers conferred upon the Minister by this Act other than the powers referred to in sections 3, 24 (1) and 35, or to exercise or perform any of the duties or functions conferred or imposed on the Minister in terms of this Act.

(2) The Director-General may in writing authorize any officer of the Department of Health to exercise or perform in general or in a particular case or in cases of a particular nature, any power, duty or function, excluding any power, duty or function referred to in subsection (1), conferred or imposed on the Director-General by or in terms of this Act.

\textsuperscript{22} National departments: Agriculture, Forestry and Fisheries, Environmental Affairs, Health and SA Police Service; Medicines Control Council, Pharmacy Council, Allied Health Professions Council and the Veterinary Council.

responsible and for what?), as well as concerns related to specific animal products, processes and service providers. Furthermore, to recognise the distinctions between compounding from the activities of manufacturing and then develop consistency in enforcement application to make sure that veterinary medicines compounding and veterinary medicines manufacturing are each regulated by the proper authorities.

E. COMPOUNDING OF VETERINARY MEDICINES

17. Numerous veterinary medicines are registered for use in animals. However, there are many species of animals (~ 60 000 vertebrates)\(^{24}\) with different diseases and conditions for which there are no registered veterinary medicines. In such circumstances, compounding of the veterinary medicine becomes a treatment option open to the veterinarian where no registered veterinary medicine is to be had.\(^{25}\)

\(^{24}\) http://www.factmonster.com/ipka/A0934288.html accessed 2016/07/17 8:50 AM.

\(^{25}\) In the US, The Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) permits veterinarians to prescribe extralabel uses of certain approved new animal drugs and approved human drugs for animals under certain conditions. Extralabel use refers to the use of an approved drug in a manner that is not in accordance with the approved label directions. Under AMDUCA and its implementing regulations published at Title 21, Code of Federal Regulations, Part 530 (21 CFR 530), any extralabel use of an approved new animal or human drug must be by or on the lawful order of a veterinarian within the context of a veterinarian-client-patient relationship (VCPR). Extralabel use must also comply with other provisions of 21 CFR 530. A list of drugs specifically prohibited from extralabel use appears in 21 CFR 530.41.

"Extralabel use" is defined as: "Actual use or intended use of a drug in an animal in a manner that is not in accordance with the approved labeling. This includes, but is not limited to, use in species not listed in the labeling, use for indications (disease and other conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from labelled withdrawal time based on these different uses." (21 CFR 530.3(a)).

Under the provisions of 21 CFR 530, the FDA recognizes the professional judgment of veterinarians, and permits the extralabel use of drugs by veterinarians under certain conditions. Extralabel use of drugs may only take place within the scope of a valid VCPR. In the absence of a valid VCPR, if an approved new animal drug is used for a use for which it is not labelled, such use has caused the drug to be deemed unsafe under
18. In recognition of the scarcity of registered veterinary medicines in South Africa and worldwide, the impetus for this policy is to clarify present understanding about the differences between compounding and manufacturing and define when veterinary compounding is acceptable and under which conditions. Bearing in mind, each situation must be determined on its own merits.

19. Veterinary compounding’s activities may be summarised as the traditional and centuries old compounding practice comprising specialist and not purely economic activities as envisaged in the Medicines Act. Compounded medicines are not sold by the Federal Food, Drug and Cosmetic Act ("the Act") (21 U.S.C. 360b), and therefore adulterated under the Act (21 U.S.C. 351(a)(5)).

An approved animal drug or approved human drug intended to be used for an extralabel use in an animal, other than a use in or on animal feed, is not unsafe under the Act (21 U.S.C. 360b) and is exempt from the labeling requirements under the Act (21 U.S.C. 502(f)), if such use is by or on the lawful written or oral order of a licensed veterinarian within the context of a valid VCPR and such use complies with the extralabel use regulation (21 CFR 530). Extralabel use is limited to circumstances when the health of an animal is threatened, or suffering or death may result from failure to treat. This means that extralabel use to enhance production is not permitted.

§530.21 Prohibitions for food-producing animals.

(a) FDA may prohibit the extralabel use of an approved new animal or human drug or class of drugs in food-producing animals if FDA determines that:

(1) An acceptable analytical method needs to be established and such method has not been established or cannot be established; or

(2) The extralabel use of the drug or class of drugs presents a risk to the public health.

(b) A prohibition may be a general ban on the extralabel use of the drug or class of drugs or may be limited to a specific species, indication, dosage form, route of administration, or combination of factors.

Rebecca J. Riley; The Regulation of Pharmaceutical Compounding and the Determination of Need: Balancing Access and Autonomy with Patient Safety Pharmacy compounding has been a central part of the practice of pharmacy for over 4000 years. One source asserts “the art of selecting, extracting, preparing and compounding medicines from vegetable, animal, and mineral substances, is an acquirement that must have been almost as ancient as man himself on earth.” Some of the oldest known prescription records are written in “hieratic writing” of ancient Egypt. A prescription on a stone tablet instructs a pharmacist to prepare a vapour for inhalation. There is also a document known as the Ebers Papyrus that translates as a sort of
wholesale\textsuperscript{27} or retail\textsuperscript{28} but under a legitimate professional triad contractual relationship\textsuperscript{29} between the pharmacist, veterinarian and owner-patient, within the ambit of the principles of veterinary medicine and pharmacy while manufactured medicines are not so restricted. So, compounding by a pharmacist or veterinarian is distinct from medicines manufacturing. Manufacturers are not obliged to, and do not extend oversight to individual patients, nor may they do so.\textsuperscript{30}

“recipe book” for compounded medications. It is thought to date back to 1552 B.C; https://dash.harvard.edu/bitstream/handle/1/8852177/Riley.html?sequence=1; 2016/07/17 2:24 PM.

\textsuperscript{27} WordWeb: The selling of goods to merchants; usually in large quantities for resale to consumers.

\textsuperscript{28} WordWeb: The selling of goods to consumers; usually in small quantities and not for resale.

\textsuperscript{29} Contract: an agreement with specific terms between two or more persons or entities in which there is a promise to do something in return for a valuable benefit known as consideration. Since the law of contracts is at the heart of most business dealings, it is one of the three or four most significant areas of legal concern and can involve variations on circumstances and complexities. The existence of a contract requires finding the following factual elements: a) an offer; b) an acceptance of that offer which results in a meeting of the minds; c) a promise to perform; d) a valuable consideration (which can be a promise or payment in some form); e) a time or event when performance must be made (meet commitments); f) terms and conditions for performance, including fulfilling promises; g) performance. Ref: contract - Collins Dictionary of Law. (2006). Retrieved July 16 2016 from http://legal-dictionary.thefreedictionary.com/contract.

\textsuperscript{30} Pharmacy Act Regulation 16. Manufacturing pharmacy. GNR.1158 of 20 November 2000: Regulation relating to the practice of pharmacy: 16. Manufacturing pharmacy. - Except as provided for in the Medicines Act, only the following services pertaining to the scope of practice of a pharmacist, may be provided in a manufacturing pharmacy—

1) the manufacturing of any medicine or scheduled substance;

2) the purchasing, acquiring, keeping, possessing, using, supplying or selling of any medicine or scheduled substance;

3) the furnishing of information and advice to any person with regard to medicine manufactured by him, her or it;

4) the application for the registration of a medicine or medical device;

5) the formulation of medicine for the purposes of registration as a medicine;

6) the distribution of medicine or scheduled substances;

7) the repackaging of medicine in accordance with the Medicines Act;

8) the initiation and conducting of pharmaceutical research and development; and

9) any other health service as may be approved by council from time to time.
F. GENERAL PRINCIPLES FOR COMPOUNDING OF VETERINARY MEDICINES

20. Veterinary medicines should only be compounded when in the patient’s therapeutic interests and not to over-service the actual needs of the animal. Before compounding, it is advisable to check whether a suitable registered veterinary or human medicine, stock remedy is available in a convenient size, volume and concentration for the species to be treated. Making exact replicates (copies) of commercially available medicines is not regarded as an acceptable practice due to the risks associated with compounded medicines.

21. One of the conditions that must be met for a compounded veterinary medicine to qualify for the Section 14(4) compounding exception (Prohibition on the sale of medicines subject to registration and are not registered) under the Medicines Act, is

31 Veterinary rule 10 “over-servicing” means the supply, provision, administration, use or prescription of any treatment or care (including diagnostic and other testing, medicines and devices) which is medically or clinically not indicated, unnecessary or inappropriate under the circumstances or which is not in accordance with current acceptable treatment protocols and procedures by the reasonable veterinarian, with due regard to the health and welfare interest of the patient.

32 14. Prohibition on the sale of medicines which are subject to registration and are not registered. - (1) Save as provided in this section or sections 21 and 22A, no person shall sell any medicine which is subject to registration by virtue of a resolution published in terms of subsection (2) unless it is registered.

(2) ...

(3) ...

(4) The provisions of subsection (1) shall not apply in respect of the sale of any medicine—

a) compounded in the course of carrying on his or her professional activities by a pharmacist, veterinarian or person who is the holder of a licence contemplated in section 22C (1) (a), for a particular patient in a quantity not greater than the quantity required for treatment as determined by the medical practitioner, pharmacist, practitioner or veterinarian; or
it must be compounded by a community pharmacist or a veterinarian that does not compound a veterinary medicine that is essentially a copy of a commercially available registered veterinary medicine.

22. A compounded veterinary medicine is considered to be essentially a copy of a commercially available registered veterinary medicine if the:

22.1. A compounded veterinary medicine has the same active pharmaceutical ingredient(s) (API) as the commercially available registered medicine;

22.2. API(s) have the same dosage strength; and

22.3. Registered and commercially available veterinary medicines can be used by the same route of administration as prescribed for the compounded drug, and

22.4. Unless a prescriber determines that there is a change, made for an identified individual veterinary patient, which produces for that patient a significant difference from the commercially available registered veterinary medicine.\(^{33}\)

\(^{33}\) Supra.
23. The term essentially a copy of a commercially available registered veterinary medicine does not include a veterinary medicine in which there is a change, made for an identified individual veterinary patient (for example removal of a dye or potency adjustment because of the mass of the animal), which produces for that patient a significant difference, as determined by the veterinarian, between the compounded veterinary medicine and the comparable commercially available registered medicine.\(^{34}\)

24. The restrictions on making veterinary medicines that are essentially copies ensure pharmacists and veterinarians do not compound veterinary medicines under the Medicines Act exception for patients who could use a commercially available registered veterinary medicine. Such a practice creates significant public health risks because patients would be exposed to veterinary medicines that have not been shown safe and effective or prepared under substandard compounding conditions.\(^{35}\)

25. Besides, limitations on producing a veterinary medicine that is essentially a copy of a commercially available registered veterinary medicine protects the integrity and

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\(^{35}\) *Ibid.*
effectiveness of the regulatory approval process the legislature\textsuperscript{36} put in place to protect patients and users of medications from unsafe, ineffective, or poor quality medicines.\textsuperscript{37}

26. A registered veterinary medicine is commercially available if it is a marketed registered veterinary medicine unless.\textsuperscript{38}

26.1. The veterinary medicine has been discontinued and is no longer marketed; or

26.2. There is a shortage of the registered veterinary medicine and is not available after enquiry and for immediate use.

27. The limitations apply to the compounding of veterinary medicines that are essentially copies of a commercially available registered veterinary medicine – not only to veterinary medicines that are exact copies or even to veterinary medicines that are nearly identical. This is to make sure that compounders do not evade the limits by making relatively small changes to a compounded veterinary medicine and then offering the veterinary medicine to the public without taking into account whether a veterinarian has determined that the change produces a significant difference for the patient.\textsuperscript{39}

\textsuperscript{36} Parliament is the legislative authority of South Africa and has the power to make laws for the country in accordance with the Constitution. It consists of the National Assembly and the National Council of Provinces (NCOP). Parliamentary sittings are open to the public.

\textsuperscript{37} \textit{Ibid.}

\textsuperscript{38} Uppsala: Pre-marketing: The stage before a drug is available for prescription or sale to the public. Post-marketing: The stage when a drug is generally available on the market.

\textsuperscript{39} Medicines Act Section 14. \textit{Prohibition on the sale of medicines which are subject to registration and are not registered.} - (1) Save as provided in this section or sections 21 and 22A, no person shall sell any medicine
28. FDA considers two drugs to have a similar dosage strength if the dosage strength of the compounded veterinary medicine is within 10% of the dosage strength of the commercially available registered veterinary medicine. About the concept of easily substitutable strength, in some cases, the same or similar dosage strength can be achieved by administration of fractional or multiple doses of a medicine while a veterinary medicine with different routes of administration is not essentially similar.

29. Last, the following factors may be the basis for concluding that a compounded veterinary medicine has regularly been compounded or in inordinate amounts:40

29.1. Inadequate precautions are taken by the compounder to review the compounding history of the compounded veterinary medicines to establish trends and whether commercially available registered veterinary medicines are obtainable to replace the compounded preparations;

29.2. The compounder routinely substitutes compounded veterinary medicines that are essentially copies of commercially available registered veterinary medicines upon receiving prescriptions for patients;

which is subject to registration by virtue of a resolution published in terms of subsection (2) unless it is registered.

40 “Health Canada may take enforcement action against either a veterinarian or a pharmacist if it appears that either is manufacturing a drug. This may occur if they compound regularly or in inordinate amounts for commercially available drugs, if they compound for resale, or if they compound inordinate amounts given their usual prescription or in-office needs, and on the basis that it is not for an individual animal or group of animals or where no veterinary-client-patient-relationship exists”. College of Veterinarians of Ontario Guidelines - Compounding of Veterinary Drugs accessed http://www.cvo.org/CVO/media/College-of-Veterinarians-of-Ontario/Resources%20and%20Publications/Position%20Statements%20and%20Guidelines/CompoundingofVeterinaryDrugs.pdf; 2016/07/17 9:21 AM.
29.3. The compounding agent offers pre-printed prescription/order pads that a prescriber can use to write a prescription for the compounded veterinary medicine that is essentially a copy without making a determination that there is a change that will produce a significant difference for a veterinary patient; and

29.4. The compounded veterinary medicine is not compounded on an as-needed basis, but on a non-historic usage routine or pre-set schedule.

30. The preceding list is not intended to be exhaustive. Other factors may be appropriate for consideration in a particular case.

31. Where no registered medicine is available, a pharmacist or veterinarian may compound a veterinary medicine in a quantity not greater than the amount required for treatment of the patient or group of patients and for not more than 30-days maximum use or where stability data proves otherwise.\(^{41}\)

32. A community pharmacist should be asked to fill a compounded veterinary medicine’s prescription only within the context of a legitimate veterinarian-client-patient-pharmacist relationship (VCPPR)\(^{42}\) or, with “in-practice” (consulting room, mobile

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\(^{41}\) Medicines Act General Regulations: 4. The conditions for and the quantity not to be exceeded by a pharmacist in compounding a medicine for sale in the retail trade. - A pharmacist compounding a medicine for sale in the retail trade in terms of section 14 (4) (b) of the Act, must only compound a quantity that is - (a) related to a treatment regimen of a particular patient; and (b) to be used by the patient for not more than 30 consecutive days from the date of dispensing.

\(^{42}\) Veterinary Rules definitions: “veterinarian-client-patient relationship” means the following -
animal service, mobile theatre, registered facility, production animal herd health facility, research animal facility and veterinary hospital/clinic use prescriptions, with a valid veterinarian-pharmacist relationship (VPR) where the pharmacist acts as a contractual agent to compound medicines on behalf of the veterinarian. If a pharmacist prepares these compounded veterinary medicines, the prescription will state for “in-practice use”. Practitioners may re-dispense or administer these medicines to individual animals, as long as a record is made noting the original community pharmacy that prepared the product and the prescription or compounding number. This will allow for trace-back to the original community pharmacy and lot if concerns arise about the product.

33. Dispensed veterinary medicines must be labelled in a package containing the following information:

33.1. The internal proprietary name (for ease of reference), approved name, or the name of each active ingredient of the compounded veterinary medicine;

i. the veterinary professional has assumed the responsibility for making professional judgments and/or treatment regimens regarding the health of a patient or improvement in the production of the animal or animals, at the request of the client;

ii. the veterinary professional has sufficient personal knowledge to initiate at least a general or preliminary assessment of the condition of the patient by virtue of a consultation with the client; and

iii. clinical records are maintained.

43 **Supra.**

44 Veterinary Act; GNR.1082 of 9 November 2015: Regulations relating to the performance of Compulsory Community Service (CCS) (Government Gazette No. 39380); See Annexure B, Rule 10 in Annex.
33.2. Name of the owner, and the name of the patient, if available, for whose treatment such compounded veterinary medicine is prepared;

33.3. Directions for the use of such medicine if not for in-practice use;

33.4. Name and business address of the dispensing pharmacist or veterinarian; and

33.5. Date of dispensing.

34. On the understanding, the compounded veterinary medicine is not intended for continued, sustained and frequent use on any one farm, by any one farm owner/farm manager/veterinarian/person as such conduct, is considered manufacturing unless the compounded veterinary medicine’s purpose is therapeutically justified and upheld by data and evidence.45

35. The compounding and use of an autogenous vaccine are restricted under various statutes and to the specific farm where the infectious agent was identified. If grounds demand an autogenous vaccine on adjacent and nonadjacent farms, then an application under the Animal Diseases Act (Act 35 of 1985) must be submitted for approval.46

45 Veterinary Rule 10 (6) A veterinarian may only use compounded veterinary medicine for a food producing animal(s), including wildlife intended for human consumption, subject to the following—

(f) It is not intended for continued, sustained and/or frequent use on any one farm, by any one farm owner, by any one farm manager, by any one veterinarian or by any one person as this constitutes manufacturing, unless the use of the compounded medicine is reasonably justifiable and substantiated by facts.

46 Veterinary Rule 10 (8) A veterinarian may only compound, or have compounded on his/her behalf an autogenous vaccine, subject to the following—

a) The veterinarian or third party contractor must be in possession of a permit in accordance with Section 20 (b) of the Animal Diseases Act 1984, Act 35 of 1984;
36. A standard operating procedure must be in place in the community pharmacy and the veterinary practice to recall any lot or product, should it be necessary? In such circumstances, the procedures in the MCC’s Veterinary Drugs Recall guideline must be followed and so for an adverse drug reaction.  

37. Compounding of a novel pharmaceutical by a pharmacist or veterinarian may infringe current patents. A veterinarian prescribing compounded medications should have an understanding of the potential legal implications of such infringement.

b) The production may only be undertaken or prescribed by a veterinarian for use in a particular patient in accordance with sections 14 (4) and 22A (5) (e) of the Medicines Act;

c) An autogenous vaccine may only be used for a disease or strain of a disease for which there is no suitable veterinary vaccine or combination thereof registered and/or sold and/or available for sale in the Republic of South Africa;

d) The use of an autogenous vaccine is restricted to the specific farm where the infectious agent was identified. If grounds exist for the use of an autogenous vaccine on adjacent and non-adjacent farms, then an application in terms of section 20 of the Animal Diseases Act (Act 35 of 1985) must be submitted for approval;

e) In a disease outbreak situation, the mass use of an autogenous vaccine may only commence in accordance with the requirements of section 20 of the Animal Diseases Act (Act 35 of 1985) and section 21 of the Medicines Act; and

f) The general sale of any autogenous vaccine to neighbouring farms or other districts/provinces must meet the requirements for general sale of a medicine in accordance with the Medicines Act and the Animal Diseases Act.

3.10 Recall of vet medicines Jan04 v1.doc January 2004; 2. REASONS FOR A RECALL: An applicant may be required to recall a particular batch or batches of a veterinary product from the market due to:

a) a report of an adverse drug reaction to a particular batch of a product by the end – user, patient or consumer,

b) product deficiencies identified as result of ongoing stability studies,

c) technical complaints experienced regarding the printed packaging material, contamination,

3.10 Recall of vet medicines Jan04 v1.doc January 2004; 2. REASONS FOR A RECALL: An applicant may be required to recall a particular batch or batches of a veterinary product from the market due to:

a) a report of an adverse drug reaction to a particular batch of a product by the end – user, patient or

b) consumer,

c) product deficiencies identified as result of ongoing stability studies,

d) technical complaints experienced regarding the printed packaging material, contamination,

e) mislabelling, counterfeit, etc or

f) when requested or instructed by the Medicines Control Council.

38. See Annex 2 for the restriction of substance use in food-producing animals and limited use.

G. DISTINCTION BETWEEN COMPOUNDING AND MANUFACTURING

39. Compounding by community pharmacy is distinct from medicines manufacturing. Medicines manufacturing is understood to consist of the mass commercialization of proprietary or patented commercially available medicines (drugs) in standard formulations and dosages for large-scale national or global markets and not for individual patients. Manufacturers routinely produce batches consisting of millions of dosage units, such as tablets or capsules, for resale utilising many staff and large-scale manufacturing equipment. These medicines are distributed through the normal channels of commerce (wholesale, distributor and retail) to people unknown to the manufacturing company.

40. Manufacturers are not obligated to, and do not give oversight to individual patients, nor may they do so.

41. One of the purposes of the Medicines Act is to regulate large-scale commercial manufacturing and aimed at preventing the production of substantial quantities of ineffective or dangerous manufactured drugs that are then introduced into commerce.

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48 Oxford dictionaries: An agent who supplies goods to retailers.

49 Supra as discussed.
The Medicines Act was passed to protect the public (and animals) at large and not individual patients in a professional relationship with a healthcare provider.50

42. By way of contrast, compounding is an expert discipline controlled under the Pharmacy Act and Veterinary and Para-Veterinary Professions Act while manufacturing is a commercial activity regulated under the Medicines Act. The standards for pharmacist compounding are set by the Pharmacy Council’s Rules Relating to Good Pharmacy Practice (GPP) and Rule 10 of the South African Veterinary Council’s Rules Relating to the Practising of Veterinary Professions while norms for manufacturing are dictated by the MCC’s Guide to Good Manufacturing Practice for Medicines in South Africa (GMP).51
43. Manufacturers of veterinary medicines in dosage form must satisfy the laws of the Medicines Act and Regulations including related standards and guidances. In particular, manufactured veterinary medicines must be registered or authorised for sale (“grandfathered”) in South Africa, meaning that the veterinary medicine’s application received is reviewed by the MCC for quality, safety and therapeutic efficacy for its effect on the health of an animal. Furthermore, the veterinary medicine must be suitable for its intended purpose before sale (pre-marketing approval or registration).

44. For sale in South Africa, a veterinary medicine will need a registration number or an application number (“grandfathered” veterinary medicine). Manufacturers, importers, exporters, wholesalers or distributors of veterinary medicines, require a

standards in practice, and any new or amended national regulations for good manufacturing practice should at least meet their level.

These standards are also intended to serve manufacturers as a basis for the elaboration of specific rules adapted to their individual needs. These standards are also intended to serve manufacturers as a basis for the elaboration of specific rules adapted to their individual needs.

In addition to the general matters of Good Manufacturing Practice outlined in the chapters of this guide, supplementary guidelines such as the Technical Series of the World Health Organisation can be used to clarify and support specific areas of activity.

The standards set out herein, apply to medicines and similar products intended for human and veterinary use.

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See Medicines Act Section 15 for the details: 15. Registration of medicines. - (1) Every application for the registration of a medicine shall be submitted to the registrar in the prescribed form and shall be accompanied by the prescribed particulars and samples of the relevant medicine and by the prescribed registration fee.

Medicines Act General Regulations: 46 Labelling for veterinary medicine. - (1) Save as provided in subregulations (2), (3) and (4), the immediate container of every package in which a veterinary medicine is sold shall have a label attached on which only the following particulars pertaining to the contents of such package shall appear, such particulars to be stated in clearly legible, indelible lettering in at least one official language –

(c) the registration number allocated to such medicine under section 15 (6) of the Act or, in the case of a medicine in respect of which an application for registration has been submitted in accordance with regulation 22, the reference number allocated to such application by the Registrar, followed by the words “(Act 101/1965)”;

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Medicines Act Section 22C licence and meet acceptable quality assurance principles, and good manufacturing and distribution practices as the MCC may determine. Compounded veterinary medicines do not call for registration before sale but may not be sold to third parties such as wholesalers, distributors or retailers for onward sale. The legal veterinarian-client-patient-pharmacist relationship (VCPPR) or valid veterinarian-pharmacist relationship (VPR) link must not be broken as the veterinarian-client-patient relationship is the foundation of effective veterinary medicine and animal care unless a medical emergency exists and immediate treatment is necessary for the patient’s interests.

45. Even though compounded veterinary medicines are exempted from registration before sale, healthcare professionals compounding veterinary medicines must meet relevant sections of the Medicines Act including the non-use of forbidden substances, restriction on advertising while the veterinary medicines must be prepared under the South

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54 Medicines Act Section 22C. Licensing - (1) Subject to the provisions of this section—
(a)...
(b) the council may, on application in the prescribed manner and on payment of the prescribed fee, issue to a manufacturer, wholesaler or distributor of a medicine or medical device a licence to manufacture, import or export, act as a wholesaler of or distribute, as the case may be, such medicine or medical device, upon such conditions as to the application of such acceptable quality assurance principles and good manufacturing and distribution practices as the council may determine.
(6) No manufacturer, wholesaler or distributor referred to in subsection (1) (b) shall manufacture, import, export, act as a wholesaler of or distribute, as the case may be, any medicine unless he or she is the holder of a licence contemplated in the said subsection.

55 See explanation above.

56 Medicines Act Section 1 “advertisement”, in relation to any medicine or Scheduled substance, means any written, pictorial, visual or other descriptive matter or verbal statement or reference—
a) appearing in any newspaper, magazine, pamphlet or other publication; or
African Pharmacy Council’s Rules Relating to Good Pharmacy Practice or Rule 10 of the South African Veterinary Council. Acceptable pharmacopoeial standards may supplement these norms.

46. Importantly, the law requires medicines to be registered. However, the law allows pharmacists and veterinarians to prepare and supply medicinal products in a registered community pharmacy or veterinary practice with no need for product registration. However, the MCC has determined that these extemporaneous preparations should be monitored in the public interest arranged quality, safety and effectiveness. An animal patient owner has every right to expect that when a medicine is prepared by, or under pharmacist supervision in a community pharmacy or by a veterinarian, is of equal quality to any registered medicine they will receive (such as those produced by a regulated and licensed manufacturer). Preparing a medicine in a community pharmacy or veterinarian clinic is an activity that can pose a significant risk to patients and the public and have potentially serious consequences when risks and processes are not managed properly. So, when a patient is supplied with a compounded veterinary medicine, it is important that the medicine is safe and suitable for its intended purpose.

b) distributed to members of the public; or

c) brought to the notice of members of the public in any manner whatsoever, which is intended to promote the sale of that medicine or Scheduled substance; and “advertise” has a corresponding meaning;
47. The pharmacovigilance monitoring obligations apply to pharmacists and veterinarians who are involved in supply and use of these compounded veterinary medicines. The pharmacovigilance forms must be completed on a six-monthly basis and can be obtained from the MCC’s website at http://www.mccza.com under the veterinary guidelines section.

48. Information required will include product information, prescriber, animal species, quantity used, the motivation for the utilization of the compounded veterinary medicine, the reason for not using a similar registered veterinary medicine or current regimen and any adverse events experienced with the compounded veterinary medicine.

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57 Uppsala: Pharmacovigilance The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problem.

58 Uppsala: Adverse Event (AE) 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.

Adverse (Drug) Reaction (ADR) A response which is noxious and unintended, and which occurs at doses normally used in humans [animals] for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. (WHO, 1972). An adverse drug reaction, contrary to an adverse event, is characterized by the suspicion of a causal relationship between the drug and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

In the EU Directive 2010/84, which is applicable from July 2012 an adverse reaction is defined as: A response to a medicinal product which is noxious and unintended.
H. PHARMACISTS AND THE COMPOUNDING OF VETERINARY MEDICINES

49. Compounding is an authorised act that falls within the scope of practice of a pharmacist but may only be done in a community pharmacy.

50. As said, a manufacturing and a wholesale pharmacy may not compound a veterinary medicine nor dispense a prescription. Pharmacists engaged in compounding in a community pharmacy must meet applicable legislation and their standards of Good Pharmacy Practice rules for these services.

51. The veterinarian’s armamentarium depends on the nature of the vet’s animal practice, location and access to compounding services. As an example, veterinarians need compounded veterinary medicines in-practice use stock for field trips to treat a range of species and for emergency treatment of animals or re-dispensing purposes depending on the nature of their practices. So, an compounded veterinary medicine may be compounded before receipt of a prescription or in-practice use order (anticipatory compounding\(^59\)) in a quantity that does not exceed the amount of veterinary medicine that the community pharmacy compounded under patient-specific

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\(^{59}\) 2015 Minnesota Statutes: Subd. 36 Anticipatory compounding. “Anticipatory compounding” means the preparation by a pharmacy of a supply of a compounded drug product that is sufficient to meet the short-term anticipated need of the pharmacy for the filling of prescription drug orders. In the case of practitioners only, anticipatory compounding means the preparation of a supply of a compounded drug product that is sufficient to meet the practitioner’s short-term anticipated need for dispensing or administering the drug to patients treated by the practitioner. Anticipatory compounding is not the preparation of a compounded drug product for wholesale distribution. Accessed https://www.revisor.mn.gov/statutes/?id=151.01 ; 2016/07/17 11:30 AM
prescriptions or in-practice use order based on a history of receipt of such patient-specific prescriptions or in-practice use orders for that compounded medicine.

52. Sometimes it is necessary for veterinarians in hospitals, clinics, consulting rooms, or other settings to have compounded veterinary medicines on hand that they can administer to a patient who presents with an immediate need (medical emergency) for the compounded veterinary medicine. In other cases, compounded veterinary medicines may need to be administered by a veterinarian in his or her consulting room because it would not be safe for the patient to take the compounded veterinary medicine home for self-administration, and it would not be practical for the patient to bring a prescription for the compounded veterinary medicine to a community pharmacy and then return to the veterinarian for administration.

53. Anticipatory compounding, or preparing compounded medications before the actual receipt of a prescription or practitioner’s order, is a major component of pharmacy

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60 A medical emergency is an acute injury or illness that poses an immediate risk to a person’s life or long-term health.

61 The following example illustrates FDA’s policy on anticipatory compounding under section 339 503A(a)(2): A compounder regularly receives valid prescription orders from a particular prescriber or prescribers, or for a particular patient or patients, for compounded drug X. The highest number of units of drug X for which the compounder has received patient-specific prescriptions in a 30-day period in the last year is 500 units. Compounding up to 500 units of drug X in advance of receiving prescriptions for the drug, and holding no more than that amount to fill new patient-specific prescriptions as the compounder receives them, would be consistent with this policy. A physician who compounds drugs for his or her own patients routinely sees patients who need compounded drug X. The highest number of units of drug X that the physician has dispensed or administered to patients after making a notation in the patients’ charts in a 30-day period in the last year is 500 units. Compounding up to 500 units of drug X in advance of making such notations in patients’ charts (i.e., before patients present at the physician’s office with a need for the compounded drug), and holding no more than that amount to dispense or administer to patients, would be consistent with this policy. Section 503A(a)(2) provides a pathway for anticipatory compounding in limited quantities... A licensed pharmacist or licensed physician can compound a drug product in advance of receiving a valid prescription order for an identified individual...
practice. It allows compounding pharmacies with a history of filling certain prescriptions to make up a larger lot and to make sure that medications will be ready when they are needed.

54. Furthermore, anticipatory compounding reduces the cost of compounded medications as economies of scale can be realised with larger lots and less waste of chemicals, dilutions, fillers, and other associated products. The practice also leads to more accuracy and uniformity in the finished medications as larger lots decrease the variation that will always exist from preparing multiple, smaller lots. In sum, anticipatory compounding can be useful because larger compounding lot sizes can reduce the likelihood of human error associated with compounding many small lots of the same compounded veterinary medicine after the receipt of individual prescriptions for the medication.

55. However, anticipatory compounding too has risks. For example, if a problem occurs during compounding, such as contaminating a compounded veterinary medicine that is supposed to be sterile, it could affect many patients, and not just one. Restricting patient, in accordance with the conditions described in section 503A(a)(2) of the FD&C Act, to have a supply of the drug product ready to provide to a patient or prescriber (or, in the case of a physician, to administer to a patient) when a patient-specific prescription order is presented for the compounded drug product. This can reduce the time it would take for a compounded drug product to be made available to a patient upon receipt of a valid prescription order for that patient. Accessed http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM496286.pdf; 2016/07/17 11:52 AM.
compounding to limited quantities serves to limit the number of patients likely to be hit by a compounding mistake.\textsuperscript{62}

56. Depending on the circumstances, a pharmacist should only supply limited amounts of compounded veterinary medicines to meet the specific needs of the veterinarian. "Limited quantity" means a quantity of compounded veterinary medicines that meet the following:

56.1. Is sufficient for that vet’s in-practice use consistent with the beyond-use date of the registered compounded veterinary medicine;

56.2. Is reasonable considering the intended use of the compounded medication and nature of the veterinarian’s practice; and

56.3. The pharmacist who provides the veterinarian with compounded veterinary medicines exercises their professional judgment as to whether the quantity of the medication is appropriate to service the practice needs of the veterinarian when considering logistics, location, lead times for delivery, medical emergencies and other unique factors attributable to the vet’s practice.

57. The pharmacist assumes the responsibility for risk arising from compounding activities in the treatment and servicing of their patients or clients. Pharmacists must be mindful

of the factors considered undesirable when compounding veterinary medicines and outlined in the section directed at veterinarians in this directive. 63

58. Compounders of veterinary medicines have a responsibility to make sure human health is not placed at risk by the presence of hazardous residues in foods. The use of compounded veterinary medicines in food animals is discouraged. 64 Compounded veterinary medicines should only be used in food animals if:

58.1. There is clinical evidence that justifies the use of such medicine; and

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63 GNR.1158 of 20 November 2000: Regulation relating to the practice of pharmacy: 18 Community or institutional pharmacy. - Except as provided for in the Medicines Act, the following services pertaining to the scope of practice of a pharmacist may be provided in a community or institutional pharmacy –

(c) the provision of animal health care services which includes:

(i) the compounding and dispensing of prescriptions written by veterinarians and ensuring the optimal use of veterinary medicines;

(ii) the immunisation of animals;

(iii) the handling of minor and/or self-limiting ailments in animals; and

(iv) the provision of information and education regarding the promotion of animal health.

64 Veterinary Rule 10: 10. Use of veterinary medicine. - (1) Whenever a veterinary professional, administers medicine to an animal or prescribes the administering thereof, he/she must satisfy himself that the administering thereof is justified with due allowance for the benefits and risks which that medicine may hold for -

a) The animal to which it is administered, including withdrawal times of residues where relevant in the animal and/or the effect on the environment;

b) The person by whom it is administered; and

c) The consumer of the products of that animal if residues of the medicine concerned should be present in those products.
58.2. A suitable withdrawal time is established, For more details, see MCC’s veterinary guideline on MRLS and Withdrawal Periods.\(^\text{65}\)

59. Moreover, compounding rights may not be exploited to evade the registration prerequisites of the Medicines Act or the Stock Remedy Act.

I. VETERINARIANS AND THE COMPOUNDING OF VETERINARY MEDICINES

60. The responsible use of veterinary medicines for therapeutic and prophylactic purposes is one of the major skills of a veterinarian and crucial to animal welfare and to support public health. To prescribe or use a compounded veterinary medicines, the patient or group of patients must be under the care of the veterinarian. In that:

\(^{65}\) MCC guideline: Residues of veterinary medicines in foodstuffs of animal origin are controlled in terms of the provisions of the Foodstuffs, Cosmetics and Disinfectants Act, 1972 (Act No 54 of 1972). One of the aims of this Act is to protect the consumer against foodstuffs, which may be harmful or injurious to human health.

It does this by, amongst others, prohibiting the importation, manufacture or sale of a foodstuff, which contains or has been treated with a substance not present in any such foodstuff when it is in a normal, pure and sound condition [Section 2. (1)(c)]

Section 15. (1)(d), however empowers the Minister of Health to make regulations “prescribing any foreign substance, that may be considered as unavoidably present in any foodstuff or cosmetic as a result of the process of its collection, manufacture or treatment, or the greatest measure in which any such substance or substances of such nature may be present in any foodstuff or cosmetic”. Accessed http://www.mccza.com/Publications/Index/1?grid-page=2 2016/07/17 4:47 PM
60.1. The veterinarian must have been given informed consent for the responsibility for the health of the animal or group of animals by the owner or the owner's agent;\(^{66}\)

60.2. Responsibility must be real and not nominal;

60.3. The animal or group of animals must have been seen immediately before prescription or recently enough or often enough for the veterinarian to have personal knowledge of the condition of the animals or current health status to make a diagnosis and prescribe; and

\(^{66}\) In recent years, patients' consent to medical treatment has particularly attracted the attention of legal doctrine and law, becoming the object of continual research and various interpretations and becoming so relevant as to gain independence from medical duty as a whole. From a paternalistic perspective, when the physician was the sole depository of medical secrets and therefore the only one who could make decisions, physicians and patients have moved on to a new relationship as collaborating peers. The principle of informed consent (IC), in fact, reflects the concept of autonomy and self-determination of a person requiring and requesting specific medical and/or surgical intervention. The theory of autonomy is defined as self-governance or self-rule, a capacity of people to reflect and choose, and freedom to express individual dual aspirations and preferences. Such a justification of IC also lies with the fact that, in most of Europe and beyond it, physicians' ethical codes see the duty to ask for IC as an expression of professional correctness itself. Informed consent in veterinary medicine: legal and medical perspectives in Italy Annamaria Passantino, Valeria Quartarone, Maria Russo, Department of Veterinary Public Health, Faculty of Veterinary Medicine, University of Messina, Polo Universitario Annunziata, Messina, Italy; passanna@unime.it Received 5 July 2011; revised 20 August 2011; accepted 3 September 2011; Vol.1, No.3, 128-134 (2011) doi:10.4236/ojas.2011.13017 Copyright © 2011 SciRes. Openly accessible at http://www.scirp.org/journal/OJAS/

Informed client consent is the basis on which veterinarians and clients confirm the veterinary services that will be provided. Informed consent is the process by which the client learns about and understands the purpose, benefits and potential risks of all recommended activities, and uses this information to make decisions concerning their animal’s care. Informed consent is a two-way dialogue in which the veterinarian provides the client with the details required to make an informed decision about whether to accept the recommended service and/or treatment. Client questions are addressed in order to clarify aspects of the proposed care and ensure that the client understands the information provided. The informed consent process requires disclosure of the purpose of the procedure, benefits, foreseeable risk(s), alternatives to the procedure and associated costs. Accessed http://cvo.org/CVO/media/College-of-Veterinarians-of-Ontario/Applicant%20Section%20Documents/ExamWorkbook.pdf; 2016/07/18 4:13 PM.
60.4. The veterinarian must keep accurate clinical records of that animal or group and allow prompt retrieval of information.

61. Although compounded veterinary medicines can serve a critical need, they pose a higher risk to patients than MCC-registered veterinary medicines. Consequently, veterinarians should only use compounded veterinary medicines where there is a legitimate medical need that in the practitioner’s professional judgment outweighs the risks involved.

62. To that end, the compounding may be outsourced to a compounding community pharmacy on condition the compounding pharmacist guarantees the purity (quality) of the ingredients used in the product. In such cases, the veterinarian retains responsibility for the compounded veterinary medicine except for a compounding error.\(^{67}\)

63. Furthermore, the veterinarian may not advertise the compounded veterinary medicine nor display it for sale to the public. Besides, veterinarians must not sell a compounded veterinary medicine to another prescriber, sell a compounded veterinary medicine to a pharmacy or return a compounded veterinary medicine to the supplying community pharmacy, unless there is a documented error or recall.

\(^{67}\) Veterinary Rule 10: (5) When using or prescribing a medicine that has been compounded, veterinarians must comply with the following –

(g) Should the compounding of medicines be outsourced to a third party, the veterinarian must make use of a registered compounding facility with the correct licensing to perform such compounding, who can contractually guarantee the purity of the ingredients, and must issue the third party with a compounding order specifying the product, quantity, packaging and labelling;
When using or prescribing a compounded veterinary medicine, veterinarians must keep to the following:

64.1. Make sure that a suitable registered veterinary medicine or any combination of such medicines or stock remedy it may be substituted with, is not available for sale in South Africa in a suitable size, volume and concentration;

64.2. Where no registered veterinary medicine is available, a veterinarian or pharmacist may only compound a veterinary medicine in a quantity not greater than the amount required for treatment of the patient for not more than 30 days;

64.3. Dispensed compounded veterinary medicines must be correctly labelled with the following information:

64.3.1. the proprietary name, approved name, or the name of each active ingredient of the medication, where applicable;

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68 Veterinary Rule 10 (5).

69 Medicines Act Section 1 “approved name”, in relation to a medicine, means the international non-proprietary name (INN) of such medicine or, where no such name exists, such other name as the council may determine, not being a brand name or trade name registered in terms of the Trade Marks Act, 1993 (Act No. 194 of 1993)

70 Medicines Act General Regulations definitions: “proprietary name”, “brand name” or “trade name” means the name which is unique to a particular medicine and by which the medicine is generally identified and which in the case of a registered medicine is the name approved in terms of section 15 (5) of the Act.
64.3.2. the name of the owner, as well as the name of the patient, if available, for whose treatment such medicine is sold;

64.3.3. the directions for the use of such medicine;

64.3.4. the name and business address of the dispensing veterinarian; and

64.3.5. date of dispensing.

64.4. A documented system for compounding is in place and inform the Veterinary Council, on request, about the therapeutic efficacy and effect of such compounded veterinary medicine, the purpose and circumstances under which and the way in which such compounded medicine should be used;

64.5. A compounded veterinary medicine may not contain substances prohibited regarding Section 36A of the Medicines Act;\footnote{Medicines Act Section 36A. Minister may prohibit the manufacture, sale or use of certain veterinary medicines. - Notwithstanding anything to the contrary in this Act or in any other law contained, the Minister may by notice in the Gazette for any reason other than the safety, quality or therapeutic efficacy of a veterinary medicine -

a) prohibit the manufacture, sale or use of any veterinary medicine containing a substance mentioned in the notice; or

b) prohibit such manufacture, sale or use, except in accordance with such conditions as may be specified in the notice,

and may in like manner repeal or amend such notice.}
64.6. The purity of the veterinary medicines is guaranteed by procuring ingredients of acceptable pharmacopoeial standards, should the veterinarian personally compound the medicines;

64.7. Otherwise, if the compounding of the medicine is outsourced to a community pharmacist skilled in veterinary compounding who must guarantee the purity of the ingredients, and must give the community pharmacist a prescription or order for the compounded veterinary medicine;

64.8. Retain full responsibility for the compounded veterinary medicine even when compounded by a community pharmacist unless such community pharmacist makes a compounding error;

64.9. Comply with aspects of Section 22A of the Medicines Act - control of medicines and Scheduled substances;

64.10. The compounded veterinary medicines are not advertised or promoted as veterinary medicine trade name products or displayed for sale to the public;
64.11. The use of compounded veterinary medicines is not intended to circumvent the registration requirements of the Medicines Act or the Stock Remedy Act.

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72 LAWSA: Volume 25(1) - Second Edition Volume; Statute Law and Interpretation; The Presumptions: 342 Statute Law is not invalid or purposeless "Intention of the legislature" can also be taken to refer to the truism that statutes are meant to be of effect. The common-law presumption that statutes do not contain invalid or purposeless provisions expresses this effect-directedness of statute law and has met with consistent approval in the case law. Oddly enough the presumption has seldom been couched in positive terms, that is, as a presumption of validity and purposefulness. The presumption has been applied in a general sense, that is without specific reference to particular circumstances deemed to be distinctively apt for its application and also in particular situations where circumstances posed an imminent threat to the validity or continued efficacy of statutory provisions.

(a) The general application of the presumption has explicitly been justified with reference to the interpretive maxim verba ita sunt intelligenda ut res magis valeat quam pereat ("the words of an instrument are to be so construed that the subject-matter may rather be of force than come to naught"). Sometimes, however, the general application of the presumption is accepted as a matter of course in instances where certain logically or linguistically feasible interpretations may render a statutory provision futile or without "business efficacy". In Esselman v Administrateur, SWA the latter conclusion was drawn in circumstances where it resulted in considerable hardship for an individual. The general application of the presumption is subject to the condition that the interpretive result arrived at by applying the presumption must be a "possible construction". If not, the presumption is taken to be rebutted.

(b) The following are examples of situations in which the presumption has been invoked almost, it seems, as a matter of course:

(v) An interpretation favouring or permitting acts or transactions in fraudem legis should be avoided, but the provisions of an enactment may well be lawfully evaded if, for instance, a transaction is genuinely and honestly arranged so as to fall outside their scope of operation. In pursuance of the maxim plus valet quod agitur quam quod simulare concipitur ("the real intention carries more weight than a fraudulent simulation") an act or a transaction is said to be in fraudem legis "when it is designedly disguised so as to escape the provisions of the law, but falls in truth within these provisions". The presumption is therefore applied in this specific way in a quest to avoid fraud.

The ratio underlying the application of this common-law presumption of validity in the sets of circumstances in (i) to (vi) above, is that legislation must be construed so that it best serves its purpose. The presumption is, in other words, consonant with and indeed conducive to purposive interpretation and therefore holds its own in the context of constitutional democracy. This appears, to begin with, from generous (albeit sometimes implicit) reliance on it in constitutional interpretation... The court inter alia laid down the requirement that the exercise of public power must be rationally connected to the purpose for which the power was granted - otherwise the power is meaningless.

73 In 1910 the Appellate Division in Zandberg v Van Zyl (1910 AD 302) laid the basis of the doctrine of substance over form, Innes J ruling as follows (at 309):

‘Not frequently, however (either to secure some advantage which otherwise the law would not give, or to escape some disability which otherwise the law would impose), the parties to a transaction endeavour to conceal its real character. They call it by a name, or give it a shape,
64.12. Inform the owner of the lack of quality control and possible deficiencies in effectiveness of the compounded veterinary medicine;  

64.13. Make sure compounding is not done without a ‘veterinarian-client-patient’ relationship; and 

intended not to express but to disguise its true nature. And when a Court is asked to decide any rights under such an agreement, it can only do so by giving effect to what the transaction really is; not what in form it purports to be.'

74 See Annex 5 and 6 for informed consent forms.

75 “valid veterinarian-client-patient relationship” means a valid VCPR exists when these conditions apply:

a) CLIENTS GIVES RESPONSIBILITY FOR ANIMAL: The client (owner or owner’s agent of the animal(s)) has given the responsibility of medical care to the veterinarian and has agreed to follow the instructions of the veterinarian, and;

b) VET ACCEPTS RESPONSIBILITY FOR ANIMAL: The veterinarian has assumed the responsibility of the client for making a clinical judgement regarding the health of the animal(s), the need for medical treatment, and for ensuring the provision of ongoing medical care for the animal(s);

c) VET KNOWS ANIMAL: The veterinarian has sufficient knowledge of the health status of the animal(s) and the care received or to be received. The knowledge has been obtained through a recent examination of the animal(s) and the premises where they are (it is) kept or through a history of medically appropriate and timely examinations and interventions, and;

d) VET OFFERS ONGOING MEDICAL CARE: The veterinarian is readily available, or has made the necessary arrangements with another veterinarian, for the ongoing medical care of adverse reactions or therapy failure.

Informed consent in a veterinarian-client relationship is vastly different from informed consent in a medical doctor-adult human patient relationship. Where in a veterinarian-client-patient relationship, the patient (animal) is not capable of making a decision for him or herself. By contrast, in a relationship between a medical doctor and an adult human patient, the patient can make the decision him or herself. Veterinarian-client informed consent is more like informed consent in a medical doctor-minor patient-caregiver situation since both require an adult human to make the final decision on the proposed treatment.

The Principles require “informed consent” from the client before the patient is treated. Getting this “informed consent” typically means the veterinarian explains both the risks and benefits associated with a particular treatment method. Then the client signs a document which states the client understands the risks and benefits. By giving informed consent to a procedure or treatment, it is assumed that the client both read and understood all of the terms in the statement. Once informed consent has been given, the patient-animal may be treated according to the conditions listed within the statement.
64.14. No compounded veterinary medicines or pharmaceutically active ingredients are imported without approval from the Medicines Control Council.

J. IS AN ACTIVITY COMPOUNDBING?

65. The following factors should be taken into consideration when assessing whether an activity is compounding:

65.1. Pharmacists and veterinarians who offer compounding related services and compounded veterinary medicines to patients/clients must be able to prove that a veterinarian-pharmacist-client-patient professional relationship exists;

65.2. Compounding activity is regulated, and relevant authorities may inspect the facility;

65.3. It is expected that pharmacists and veterinarians who compound veterinary medicines will have suitable risk management processes in place to manage risks associated with the compounded veterinary medicines and the workplace (facilities, safety, etc.), in line with the standards set by legislation and guidelines;

65.4. A community pharmacy may prepare compounded veterinary medicines in quantities enough for a patient or group of patients awaiting a prescription or in-practice order or based on historical usage trends. For this Policy, preparation involves compounding or repackaging of multiple units, not for
immediate use, in a single process, by the same operator under a standardised operating procedure;

65.5. Compounding should only be done because of a therapeutic need or lack of product availability after enquiry;

65.6. The compounded veterinary medicine must provide a personalised therapeutic solution to improve patient care;

65.7. When there is a shortage or no supply of a registered veterinary medicine and the pharmacist or veterinarian has determined a medical need for this medication, the compounded veterinary medicine may be compounded during shortage or no supply only;

65.8. Veterinary medicines should not be compounded to be sold to third parties who will sell/deliver to patients outside of their defined patient-healthcare professional relationship. Pharmacists and veterinarians that do not offer specific compounding services may contract this activity to another pharmacist who provides this specialised compounding service;

65.9. Compounding of clinical trial veterinary medicines is only permitted if this activity is authorised in the clinical trial application or experimental or investigational authorization;
65.10. Product should be compounded from a registered medicine or Active Pharmaceutical Ingredient (API) used in a registered medicine for use in South Africa or listed in a recognized Pharmacopoeia;

65.11. Compounding of sterile products is only permitted in practice settings where established standards to run clean rooms, preparation of sterile products are in place and processes follow standard operating procedures. The compounded veterinary medicines are dispensed directly to patients or to those who administer to patients and are operating within a demonstrated patient-healthcare professional relationship. Pharmacists may delegate some of the compounding responsibilities to registered pharmacy technicians if they are trained in compounding sterile products and as permitted under the Pharmacy Act. Those engaged in sterile compounding should be knowledgeable and have specialised technical training in aseptic compounding techniques;

65.12. The compounded veterinary medicine must meet relevant provisions of the Medicines Act; and

65.13. The expiry date of the compounded veterinary medicine is based on known stability data. If stability data is not available, the expiry date or use by date should be short, limited to the life of the prescription or use.
K. IS AN ACTIVITY MANUFACTURING?

66. The following factors should be taken into consideration when assessing whether an activity is manufacturing:

66.1. Healthcare professionals who cannot prove that a patient-healthcare professional relationship exists;

66.2. Producing an identical compounded veterinary medicine that is registered and commercially available unless there is a shortage;

66.3. Producing or selling the compounded veterinary medicine by a third party;

66.4. Healthcare professionals who produce compounded veterinary medicines intended for distribution or sale outside the demonstrated patient-healthcare professional relationship;

66.5. Producing compounded veterinary medicines made on such a scale, time and frequency to fall outside of a patient-healthcare professional relationship;

66.6. Clinical trial application, experimental or investigational authorization does not specify permission to compound clinical trial drugs;

66.7. Producing a compounded veterinary medicine that requires only minor change before direct administration when such change amounts to mere directions for use. Examples of such include adding liquid to a powder or adding a powder to animal drinking water. Compounding does not include mixing, reconstituting,
or any other manipulation that is performed under the directions for use on an approved medicine’s labelling material; and

66.8. Repackaging commercially available medicines in finished dosage form outside the normal dispensing activities within the practice of pharmacy.

67. General guidance on compounding and manufacturing activities is summarised in the Annex 3 checklist.
L. DEFINITIONS

68. Glossary of terms used in this document.

“animal” means any vertebrate other than man;

“anticipation of a prescription” means that community pharmacies may prepare veterinary medicines in quantities before receiving a valid prescription or order, provided they can document a history of receiving valid prescriptions or orders that have been generated solely within an established patient-healthcare professional relationship, and provided further that they maintain the prescription on file as required by law;

“anticipatory compounding” means preparing a compounded medication before the actual receipt of a prescription or practitioner’s order;

“autogenous vaccine” means a non-registered veterinary vaccine prepared from biological material or cultures derived from a lesion or disease of an animal or animals and intended for use in the flock or farm where the material was procured;

“beyond use date” means the date up to which a medicine will retain the strength and other properties which are mentioned on the label which strength and other properties can change after the lapse of time and after which date the medicine shall not be sold to the public or used;

“client” means a person who uses the professional services of a veterinarian, para-veterinary professional or pharmacist;

“client consent” means consent given by the owner of the patient after the veterinary professional informing the owner in a manner understood by a reasonable person of the following:

a) the presumptive diagnosis; and
b) the available treatment options and expected prognosis;

“client” means a person who uses the professional services of a veterinarian, para-veterinary professional or pharmacist;
“community pharmacy” means a pharmacy wherein or from which some or all of the services as prescribed under the Pharmacy Act are provided to persons requiring pharmaceutical services, but excludes an institutional pharmacy;

“compounding” means to prepare, mix, combine, package, and/or label a non-registered medicine(s), or to mix or combine a registered medicine with a non-registered medicine for dispensing as a result of a prescription for an individual patient by a pharmacist or a veterinarian authorised in terms of the Medicines Act. Compounded medicines are not intended as a replacement for a registered medicine or stock remedy, or for the treatment of a patient for more than 30 consecutive days from the date of compounding. The latter, however, does not preclude a pharmacist/veterinarian from continuing treatment for a period longer than 30 days, provided that a new lot of medicine is compounded for the patient in question every 30 days, except if the stability of the compounded product has been proven by accepted stability trials to extend beyond the 30-day period;

“consultancy” means an interaction between a veterinarian and an owner, farmer, client or group of clients where animals may be examined away from a registered physical facility; treatment protocols drawn up, medicines prescribed and/or provided and professional advice given regarding an ongoing health, production concern/entity or animal behaviour;

“consulting room” means a veterinary facility that complies with all the general requirements set out in the Veterinary Rules;

“dispensing” means the interpretation and evaluation of a prescription, the selection, manipulation or compounding of the medicine, the labelling and supply of the medicine in an appropriate container according to the Medicines Act and the provision of information and instructions by a pharmacist to ensure the safe and effective use of medicine by the patient and “dispense” has a corresponding meaning;

“food-producing animal” is an animal that is fed, bred, kept or utilised for the production of food for human consumption, including an animal that is not used for human consumption, but which animal belongs to a species that is normally used for human consumption in the community;

“informed consent” means consent of a patient (owner or authorised agent of the animal) or other recipient of services based on the principles of autonomy and privacy. Seven criteria define informed consent:
1) competence to understand and to decide;
2) voluntary decision making;
3) disclosure of material information, (4) recommendation of a plan;
4) comprehension of terms (3) and (4);
5) decision in favour of a plan; and
6) authorization of the plan.

A person gives informed consent only if all of these criteria are met. If the criteria are met except that the person rejects the plan, then that person makes an informed refusal.

“in-practice use” means the use of medicine for a bona fide client or patient of a veterinary practice by a veterinarian affiliated with the practice.

“label”, when used as a verb, means brand, mark or otherwise designate or describe, and when used as a noun, means any brand or mark or any written, pictorial or other descriptive matter appearing on or attached to or packed with and referring to any article or the package containing any item;

“manufacture” means all operations including purchasing of raw material, processing, production, packaging, releasing, storage, quality assurance, importation, exportation of medicine and scheduled substances and related control and “manufacturing” has a corresponding meaning;

“manufacturing pharmacy” means a pharmacy wherein or from which some or all of the services as prescribed under the Pharmacy Act are provided and which shall sell medicine only to a wholesale pharmacy or a community pharmacy or an institutional pharmacy or to persons who are authorised to purchase medicines in terms of the Medicines Act or to an organ of State;

“mobile animal service” means a veterinary practice facility, which is registered with the South African Veterinary Council in the name of the principal of the base veterinary facility from which it operates;

“mobile theatre” means a vehicle or trailer, which could consist of either a self-propelled facility or be mounted on a base which is transported to a site, and which is appropriately equipped to perform sterilisations and other surgical procedures in a controlled environment to poor or isolated communities;
“over-servicing” means the supply, provision, administration, use or prescription of any treatment or care (including diagnostic and other testing, medicines and devices) which is medically or clinically not indicated, unnecessary or inappropriate under the circumstances or which is not in accordance with current acceptable treatment protocols and procedures by the reasonable veterinarian, with due regard to the health and welfare interest of the patient.

“owner” means any person over the legal age having the possession, charge, custody or control of an animal for which veterinary services are rendered, or the owner’s representative;

“para-veterinary profession” means a profession referred to in a notice under section 21 of the Veterinary and Para-Veterinary Professions Act No. 19 of 1982;

“patient” means an individual animal or group of animals as a unit examined and/or treated, operated or consulted on by a veterinary professional by a ‘veterinarian-client-patient’ relationship;

“pharmacist” means a person registered as such under the Pharmacy Act, 1974;

“prescription” means an order given by a practitioner directing that a stated amount of any drug or mixture of drugs (medicines) specified therein be dispensed for the person/patient named in the order;

“production animal” means an animal whose products are used by humans and/or which may enter the food chain for consumption;

“production animal herd health facility” means a base facility where no clinical work is done and where the primary service is rendered essentially from an equipped vehicle to ruminant livestock, wildlife, poultry, pig or aquatic production units;

“products” means animal related products;

“public” includes a section of the public concerned with manufacturing, dispensing, selling or administering, or the issue of prescriptions for, medicines or a Scheduled substance;

“re-dispensing” means the dispensing of a medicine, stocked in the pharmacy or the dispensary of a veterinary practice, which was previously dispensed by a pharmacist of a wholesale or of a community pharmacy to a veterinarian of a veterinary practice, by
a veterinarian affiliated with the veterinary practice to a bona fide client or patient of
the practice.

“registered facility” means a pharmacy or veterinary facility which complies with the
minimum standards as applicable to the category of service rendered there, and is
registered with a Professional Council;

“re-packaging” means the removing of a medicine from its original container and
placing it into a patient ready pack and “pre-packaging” have corresponding meanings;

“research animal facility” means any facility or area where animals may be used,
maintained or bred for scientific purposes, including for research, testing, teaching,
validation, production or observation;

“scheduled substance” means any medicine or other substance prescribed by the
Minister under section 22A of the Medicines Act;

“scope of practice” means the extent of work which a pharmacist, veterinary
professional or para-veterinary professional may perform by law or chooses to restrict
himself/herself to, and defines the minimum standards of the facility that will be
registered for that purpose;

“sell” means sell by wholesale or retail and includes import, offer, advertise, keep,
expose, transmit, consign, convey or deliver for sale or authorize, direct or allow a sale
or prepare or possess for purposes of sale, and barter or exchange or supply or dispose
of to any person whether for a consideration or otherwise; and “sale” and “sold” have
corresponding meanings;

“Stock Remedy Act” means the Fertilisers, Farm Feeds, Agricultural Remedies and Stock
Remedies Act 1947, Act No. 36 of 1947, or any relevant Act it may be substituted with;

“stock remedy” means a substance intended or offered to be used in domestic animals,
livestock, poultry, fish or wild animals (including wild birds), for the diagnosis,
prevention, treatment or cure of any disease, infection or other pathological condition,
or for the maintenance or improvement of health, growth, production or working
capacity, but excluding any substance in so far as it is controlled under the Medicines
Act;

“third party” means any individual, organisation, or company outside of a patient-
healthcare professional or valid veterinarian-client-patient relationship.
“valid veterinarian-client-patient relationship” means a valid VCPR exists when these conditions apply:

a) The client (owner or owner’s agent of the animal(s)) has given the responsibility of medical care to the veterinarian and has agreed to follow the instructions of the veterinarian, and;
b) the veterinarian has assumed the responsibility of the client for making a clinical judgement regarding the health of the animal(s), the need for medical treatment, and for ensuring the provision of ongoing medical care for the animal(s);
c) the veterinarian has sufficient knowledge of the health status of the animal(s) and the care received or to be received. The knowledge has been obtained through a recent examination of the animal(s) and the premises where they are (it is) kept or through a history of medically appropriate and timely examinations and interventions, and;
d) the veterinarian is readily available, or has made the necessary arrangements with another vet, for the ongoing medical care of adverse reactions or therapy failure;

“veterinarian” means a person registered as such under the Veterinary and Para-Veterinary Professions Act, 1982 (Act No. 19 of 1982);

“veterinary hospital/clinic” means a veterinary facility where veterinary services are available at selected times and wherein examination, diagnostic, prophylactic, medical, surgical and extended accommodation services for hospitalised animals are provided;

“veterinary medicine” means any substance or mixture of substances, other than a stock remedy or farm feed to be registered in terms of the Stock Remedies Act, used or purporting to be suitable for use or manufactured or sold for use in connection with vertebrates, for the treatment, diagnosis, prevention or cure of any disease, infection or other pathological condition, or for the maintenance or improvement of health, growth, production or working capacity, or for curing, correcting or modifying any somatic or organic function, or for correcting or modifying behaviour;

“wholesale pharmacy” means a pharmacy wherein or from which some or all of the services as prescribed under the Pharmacy Act are provided and who shall sell medicine only to a wholesale pharmacy or a community pharmacy or an institutional pharmacy or to persons who are authorised to purchase medicines in terms of the Medicines Act or to an organ of State;
“wildlife” means all non-domesticated species of animals, whether free-living or kept in captivity;

“withdrawal period” means the length of time between the last administration of a drug to an animal and the time when tissues or products collected from the treated animal for consumption as food contain a level of residue of the drug that would not likely cause injury to human health.
ANNEX 2

PROHIBITED SUBSTANCES FOR USE IN FOOD-PRODUCING ANIMALS

The following veterinary medicines or substances are prohibited for use in food-producing animals:

- Phenylbutazone;
- Chloramphenicol;
- Aristolochia spp. and preparations;
- Carbadox;
- Cefuroxime*;
- Chloroform;
- Chlorpromazine;
- Colchicine;
- Dapsone;
- Diethylstilboestrol;
- Ipronizadole;
- Metronidazole;
- Nitrofurans (including Furazolidone);
- Organic arsenicals; and
- Phoxim.

*The new maximum residue limit (MRL) applies for use in cattle only.

RESTRICTED USE OF PHENYL BUTAZONE

Administration of phenylbutazone must comply with the following conditions:

An electronic microchip must identify the patient;

All records must be kept as prescribed by the Medicines Act for Schedule 6 medicines;

The veterinarian must obtain a written undertaking signed by the owner, that he/she will:

i. prevent the patient from entering into the food chain when it dies and that, at that time, proof will be submitted that it was buried, burned or fed to carnivores, subject to the
condition that irrespective of the method of disposal, it is incumbent on the veterinarian to ensure that any such disposal poses no danger to the environment or the predators and/or vultures therein.

ii. that a further written undertaking will be obtained from any third party that is contracted to remove the carcase from the premises, that the carcase will be buried or burned; and that the owner will submit such signed undertaking to the treating veterinarian;

that, if the animal is sold on, the responsibility of the seller will be taken over by the buyer who will give a written undertaking to the same effect, and which must be submitted to the treating veterinarian;

that, if the treatment of the animal is taken over by another veterinarian, copies of the written undertakings must be forwarded to same; and

that defaulting on the given undertaking will be seen in a serious light as public health is at stake.

The veterinarian must file these undertakings with the relevant clinical records for five years after the death of the animal;

Non-compliance with Rule 10(12) constitutes very serious unprofessional conduct and on conviction may attract the maximum published fine and/or removal from the register to practice as a veterinarian.
# ANNEX 3

## DIFFERENCES BETWEEN COMPOUNDING AND MANUFACTURING ACTIVITIES CHECKLIST

<table>
<thead>
<tr>
<th>NUMBER</th>
<th>QUESTION</th>
<th>COMPOUNDING</th>
<th>MANUFACTURING</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Is there a demonstrated patient-healthcare professional relationship?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>2.</td>
<td>Is there third party reselling of the product outside of the patient-healthcare professional relationship?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>3.</td>
<td>Is the activity regulated, and facility inspected, by the Pharmacy Council as a community pharmacy or the South African Veterinary Council?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4.</td>
<td>Is producing a product in anticipation of a prescription or order, is the amount produced consistent with the history of prescriptions or orders received?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>5.</td>
<td>Is there an inordinate amount of product produced or on a regular basis?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>6.</td>
<td>Is an identical product (e.g. dosage form, strength, formulation) commercially available?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>7.</td>
<td>Is the product and/or compounding service promoted or advertised to the general public rather than strictly to healthcare professionals?</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>8.</td>
<td>Does the product require only minor modification before direct administration when such modification amounts to mere directions for use?</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
ANNEX 4

GNR 1082 of 9 November 2015: Regulations relating to the performance of Compulsory Community Service (CCS) (Government Gazette No. 39380)

10. Use of veterinary medicine. - (1) Whenever a veterinary professional, administers medicine to an animal or prescribes the administering thereof, he/she must satisfy himself that the administering thereof is justified with due allowance for the benefits and risks which that medicine may hold for—

   a) The animal to which it is administered, including withdrawal times of residues where relevant in the animal and/or the effect on the environment;
   b) The person by whom it is administered; and
   c) The consumer of the products of that animal if residues of the medicine concerned should be present in those products.

(2) To tranquilise, sedate, chemically immobilise or anaesthetise wildlife, any schedule 5 or 6 medicine to be administered parenterally, must be administered by a veterinary professional personally.

(3) Notwithstanding the provisions of 10 (2) a veterinary professional may prescribe, sell, or dispense the following substance(s) or medicine(s) to a client within a ‘client- patient-veterinarian’ relationship for the purposes of the treatment of a specified patient on condition that the requirements of the Medicines Act are complied with and said substance/medicine may only be made available for a reasonably acceptable period, but in any event for no longer than thirty (30) days consecutive treatment at a time—

   a) Perphenazine enanthate;
   b) Haloperidol;
   c) Zuclopenthixol acetate;
   d) Diazepam; and/or
   e) Azaperone.
(4) A veterinary professional must inform the owner of an animal to which medicine is administered, fully with regard to -

a) The application and effect of and precautionary measures in connection with that medicine;

b) The period, if any, during which the products of that animal are to be withheld from human consumption; and

c) The period, if any, (also referred to as the detection time) during which the animal should not be entered for sports competitions where prohibited substance rules apply.

(5) When using or prescribing a medicine that has been compounded, veterinarians must comply with the following -

a) Ensure that a suitable registered veterinary medicine or any combination of such medicines, as defined in the Medicines Act, or stock remedy, as defined in the Stock Remedy Act, or any relevant Act it may be substituted with, is not available for sale within the Republic of South Africa in a suitable size, volume and concentration; including extra-label medicine use;

b) Ensure that where there is no registered veterinary medicine available, a veterinarian may only compound medicine in a quantity not greater than the quantity required for treatment of the patient for a period of not more than 30 days;

c) Ensure that the preparation labelling of the medicines is done in labelling in accordance with Rule 21 (4) (l);

d) Ensure that there is a documented system for compounding in place and inform the Council, on its request, on the therapeutic efficacy and effect of such compounded medicine, the purpose and circumstances under which and the manner in which such compounded medicine should be used;
e) Ensure that a compounded product does not contain substances as prohibited in terms of Section 36A of the Medicines Act in South Africa;

f) Ensure that the purity of the medicines is guaranteed by procuring such medicines from a manufacturer(s) accredited for Good Manufacturing Practice, should the veterinarian personally compound the medicines;

g) Should the compounding of medicines be outsourced to a third party, the veterinarian must make use of a registered compounding facility with the correct licensing to perform such compounding, who can contractually guarantee the purity of the ingredients, and must issue the third party with a compounding order specifying the product, quantity, packaging and labelling;

h) Retain full responsibility for the product even when it is compounded by a third party, unless such third party commits a manufacturing error;

i) Comply with all aspects of Section 22A of the Medicines Act;

j) Ensure that the compounded products are not advertised or promoted as veterinary medicine trade name products or displayed for sale to the general public;

k) The use of compounded medicine is not intended to circumvent the registration requirements of the Medicines Act and/or the Stock Remedy Act;

l) Inform the owner of the lack of quality control and possible deficiencies in efficacy of the compounded product;

m) Ensure that compounding is not done in the absence of a ‘veterinarian-client-patient’ relationship; and/or

n) No compounded veterinary medicines or actives may be imported without approval from the Medicines Control Council.

(6) A veterinarian may only use compounded veterinary medicine for a food producing animal(s), including wildlife intended for human consumption, subject to the following—
a) The use of the compounded medicine is limited to the emergency management of a new disease/condition or the management of a disease/condition to which no local registered product exists, or is not readily accessible at the time, as restricted by the conditions in Rule 10 (5) (a) to 10 (5) (g) above;

b) The reason for compounding is not an attempt to enhance growth promotion in any food producing species in the absence of disease;

c) The withdrawal period associated with its use as prescribed by the veterinarian must be approved in writing by the Food Safety and Security Committee of the Council or the Veterinary Clinical Committee of the Medicines Control Council, as the case may be, in accordance of the requirements of the Foodstuffs, Cosmetics and Disinfectants Act, Act 54 of 1972 or hundred and twenty (120) days, or otherwise ten times the half-life of the medicine, unless another withdrawal period is set by one of the two Committees;

d) The food produced by said animal is unsuitable for human consumption until such time that the withdrawal time is approved by either or both of the Committees listed in Rule 10 (6) (c), unless any one of the conditions in Rule 10 (6) (c) is met;

e) Medicines prohibited for use in food producing species as set out in Rule 10 (11) may not be used in compounded medicines; and

f) It is not intended for continued, sustained and/or frequent use on any one farm, by any one farm owner, by any one farm manager, by any one veterinarian or by any one person as this constitutes manufacturing, unless the use of the compounded medicine is reasonably justifiable and substantiated by facts.

(7) When a veterinarian compounds a veterinary medicine, it must be done from a registered suitable facility, unless the circumstances dictate otherwise.

a) (8) A veterinarian may only compound, or have compounded on his/her behalf an autogenous vaccine, subject to the following—
b) The veterinarian or third party contractor must be in possession of a permit in accordance with Section 20 (b) of the Animal Diseases Act 1984, Act 35 of 1984;

c) The production may only be undertaken or prescribed by a veterinarian for use in a particular patient in accordance with sections 14 (4) and 22A (5) (e) of the Medicines Act;

d) An autogenous vaccine may only be used for a disease or strain of a disease for which there is no suitable veterinary vaccine or combination thereof registered and/or sold and/or available for sale in the Republic of South Africa;

e) The use of an autogenous vaccine is restricted to the specific farm where the infectious agent was identified. If grounds exist for the use of an autogenous vaccine on adjacent and non-adjacent farms, then an application in terms of section 20 of the Animal Diseases Act (Act 35 of 1985) must be submitted for approval;

f) In a disease outbreak situation, the mass use of an autogenous vaccine may only commence in accordance with the requirements of section 20 of the Animal Diseases Act (Act 35 of 1985) and section 21 of the Medicines Act; and

g) The general sale of any autogenous vaccine to neighbouring farms or other districts/provinces must meet the requirements for general sale of a medicine in accordance with the Medicines Act and the Animal Diseases Act.

(9) If a veterinarian compunds a veterinary medicine, he/she must do so from a registered facility, suitable for compounding, unless the circumstances dictate otherwise.

(10) Extra label use: A veterinarian may use a registered medicine, veterinary medicine or stock remedy in a manner other than stated on the approved label or package insert, provided that there is justifiable reason for doing so. The veterinarian takes full responsibility for the supervision of the preparation, application and outcome of the application/administration of the said medicine, and must be available to advise or intervene if there are any aberrant reactions to the said application/administration. If there is reason to expect any such aberrant reactions from the extra label use, the
veterinarian must first explain his/her reasons to the client, and receive permission from the client to proceed.

(11) The following medicines are prohibited for use in food producing animals—

a) Phenylbutazone;
b) Chloramphenicol;
c) Aristolochia spp. and preparations;
d) Carbadox;
e) Cefuroxime*;
f) Chloroform;
g) Chlorpromazine;
h) Colchicine;
i) Dapsone;
j) Diethylstilboestrol;
k) Ipronizadole;
l) Metronidazole;
m) Nitrofurans (including Furazolidone);
n) Organic arsenicals; and
o) Phoxim.

*The new maximum residue limit (MRL) applies for use in cattle only.

(12) Administration of phenylbutazone must comply with the following conditions—

a) The patient must be identified by an electronic microchip;
b) All records must be kept as prescribed by the Medicines Act for Schedule 6 medicines;
c) The veterinarian must obtain a written undertaking signed by the owner, that he/she will—
i. prevent the patient from entering into the food chain when it dies and that, at that time, proof will be submitted that it was buried, burned or fed to carnivores, subject to the condition that irrespective of the method of disposal, it is incumbent on the veterinarian to ensure that any such disposal poses no danger to the environment or the predators and/or vultures therein.

ii. that a further written undertaking will be obtained from any third party that is contracted to remove the carcase from the premises, that the carcase will be buried or burned; and that such signed undertaking will be submitted by the owner to the treating veterinarian;

iii. that, if the animal is sold on, the responsibility of the seller will be taken over by the buyer who will give a written undertaking to the same effect, and which must be submitted to the treating veterinarian;

iv. that, if the treatment of the animal is taken over by another veterinarian, copies of the written undertakings must be forwarded too same; and

v. that defaulting on the given undertaking will be seen in a serious light as public health is at stake.

d) The veterinarian must file these undertakings with the relevant clinical records for a period of five years after the death of the animal;

e) Non-compliance with Rule 10 (12) constitutes very serious unprofessional conduct and on conviction may attract the maximum published fine and/or removal from the register to practice as a veterinarian; and

f) This Rule will become operative when the conditions set out in Rule 47 (3) are met.
# ANNEX 5

**CONSENT TO DISPENSE OR USE COMPOUNDED VETERINARY MEDICINES**

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<th>Client Name:</th>
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<table>
<thead>
<tr>
<th>Animal Identification:</th>
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<tr>
<th>Description of the compounded veterinary medicine:</th>
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<tr>
<th>Community pharmacy that prepared the compounded veterinary medicine (if applicable):</th>
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<th>Rx Number (if applicable)</th>
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<td>_______________</td>
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<thead>
<tr>
<th>Prescribed Directions for Use:</th>
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I give consent for the compounded veterinary medicine (s) described above.

a) I understand the proposed compounded veterinary medicine is not approved by the South African Medicines Control Council and so may provide a greater risk level to the animal (s). This compounded veterinary medicine has not undergone rigorous testing for efficacy and stability.

b) I understand the reasons for utilising the compounded veterinary medicine, its potential risks and benefits, other alternative treatment (s) and the probable consequences, which may occur if the proposed medication is not administered.

c) I am willing to accept the risks associated with this compounded veterinary medicine that my veterinarian has discussed with me.

d) By this allow Dr. _________________________________ to dispense or use the compounded veterinary medicine described above to my animal.
(s). This consent is valid until I revoke it or conditions change to the point that all risks and benefits are significantly different.
ANNEX 6
CONSENT TO DISPENSE OR USE COMPOUNDED VETERINARY MEDICINES FOR FOOD-PRODUCING ANIMALS & POULTRY

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<th>Client Name:</th>
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<th>Animal Identification:</th>
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<td>Community pharmacy that prepared the compounded veterinary medicine (if applicable):</td>
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<td>Rx Number (if applicable) _________________</td>
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<th>Prescribed Directions for Use:</th>
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<tr>
<th>Withdrawal instructions:</th>
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<tbody>
<tr>
<td>Milk from this animal, taken at the am/pm milking, may go into the tank on DD/MM/YYYY:</td>
</tr>
<tr>
<td>This animal may be shipped for slaughter on DD/MM/YYYY:</td>
</tr>
<tr>
<td>Eggs may be marketed on DD/MM/YYYY:</td>
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</tbody>
</table>
I give consent for the compounded veterinary medicine(s) described above.

a) I understand the proposed compounded veterinary medicine is not approved by the South African Medicines Control Council and so may provide a greater risk level to the animal(s). This compounded veterinary medicine has not undergone rigorous testing for efficacy and stability.

b) I understand the reasons for utilising the compounded veterinary medicine, its potential risks and benefits, other alternative treatment(s) and the probable consequences, which may occur if the proposed medication is not administered.

c) I am willing to accept the risks associated with this compounded veterinary medicine that my veterinarian has discussed with me.

d) By this allow Dr. ________________________________ to dispense or use the compounded veterinary medicine described above to my animal(s). This consent is valid until I revoke it or conditions change to the point that all risks and benefits are significantly different.

<table>
<thead>
<tr>
<th>Client Signature:</th>
<th>Date:</th>
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<tbody>
<tr>
<td>Address:</td>
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