



Certified Responsible Antibiotic Use Standard (CRAU): Beef

.....

In working to improve husbandry and optimize animal health, the beef industry can reduce the need for antibiotics, while improving antibiotic stewardship and helping to preserve the future efficacy of life-saving medicines. The attached Certified Responsible Antibiotic Use standard for beef production provides a clear, actionable definition for responsible antibiotic use and stewardship for producers who choose to reduce antimicrobial use, improve their management practices and provide more accountability to their buyers and the public.

Consistent with our commitment to the protection of public and animal health, we support conformance with the attached Certified Responsible Antibiotic Use standard for beef production.

We urge the beef industry and its customers to incorporate the standard into production and purchasing decisions. We look forward to collaborating with beef producers interested in responsible antibiotic use to finalize implementation details to meet the requirements of this CRAU standard.



CRAU is managed by the Antibiotic Resistance Action Center at the Milken Institute School of Public Health at the George Washington University.

The beef standard was developed by the Natural Resources Defense Council.

CERTIFIED RESPONSIBLE ANTIBIOTIC USE STANDARD FOR BEEF PRODUCTION

OVERVIEW

Increasingly scientists, medical associations, public interest organizations, business leaders and consumers are calling for livestock and poultry production that relies on responsible antimicrobial use practices. In conformance with the clear and auditable practices encompassed by this standard, beef producers can improve animal husbandry and optimize cattle health while reducing the need for antimicrobials and minimizing the potential for antimicrobial resistance. This will help to ensure that existing antimicrobials remain effective longer for treating sick humans and animals.

SCOPE

Under this standard, a beef producer certifies the production of cattle at one of three levels, in conformance with all provisions set forth below (summarized in Table 1).

DEFINITION OF TERMS:

Antimicrobials refer to agents used against microbial infections, and include antibacterials, antifungals, and antiparasitic drugs and metals. This document uses antibiotic interchangeably with antimicrobial, unless otherwise noted.

Medically important antimicrobials means any antimicrobial drug composed wholly or partly of any drug or derivative of a drug from a class listed as “Important”, “Highly Important” or “Critically Important” by the World Health Organization (WHO) in the most recent version of its *Critically Important Antimicrobials for Human Medicine* publication. (Summarized in Tables 2 and 3)¹

Non-medically important antimicrobials are those antimicrobials added to animal feed that do not belong to drug classes also used in human medicine, including ionophores or coccidiostats, as well as metals added to animal feeds such as copper and zinc.

Based on language adopted in May 2018 by the World Organization for Animal Health (OIE)², the standard defines the following terms:

Disease prevention means antimicrobial use in an individual or group of animals in the absence of clinical infectious disease in any individual or group of animals.

Disease control (also called metaphylaxis) means antimicrobial use in a group of animals containing both sick and healthy animals, to reduce or resolve the clinical signs of infection and to prevent further spread of the disease. Under this standard, disease control is not to be considered a form of disease prevention.

Disease treatment means antimicrobial use in an individual or group of animals showing documented, clinical signs of an infectious disease. Once infection resolves, application of the antimicrobial ceases.

Entry Level

1. Level of production

- a. Entry Level requirements apply for the last 180 days of life of any cattle produced in the facility or facilities being certified under the Standard. Cattle may spend the entire 180 days on a feedlot; if cattle under the standard have spent a portion of those 180 days at another facility, prior to entering the feedlot, then records must be available to auditors confirming conformance with the standard's requirements at all facilities.
- b. All cattle falling under Entry Level requirements must be kept segregated and readily identifiable for the purpose of animal management and veterinary oversight.

2. Veterinary oversight. All antimicrobial use is directed by a licensed veterinarian in the context of a valid veterinarian client-patient relationship (VCPR), as defined in federal code.³

- a. Producers shall develop a stewardship plan with their veterinarian(s) that includes production practices to reduce, and where possible eliminate, the need for antimicrobials.⁴ Examples could include (but are not limited to) a focus on healthy breeding stock; sourcing of healthy animals; vaccination; use of non-antimicrobial feed agents such as prebiotics, probiotics or other approved alternatives to antimicrobials; reductions in animal density; reduced stress from changes made to stocking density, cattle mixing or transportation practices; improved hygiene and biosecurity; improved feed nutrition; and close observation for early signs of disease.
- b. When antimicrobials are used, they should be administered to as few cattle as possible, and only for as long as necessary (e.g. shortest duration).⁵

3. Permitted uses of medically important antimicrobials: Medically important antimicrobials may be used only when administered:

- a. Under a veterinary prescription or veterinary feed directive, and when the antimicrobial in question is *both* FDA-approved for use in the U.S.

- as well as approved for use by the equivalent agency in the country where the certified facility is in operation.
- b. To individual cattle, in relation to a specific surgery or medical procedure carrying risk of infection, e.g. castration, dehorning, caesarian section.
 - c. For disease treatment and disease control, as previously defined, with the following limitations:
 - i. Antimicrobials classified by the WHO as Critically Important in human medicine (Table 3) should only be used for disease treatment or disease control when the most recent culture and sensitivity results for the bacterium known to have caused the disease indicate that the antimicrobial in question is the only option⁶; and further
 - ii. Highest-Priority Critically Important Antimicrobials, or HPCIAAs, more specifically are not permitted for disease control use.
 - d. Medically important antimicrobials are not permitted for growth promotion, feed efficiency, weight gain, disease prevention, reduction in incidence of liver abscesses, or any other repeated or regular pattern of use.
4. **Record-keeping.** In seeking initial recognition under the standard, a producer must submit the following:
- a. A stewardship plan that also demonstrates the facility's ability to comply with data collection requirements outlined below;
 - b. Documentation, beginning with the 12-month period preceding the facility's entrance into the program, updated no less than every 3 months thereafter, of:
 - i. The total number of cattle produced in the facility for each year, broken down by # of slaughtered steers/bullocks/bulls; # of slaughtered heifers and cows; and # of slaughtered calves/young cattle;
 - ii. The number, age and type of cattle arriving at the facility;
 - iii. The number, age and type of cattle having left the facility, due to death or other reason, prior to slaughter.
 - iv. Documentation of veterinary approval for each medically important antimicrobial administered, as well as its intent or purpose;
 - v. Age and number of cattle to which this medically important antimicrobial was administered (i.e., receiving this antimicrobial at least once).

- vi. Amount of active ingredient (in milligrams) of each medically important antimicrobial product used;
- c. Written treatment protocols including requirements for non-antimicrobial preventive measures, diagnosis and susceptibility testing for treatment of expected conditions.

LEVEL TWO

For recognition at Level Two, all Entry Level criteria must continue to be met.

In addition, medically important antimicrobials may not have been administered to more than one in every 4 cattle (25%) on all facilities enrolled by the producer under this standard. All cattle that have spent any time on the facilities covered under the standard shall count towards the total number of cattle in the calculation.

A facility previously certified at Level Two where a subsequent annual audit finds that greater than 25% of cattle have been administered at least one medically important antimicrobial over the previous year will be placed on probation. If the 25% threshold has not been met by the next annual audit, the facility will lose its Level Two certification.

LEVEL THREE

For recognition at Level Three, all Entry Level criteria must continue to be met.

For Level Three, the Entry Level documentation requirements (under paragraph 4b) apply to animal-only antimicrobials including ionophores and aminocoumarins, in addition to medically important antimicrobials.

In addition, over the previous 12 months antimicrobials of *any* class, including animal-only antimicrobials, may not have been administered to more than 5% of cattle from all facilities enrolled by the producer under this standard. Any cattle that have spent any time on the facilities covered under the standard shall count towards the total number of cattle in the calculation.

ASSURANCE OF CONFORMANCE

A third-party certifier will verify that the producer is in conformance with the above requirements. Auditors are:

- Independent;
- Allowed access to records documenting conformance with the standard;
- Expected to comply with biosecurity procedures at producers' facilities;
- Permitted to conduct spot checks of the premises and contents, including any testing deemed appropriate;

- Expected to conduct on-site audits of production facilities no less than once every 12 months;

RAISING ANIMALS UNDER DIFFERENT PRODUCTION SYSTEMS

Certified and non-certified facilities must be physically separated and cattle may not be co-mingled between them.

© 2019 Natural Resources Defense Council

TABLE 1: RESPONSIBLE ANTIMICROBIAL USE STANDARD – SUMMARY

	Entry Level	Level 2	Level 3
1. Level of production	Last 180 days of life prior to slaughter.		For lifespan
2. Antimicrobial administration is under veterinary supervision.	Yes. Veterinary supervision must include an antimicrobial stewardship plan (ASP), under which antimicrobials may not be used if a viable non-antimicrobial alternative exists.	<p>Same as Entry Level. But ≤ 25% of cattle have received medically important antimicrobials for any purpose.</p>	<p>Same as Entry Level. But ≤ 5% of cattle have received antimicrobials from any class for any purpose.</p>
3. Limited allowed uses of medically important antibiotics:	All require a veterinary prescription, or a veterinary feed directive (VFD).		
a. For disease treatment, and disease control	With certain specified limitations on the use of Critically Important Antimicrobials, and Highest-Priority Critically Important Antimicrobials (see text).		
b. For certain other limited, exceptional (non-routine) purposes:	Permitted when determined by the veterinarian to be necessary in the case of surgical or medical procedures, e.g. castration, dehorning, caesarian section.		
c. For growth promotion or disease prevention	Not permitted.		
4. Record-keeping	Records kept for all antimicrobials used, and total cattle produced under the standard. Total cattle should be delineated by # of slaughtered cows/bullocks/bulls, # of slaughtered heifers, and # of slaughtered calves/young cattle. Records must be maintained and updated no less than quarterly.		
5. Third party verification	Yes.		

TABLE 2: Approved Medically Important^a Antibiotics for U.S. Cattle Use, and By Delivery Route (Last Updated, 2017)

	Class	Antibiotic	Feed	Water	Injection	Intra-mammary	Topical	Other
Medically important								
	Aminoglycosides	Dihydrostreptomycin			X	X		
		Gentamicin					X	
		Neomycin	X	X			X	X
		Spectinomycin			X			X
	Amphenicols	Florfenicol			X			
	Cephalosporins	Ceftiofur				X		
	Fluoroquinolones	Danofloxacin			X			
		Enrofloxacin			X			
	Lincosamides	Pirlimycin				X		
	Macrolides	Gamithromycin			X			
		Tildipirosin			X			
		Tilmicosin	X		X			
		Tulathromycin			X			
		Tylosin	X					
	Penicillins	Amoxicillin			X			X
		Ampicillin			X			X
		Cloxacillin				X		
		Penicillin			X	X		
	Polymyxins	Polymyxin					X	
	Polypeptides	Bacitracin ^b	X					
	Streptogramins	Virginiamycin	X					
	Sulfonamides (Sulfas)	Sulfadimethoxine		X	X			X
		Sulfamethazine	X	X	X			X
	Tetracyclines	Chlortetracycline	X	X				X
		Oxytetracycline	X	X	X		X	X
		Tetracycline		X			X	X
Non-medically important								
	Aminocoumarins	Novobiocin				X		
	Ionophores	Laidlomycin	X					
		Lasalocid	X					
		Monensin	X					

^a This table is based on medical importance as determined by the World Health Organization, Critically Important Antimicrobials in Human Medicine: Ranking of Medically Important Antimicrobials for Risk Management of Antimicrobial Resistance Due to Non-human Use, 6th ed., 2019. <https://www.who.int/foodsafety/publications/antimicrobials-sixth/en/> (accessed September 24, 2019).

^b While the WHO list is updated frequently, the FDA operates according to a list of medically important drugs last updated in 2003, and which does not consider polypeptides like bacitracin to be important to human medicine.

TABLE 3: Critically Important Antimicrobials (*Designated as “Highest Priority Critically Important Antimicrobials”)

- Aminoglycosides
- Ansamycins
- Carbapenems and other penems
- Cephalosporins (3rd, 4th, 5th generation)*
- Glycopeptides*
- Glycylcyclines
- Lipopeptides
- Macrolides and Ketolides*
- Monobactams
- Oxazolidinones
- Penicillins (antipseudomonal, aminopenicillins, and aminopenicillin with beta-lactamase inhibitors)
- Polymyxins*
- Quinolones and Fluoroquinolones*
- Drugs used solely to treat tuberculosis or other mycobacterial diseases

Source: World Health Organization, Critically Important Antimicrobials in Human Medicine: Ranking of Medically Important Antimicrobials for Risk Management of Antimicrobial Resistance Due to Non-human Use, 6th ed., 2019. <https://www.who.int/foodsafety/publications/antimicrobials-sixth/en/> (accessed September 24, 2019).

REFERENCES

- ¹ World Health Organization, *Critically Important Antimicrobials in Human Medicine: Ranking of Medically Important Antimicrobials for Risk Management of Antimicrobial Resistance Due to Non-human Use*, 6th ed., 2019. <https://www.who.int/foodsafety/publications/antimicrobials-sixth/en/> (accessed September 24, 2019).
- ² World Organization for Animal Health (OIE). Press Release: Three new steps in the fight against antimicrobial resistance. May 25, 2018. Accessed at <http://www.oie.int/en/for-the-media/press-releases/detail/article/oie-general-session-three-new-steps-in-the-fight-against-antimicrobial-resistance/>
- ³ Medically important antimicrobials administered under a VFD are only lawful if issued in the context of a valid VCPR. See <http://www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/ucm460406.htm>. A valid VCPR is defined in federal code, at CFR 21, Subpart A, §530.3(i).
- ⁴ Non-antimicrobial approaches to reducing the need for antimicrobials, and their effectiveness in doing so, are described comprehensively in the following; EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (hereinafter RONAFA Report). [EMA/CVMP/570771/2015]. *EFSA Journal* 2017;15(1):4666, 245 pp. doi:10.2903/j.efsa.2017.4666; and Health and Food Safety Directorate-General, *Overview Report: Measures to Tackle Antimicrobial Resistance Through the Prudent Use of Antimicrobials in Animals* (hereinafter DG Health and Food Safety, Overview Report), Luxembourg: European Union, 2018, http://ec.europa.eu/food/audits-analysis/overview_reports/act_getPDF.cfm?PDF_ID=1190.
- ⁵ *Ibid*, page 3. As this important EU report clearly states, the ultimate goal is to reduce the need for antibiotics by preventing disease in the first place (i.e. ‘prevention is better than cure’). Animal diseases and infections should primarily be prevented by ensuring biosecurity, following good production and good management practices, and implementing integrated disease control programs to minimize the occurrence of diseases and eradicate endemic disease. The final outcome of this prudent/responsible approach to use of antibiotics in livestock production is an overall reduction in use, described by the motto ‘as little as possible, as much as necessary’.
- ⁶ Commission Notice, 2015 O.J. C 299/04 [hereinafter Guidelines for Prudent Use of Antimicrobials]. Official Journal of the European Union. http://ec.europa.eu/health/antimicrobial_resistance/docs/2015_prudent_use_guidelines_en.pdf. The standard’s language in this section reflect these 2015 guidelines.