PROPOSED CATEGORIZATION OF ANTIMICROBIAL DRUGS

Antimicrobial drugs are used primarily in human and veterinary medicine for the treatment, control and prevention of bacterial diseases.   In addition, some of these drugs are also used for other purposes in the agri-food industry for instance,   growth promotion and improving feed efficiency. It is well recognized that many of the same chemical classes of antimicrobial drugs used in animals are also used in humans.   Some of these antimicrobials are the drugs of last resort for the treatment of serious life-threatening infections in humans.   If these drugs become ineffective due to the development of bacterial resistance, alternative antimicrobials may not be available to treat infections caused by resistant bacteria. Therefore, it is imperative to develop measures   to mitigate the loss of effectiveness of these life saving drugs. In the context of ensuring prudent and judicious use of antimicrobials, careful attention needs to be placed on how these drugs are used both in human and animals.

Health Canada recognizes that all available antimicrobial drugs are important.   However, some drugs are considered more important than others in the treatment of bacterial infections.   The rationale used to rank the antimicrobial drugs according to their relative importance in human medicine is given below.   For the sake of simplicity, the drugs have been ranked according to their chemical class and have been placed in a category where majority of the drugs within the class may fall. It is understood that some of the individual drugs in a particular class may not fall in the same category as other drugs of the same class and such exceptions will be treated on a case by case basis.

This categorization system is a guide for the evaluation of veterinary new antimicrobial drug submissions. Sponsors are encouraged to take into consideration this categorization system when preparing their veterinary new drug submissions. As a general rule, drugs belonging to a higher category will receive more rigorous scrutiny as compared to the drug of a lower category. This categorization will be updated periodically as new relevant scientific information/evidence is obtained by the Directorate.

Rationale for categorization:

The criteria for categorization of antimicrobials is mainly based on the following factors:

- **Indication and availability of alternative antimicrobial therapy**: A drug which is used for serious life-threatening condition will be given a higher score over a drug which is used routinely for common non-life-threatening infections. Consideration will be given on whether there are any suitable alternative drugs available in case bacteria develop resistance to these drugs. For example, for a drug belonging to category I, there are limited and/or no alternatives available or the alternative drugs available are within the same category.
- **Activity and mode of action**: This includes a consideration of the spectrum of

activity as well as the efficacy of a particular drug   A drug with a novel mode of action is given a higher score.

- **Mechanism of resistance and potential for transfer**: This factor encompasses a consideration of resistance mechanism(s) by which bacteria develop resistance to a particular drug as well as the potential to develop cross and co-resistance.   For the potential for transfer of resistance, resistance mechanisms which are encoded on transmissible elements are given a higher score than the chromosomal encoded mechanisms.

## 1.	Category I: Very High Importance

These are antimicrobials of highest importance in human medicine and are used for the treatment of life-threatening bacterial infections.   There may be no alternative antimicrobials in case of emergence of resistance to these agents. Some of these agents have unique mechanism of action and hence should be reserved for the treatment of serious infections. New antimicrobial drugs with the spectrum of activity against serious life threatening infections and/or unique mode of action will fall in this category. Examples include:

1.1	Carbapenems
1.2	Cephalosporins -third and fourth generation
1.3	Fluoroquinolones
1.4	Glycopeptides
1.5	Ketolides
1.6	Monobactams
1.7	Oxazolidinones
1.8	Streptogramins

## 2.	Category II: High Importance

Antimicrobials classified as category II consist of those that can be used to treat severe infections and for which alternatives are generally available.   Examples include:

2.1	Aminoglycosides Group 1 (amikacin, gentamicin, kanamycin, netilmicin, tobramycin)
2.2	Cephamycins
2.3	Lincosamides
2.4	Macrolides
2.5	Penicillins Group 1 (penicillins - β lactamase inhibitor combinations, carboxypenicilins, ureidopenicillins)
2.6	Rifamycins

3.   Category III: Medium Importance

Majority of these antimicrobials are generally used for treatment of non-life-threatening yet common bacterial infections.   Bacteria that are resistant to these drugs can be treated by category II or I antimicrobials.   Examples include:

    3.1   Aminoglycosides Group 2 (neomycin, streptomycin, spectinomycin)
    3.2   Amphenicols
    3.3   Cephalosporins -first and second generation except cephamycin
    3.4   Penicillins Group 2 (natural penicillins, aminopenicillins, penicillinase resistant penicillins)
    3.5   Polymyxins
    3.6   Quinolones except fluoroquinolones
    3.7   Sulphonamides
    3.8   Tetracyclines
    3.9   Trimethoprim

4.   Category IV: Low Importance

Some of these antimicrobials are currently of limited use in human medicine while others such as the ionophores, are not used in human medicine.   Examples in this category include:

    4.1   Bacitracin
    4.2   Coumarins
    4.3   Flavophospholipols
    4.4   Ionophores
    4.5   Nitrofurans
    4.6   Quinoxalines