Chapter 8. Synthetic Antibacterials

【Outline of synthetic antibacterials】

Antibacterial substance is one of feed additives to be used in order to promote beneficial use of nutrient components in feed. “Antibacterial substance” is a collective term of substances having antibacterial activity, which includes synthetic antibacterials (synthesized antibacterials specified as a feed additive are referred to as “synthetic antibacterial agents”), antibiotics as well as, fungicides such as propionic acid specified as antibacterial substances in Feed Safety Act. However, in general, this term is used as that including synthetic antibacterial agents and antibiotics permitted to use in order to increase the productivity by improving the growth and feed conversion and by disinfesting Coccidia and endoparasites, and those synthesized chemically are defined as synthetic antibacterials being discriminated from antibiotics which are made from microorganisms.

The standards based on Feed Safety Act specified that feeds never contain antibacterial substances other than those set down as feed additives.

Easy use of antibacterial substances can cause public health problems such as the residue in animal products and emergence of drug-resistant strains of bacteria even if they have been set down as feed additives; therefore, there are many items to keep in mind at the time of use to be strictly controlled in respective steps, manufacture, distribution and usage. The basic items which persons handling feed additives must know are as follows.

I Synthetic antibacterial agents and antibiotics available for respective animal species, types of feed, and additive amounts were specified individually; should not be used in other feed than specified.

II Synthetic antibacterial agents and antibiotics should not be used in feeds for cultured fish.

III Those capable and incapable of combination use of 2 types or more are specified, respectively.

IV Antibiotics are designated to the specific feed additive, which cannot be sold except for those with a special label describing that the article has approved by FAMIC or has manufactured in a facility licensed by the Minister of Agriculture, Forestry and Fisheries.

V Synthetic antibacterial agents and antibiotics cannot be used for animals other than indicated by description on the package.

VI Feeds containing synthetic antibacterial agent(s) and/or antibiotic(s) should not be supplied to milking cows, laying hens or quails, or domestic animals or chickens to be killed for edible use within 7 days.

Target animal types, usage levels and the like for each synthetic antibacterial agent were specified by Ministerial Ordinance Concerning Compositional Standards, and the specifications are sequentially canceled or added. As of November, 2009, a total of 6 articles (7 components) including amprolium ethopabate, amprolium ethopabate sulfaquinoxaline, morantel citrate, decoquinate, nicarbazin and halofujinon calcium polystyrene-sulfonate have been specified as the synthetic antibacterial agents.

As for canceled articles, some of them are still in distribution as animal drugs, and the analysis methods have been available in the Feed Analysis Standards because of possible use as feed additives.

Furthermore, this section also specifies the analytical methods of residual synthetic antibacterials in

animal feeds for articles possibly used abroad for domestic animals or cultured fish.

Standard preparations of synthetic antibacterial agents specified as feed additive are commercially available at Japan Scientific Feeds Association (TEL: 03-3297-5631, FAX: 03-3297-5633)

《Summary Table of analytical methods of synthetic antibacterials》

Analytical methods of synthetic antibacterials which currently listed in Feed Analysis Standards (FAS) are summarized in Tables 8-1 to 8-3.

Table 8-1 Summary Table of analytical methods of synthetic antibacterials

Name of synthetic antibacterial agent	Date of designation	Scope of application	Analytical method listed in FAS [Note]				Other mrthod
			Quantification to labeled amount			Micro-determination	
			LC method	Absorbance/fluorometry			
Amprolium	24/7/1976	Premix	1.1.1(1)	1.1.2(1)	Absorbance		
		Formula feed	1.1.1(2)	1.1.2(2)	Absorbance	1.2.1	
Ethopabate	24/7/1976	Premix	2.2.1(1)				
		Formula feed	2.2.1(2)			2.2.1	
Morantel citrate	15/10/1985	Premix	7.1.1(1)			7.2.1	
		Formula feed	7.1.1(2)			7.2.1	
Sulfaquinoxaline	24/7/1976	Premix	10.1.1(1)			10.2.1	Quantification (Absorbance)
		Formula feed	10.1.1(2)			10.2.1	
Decoquinate	24/7/1976	Premix	11.1.1(1)	11.1.2(1)	Fluorometry	11.2.1(1)	
		Formula feed	11.1.1(2)	11.1.2(2)	Fluorometry	11.2.1(2)	
Nicarbazin	24/7/1976	Premix	12.1.1(1)	12.1.2(1)	Absorbance		
		Formula feed	12.1.1(2)	12.1.2(2)	Absorbance	12.2.1	
Halofujinon calcium polystyrene-sulfonate	25/12/1987	Premix	13.1.1(1)				
		Formula feed	13.1.1(2)			13.2.1	Control assay (Absorbance)

Note: Figures indicate the listing no. (Feed Analysis Standards Chapter 8, Section 1)

Table 8-2 Summary Table of analytical methods of synthetic antibacterials cancelled from specification as a feed additive

Name of synthetic antibacterial agent	Date of cancel	Scope of application	Analytical method listed in FAS [Note 1]				Other method
			Quantification to added amount			Micro-determination	
			LC method	Absorbance/fluorometry			
Lobenidine hydrochloride	27/7/1981	Premix		3.1	Absorbance		
		Formula feed		3.1	Absorbance		
Oraquindox	7/3/2001	Premix	5.1.1(1)			5.2.1	
		Formula feed	5.1.1(2)			5.2.1	
Carbadox	27/7/1981	Premix		6.1	Absorbance		
		Formula feed		6.1	Absorbance		Quantification (LC method)
Clopidol	20/3/2002	Premix	8.1				
		Formula feed	8.1				
Dinitolmide	27/7/1981	Premix		9.1			
		Formula feed		9.1			
Furazolidone	Note 2	Formula feed	14.2				

Note 1: Figures indicate the listing no. (Feed Analysis Standards Chapter 8, Section 1).

Note 2: Cancelled from specification as a feed additive at the time of revision of Feed Safety Act, in1976, when feed additives became designation basis by Minister of Agriculture, Forestry and Fisheries.

See Paragraph 14, Section 1 in this Chapter.

Table 8-3 Summary Table of analytical methods of other synthetic antibacterials

Name of synthetic antibacterial agent	Scope of application	Listing no. in FAS		Reference
		LC method	LC-MS/MS method	
Oxolinic acid	Fish meal and formula feed	4.1		Simultaneous determination (Paragraph 2, Section 2)
Flumequine	Fish meal and formula feed	15.1		
Malachite green	Fish meal and formula feed		16.1	Simultaneous determination (Paragraph 2, Section 2)
	Fish oil		16.2	Simultaneous determination (Paragraph 3, Section 2)
Leucomalachite green	Fish meal and formula feed		17.1	Simultaneous determination (Paragraph 2, Section 2)
	Fish oil		17.2	Simultaneous determination (Paragraph 3, Section 2)