WHO Guidelines on use of Medically Important Antimicrobials in Food-Producing Animals

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WHO: Global Action Plan on AMR

Goal: "To ensure… continuity of successful treatment ….of infectious diseases with effective and safe antimicrobial agents”

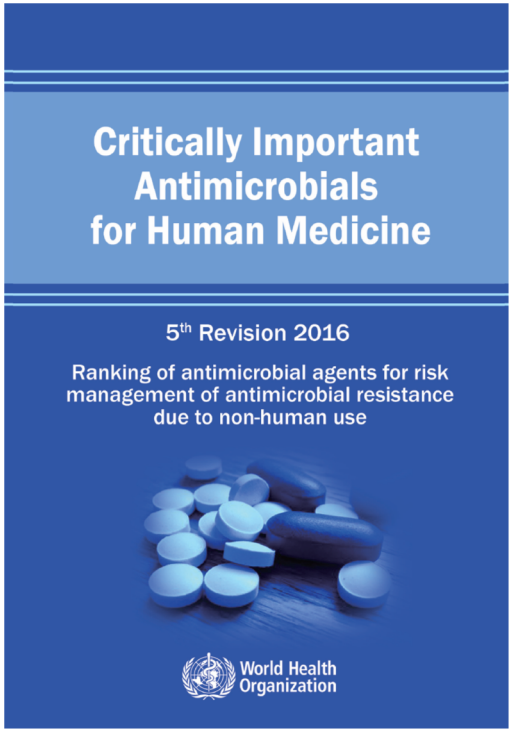
Adopted by World Health Assembly, May 2015

GAP Strategic Objectives

1. Improve awareness and understanding of AMR through education and training
2. Strengthen knowledge and evidence base through surveillance and research
3. Reduce the incidence of infection through effective hygiene and IPC measures
4. Optimize the use of antimicrobial medicines in human and animal health
5. Ensure sustainable investment through research and development

The WHO CIA list

- Ranking of antimicrobials according to their importance in human medicine
- For risk management and containment of antimicrobial resistance in the context of non-human antimicrobial use
- First developed by WHO in 2005
- Updated on regular basis (2007, 2009, 2013, 2016 and 2018 (currently in draft))
- Component of WHO's Global Action Plan on AMR



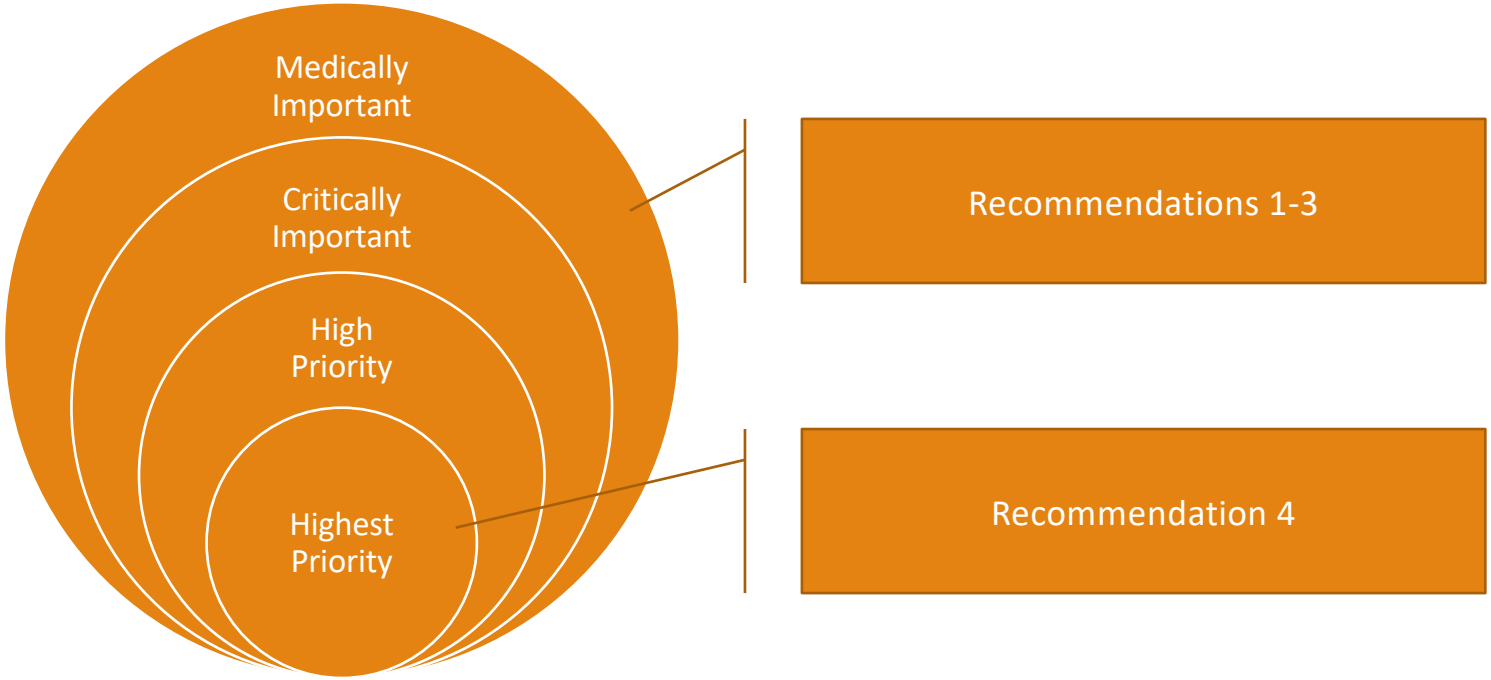
5th Revision 2016

Antimicrobial class	Criterion (Yes=)				
CRITICALLY IMPORTANT ANTIMICROBIALS	C1	C2	P1	P2	P3
HIGHEST PRIORITY					
Cephalosporins (3rd, 4th and 5th generation)					
Glycopeptides					
Macrolides and ketolides					
Polymyxins					
Quinolones					
HIGH PRIORITY					
Aminoglycosides					
Ansamycins					
Carbapenems and other penems					
Glycylcyclines					
Lipopeptides					
Monobactams					
Oxazolidinones					
Penicillins (natural, aminopenicillins, and antipseudomonal)					
Phosphonic acid derivatives					
Drugs used solely to treat tuberculosis or other mycobacterial diseases					

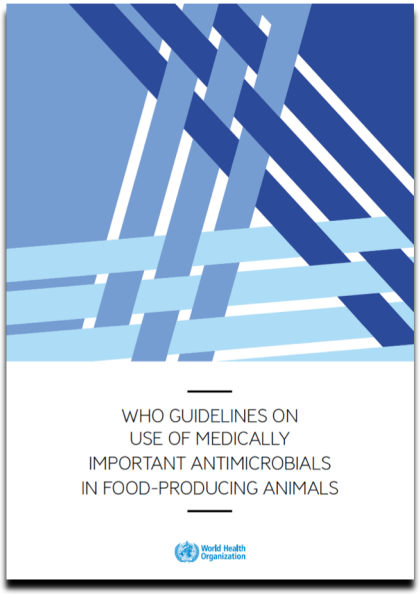
Antimicrobial class	Criterion (Yes=)				
HIGHLY IMPORTANT ANTIMICROBIALS	C1	C2	P1	P2	P3
Amidinopenicillins			NA		
Amphenicols					
Cephalosporins (1st and 2nd generation) and cephamycins					
Lincosamides					
Penicillins (anti-staphylococcal)					
Pseudomonic acids					
Riminofenazines					
Steroid antibacterials					
Streptogramins					
Sulfonamides, dihydrofolate reductase inhibitors and combinations					
Sulfones					
Tetracyclines					
IMPORTANT ANTIMICROBIALS	C1	C2	P1	P2	P3
Aminocyclitols			NA		
Cyclic polypeptides					
Nitrofurantoins					
Nitroimidazoles					
Pleuromutilins					

Note: Does not include non-medically important antimicrobials (e.g. ionophores, phosphoglycolipids).

Categories Subject to Recommendations



The Guidelines



Published 2017

- Aim to preserve the effectiveness of medically important antimicrobials, particularly those critically important to human medicine
- Public health focus, but due consideration given to factors such as animal health and welfare
- Evidence-based: systematics reviews, literature reviews, GRADE approach, an independent multidisciplinary group of experts, external peer review

http://apps.who.int/iris/bitstream/10665/258970/1/9789241550130-eng.pdf?ua=1

What are WHO Guidelines?

WHO procedure established in 2007

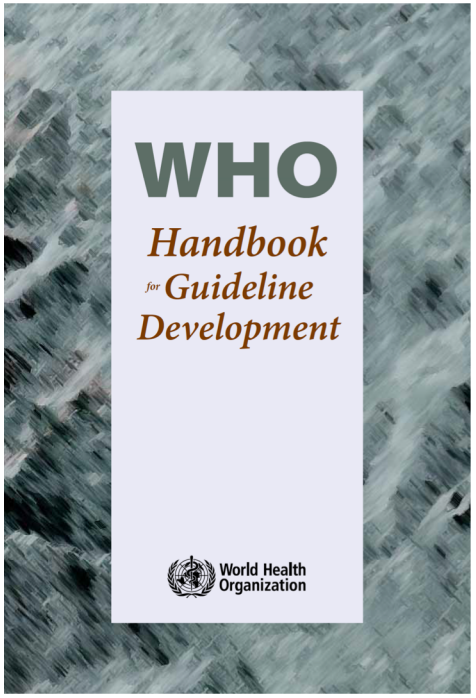
Applies to any document developed by the WHO containing recommendations for clinical practice or public health policy

A recommendation tells the intended end-user of the guideline what to do in specific situations to achieve the best health outcomes possible, individually or collectively

Uses evidence-based standards

Minimize bias, conflict of interest

Transparency in judgments

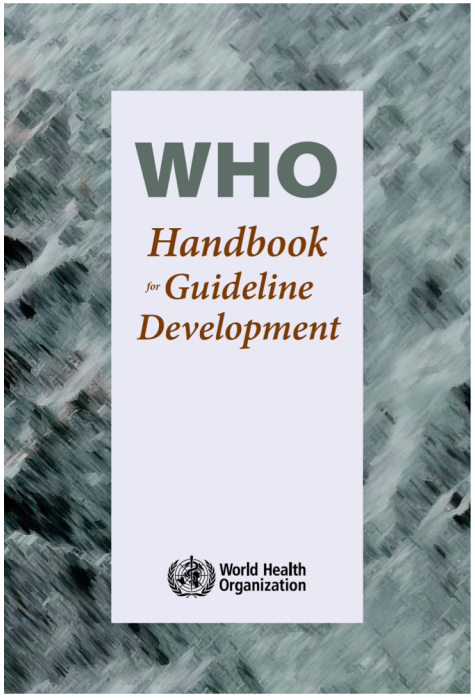


How Differ from Treatment Guidelines?

WHO Guidelines on use of Medically Important Antimicrobials in Food-Producing Animals are not the same as treatment guidelines (also known as clinical practice guidelines)

Treatment guidelines are normally produced locally / regionally

Take into account national regulations (e.g. drug approvals), animal species, route of administration, indication, local AMR patterns in target pathogens, other factors



PRIORITY QUESTION 1: Human Populations

For human populations of any age in any setting, does a limitation compared to not having that limitation of use of antimicrobial(s) in food-producing animals reduce the presence of antimicrobial resistant genetic elements and/or antimicrobial-resistant bacteria in human populations?

PRIORITY QUESTION 2: Animal Populations

For food-producing animals of any age in any setting, does a limitation compared to not having that limitation of use of antimicrobial(s) in food-producing animals reduce the presence of antimicrobial resistant genetic elements and/or antimicrobial-resistant bacteria in food producing animals?

Identify Important Outcomes: Benefits and potential harms from limitations on AMU.

Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis

Karen L Tang, Niamh P Caffrey, Diego B Nóbrega, Susan C Cork, Paul E Ronksley, Herman W Barkema, Alicia J Polachek, Heather Ganshorn, Nishan Sharma, James D Kellner, William A Ghali

Summary

Background Antibiotic use in human medicine, veterinary medicine, and agriculture has been linked to the rise of antibiotic resistance globally. We did a systematic review and meta-analysis to summarise the effect that interventions to reduce antibiotic use in food-producing animals have on the presence of antibiotic-resistant bacteria in animals and in humans.

Lancet Planet Health 2017
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November 6, 2017
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journal homepage: www.elsevier.com/locate/ijantimicag

Review

Is antimicrobial administration to food animals a direct threat to human health? A rapid systematic review

Anna Mae Scott, (PhD)[a,*], Elaine Beller, (MAppStat)[a], Paul Glasziou, (PhD)[a], Justin Clark, (BA)[a], Respati W. Ranakusuma, (MD)[a], Oyungerel Byambasuren, (MD)[a], Mina Bakhit, (MD)[a], Stephen W. Page, (MVetClinStud)[b], Darren Trott, (PhD)[c], Chris Del Mar, (MD)[a]

F1000Research

F1000Research 2017, 6:1805 Last updated: 14 NOV 2017

Check for updates

REVIEW

Illustrative examples of probable transfer of resistance determinants from food animals to humans: Streptothricins, glycopeptides, and colistin [version 1; referees: 2 approved]

Hattie E. Webb[1], Frederick J. Angulo[2], Sophie A. Granier[3], H. Morgan Scott[4], Guy H. Loneragan[1]

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[3]Laboratory for Food Safety, Anses, Université Paris-Est, Maisons-Alfort, F-94701, France
[4]Department of Veterinary Pathobiology, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, 77843, USA

v1 **First published:** 05 Oct 2017, **6**:1805 (doi: 10.12688/f1000research.12777.1)
Latest published: 05 Oct 2017, **6**:1805 (doi: 10.12688/f1000research.12777.1)

Open Peer Review

Comment

Unintended consequences associated with national-level restrictions on antimicrobial use in food-producing animals

www.thelancet.com/planetary-health **Vol 2 July 2018**

Formulation of Recommendations

Considering:

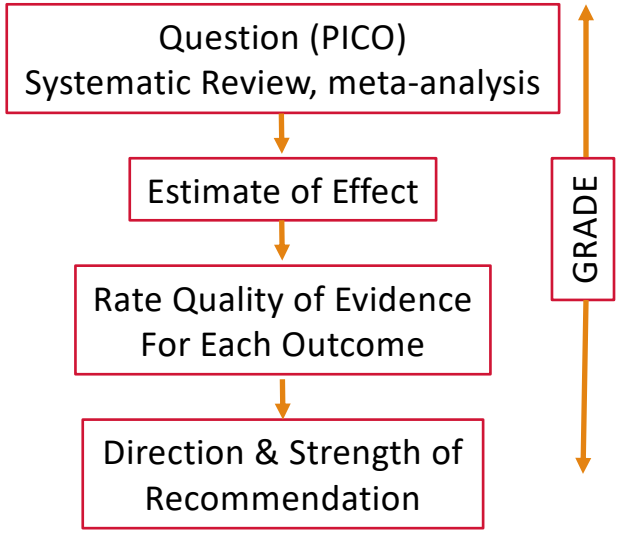
- Quality of supporting evidence
- Importance of the problem
- Balance between benefits and harms
- Values and preferences of stakeholders
- Resource implications of the intervention
- Equity and rights
- Acceptability and feasibility

Strength of Recommendation (public health policy)

Strong	**Desirable consequences clearly outweigh the undesirable consequences. Can be adopted as policy in most situations.**
Conditional	Uncertain about balance of desirable / undesirable consequences. Policy-making will require substantial debate and involvement of various stakeholders

Quality of Evidence

- Systematic reviews (intervention effects), narrative reviews (harms, biological plausibility, examples)
- Quality assessment (GRADE - Grading of Recommendations Assessment, Development and Evaluation)



GRADE Quality Assessment Criteria

Design	Quality of Evidence	Lower if:	Higher if:
Randomized Trial	High	Risk of bias Inconsistency Indirectness Imprecision Publication bias	Large effect Dose response All plausible confounding
	Moderate		
Observational Study	Low		
	Very Low		

RECOMMENDATION 1: Overall antimicrobial use

We recommend an overall reduction in use of all classes of medically important antimicrobials in food-producing animals.

Strong recommendation, low quality evidence

Recommendation 2: Growth promotion use

We recommend complete restriction of use of all classes of medically important antimicrobials in food-producing animals for growth promotion.

Strong recommendation, low quality evidence

Recommendation 3: Prevention use (in the absence of disease)

We recommend complete restriction of use of all classes of medically important antimicrobials in food-producing animals for prevention of infectious diseases that have not yet been clinically diagnosed.

Strong recommendation, low quality evidence

Remarks: When a veterinary professional judges that there is a high risk of spread of a particular infectious disease, use of antimicrobials for disease prevention is justified, if such a judgement is made on the basis of recent culture and sensitivity testing results.

RECOMMENDATION(s) 4: Control and treatment use (in the presence of disease)

Recommendation 4a

We suggest that antimicrobials classified as highest-priority critically important for human medicine should not be used for control of the dissemination of a clinically diagnosed infectious disease identified within a group of food-producing animals.

Conditional recommendation, very low quality evidence

Recommendation 4b

We suggest that antimicrobials classified as highest-priority critically important for human medicine should not be used for treatment of food-producing animals with a clinically diagnosed infectious disease.

Conditional recommendation, very low quality evidence

Remarks: To prevent harm to animal health and welfare, exceptions to recommendations 4a and 4b can be made when, in the judgment of veterinary professionals, bacterial culture and sensitivity results demonstrate that the selected drug is the only treatment option.

Best Practice Statements

Best practice statement 1

Any new class of antimicrobials or new antimicrobial combination developed for use in humans will be considered critically important for human medicine unless categorized otherwise by WHO.

Best practice statement 2

Medically important antimicrobials that are not currently used in food production should not be used in the future in food production including in food-producing animals or plants.

Guideline Implementation and Evaluation

Member states, international organizations (e.g. Codex Alimentarius) and other stakeholders are urged to take these Guidelines into account when developing standards and policies.

- Regulators: licensing, labelling, off-label restrictions
- Veterinarians: development of national and local clinical antimicrobial use guidelines / formularies
- Food industry and animal industry policies: voluntary restrictions

Implementation in low- and middle-income countries may require support (e.g. antimicrobial susceptibility testing, translation of knowledge and technologies for reducing antimicrobial use in food-producing animals).

Guidelines will be evaluated by WHO as part of its monitoring of efforts by member states related to the WHO Global Action Plan on Antimicrobial Resistance.

WHO will review and update the Guidelines within 5 years.

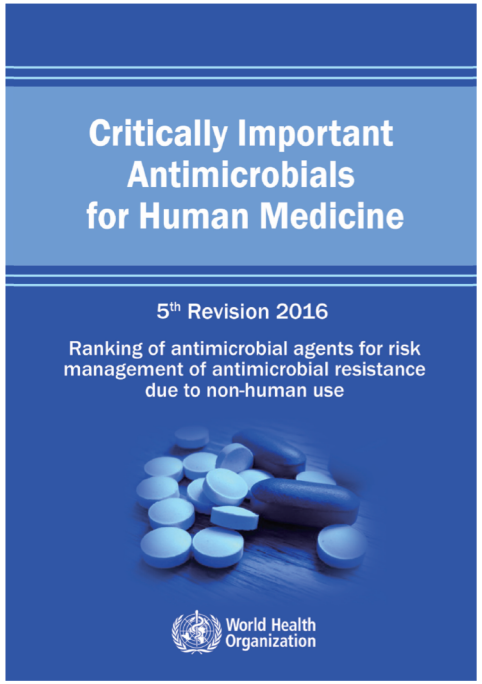
Summary

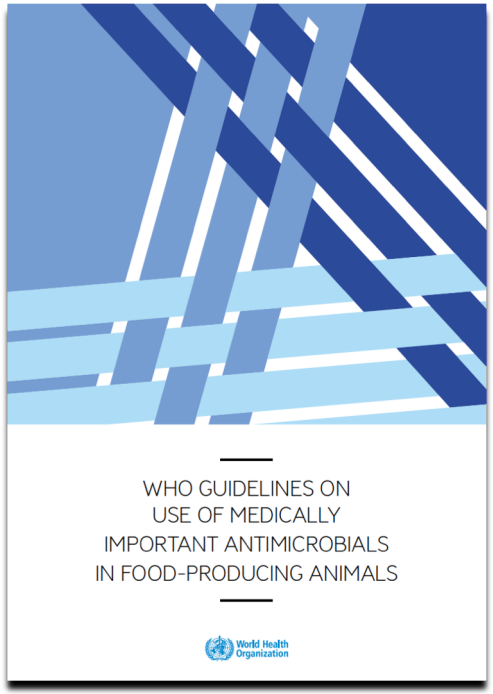
The WHO Guideline for Use of Medically Important Antimicrobials in Food-Producing Animals

- Provide specific evidence-based recommendations to further support the Global Action Plan by preserving the effectiveness of medically important antimicrobials

Thank you!


GLOBAL ACTION PLAN
ON ANTIMICROBIAL
RESISTANCE
World Health Organization


Critically Important Antimicrobials for Human Medicine
5th Revision 2016
Ranking of antimicrobial agents for risk management of antimicrobial resistance due to non-human use
World Health Organization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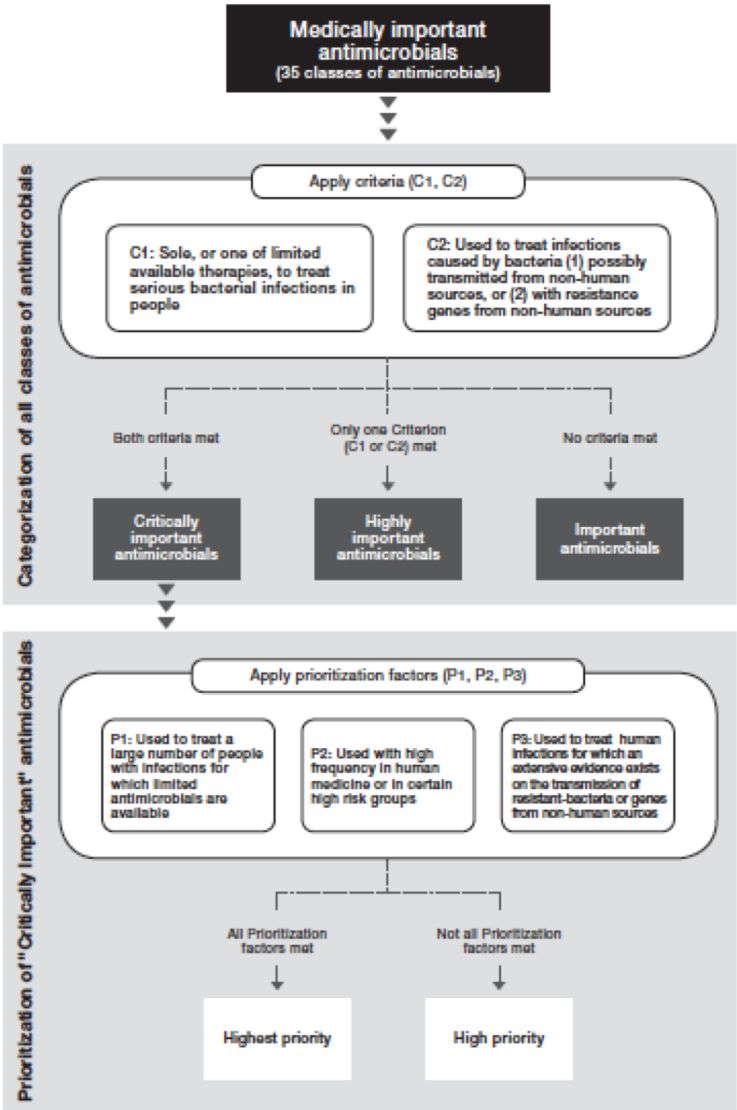
Medically important antimicrobials
(35 classes of antimicrobials)
Categorization of all classes of antimicrobials
Apply criteria (C1, C2)
C1: Sole, or one of limited available therapies, to treat serious bacterial infections in people
C2: Used to treat infections caused by bacteria (1) possibly transmitted from non-human sources, or (2) with resistance genes from non-human sources
Both criteria met
Only one Criterion (C1 or C2) met
No criteria met
Critically important antimicrobials
Highly important antimicrobials
Important antimicrobials
Prioritization of "Critically Important" antimicrobials
Apply prioritization factors (P1, P2, P3)
P1: Used to treat a large number of people with infections for which limited antimicrobials are available
P2: Used with high frequency in human medicine or in certain high risk groups
P3: Used to treat human infections for which an extensive evidence exists on the transmission of resistant-bacteria or genes from non-human sources
All Prioritization factors met
Not all Prioritization factors met
Highest priority
High priority