NEOMYCIN

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IDENTITY

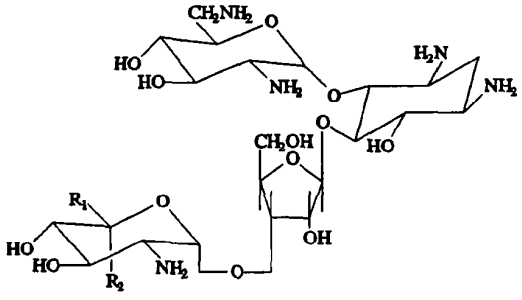
Chemical name: Neomycin sulfate

Classification: Aminoglycoside antibiotic

Chemical Abstracts Service Name: D-Streptamine, O-2,6-diamino-2,6-dideoxy-.alpha.-D-glucopyranosyl-(1→4)-O-[O-2,6-diamino-2,6-dideoxy-.beta.-L-idopyranosyl-(1→3)-.beta.-D-ribofuranosyl-(1→5)]-2-deoxy-, sulfate (1:1)(salt)

Chemical Abstracts Registry Number: 25389-98-4

Structural formula:



Neomycin B: R_1 = H and R_2 = CH_2NH_2
Neomycin C: R_1 = CH_2NH_2 and R_2 = H

Molecular formula: $C_{23}H_{46}N_6O_{13}H_2O_4S$

Molecular weight: 712.73

OTHER INFORMATION ON IDENTITY AND PROPERTIES

Pure active ingredient: Neomycin B Sulfate

BP and EP Specification:	Not less than 680 μg/mg
USP Specification:	Not less than 600 μ/mg
Agriculture grade:	571 μg/mg
Technical grade:	571 μg/mg

Impurities: BP and EP specifications:

Neomycin C:	3-15%
Neamine:	Not more than 2%

Appearance: White or off-white amorphous powder

Optical Rotation:	BP and EP Specifications:	+53.5 - +59.0°
pH:	BP and EP Specifications:	5.0 - 7.5
Solubility:	mg/mL at 28°C	
	Water	6.3
	Methanol	0.225
	Ethanol	0.095
	Isopropanol	0.082
	Isoamyl alcohol	0.247
	cyclohexane	0.08
	benzene	0.05

RESIDUES IN FOOD AND THEIR EVALUATION

CONDITIONS OF USE

General

Neomycin has been used for more than 40 years as a human therapeutic for bacterial gastro-intestinal infections. The sulfate salt of neomycin has been in constant use for over 35 years on a worldwide basis for combating bacterial gastro-intestinal infections in cattle, sheep, goats, swine and poultry. Neomycin sulfate is also used in intrammary infusions to treat mastitis. Various formulations include premixes, water soluble products and intrammary infusions. Its spectrum of activity includes many gram-negative and gram-positive organisms.

Dosages

A dose of 10 mg neomycin sulfate/kg body weight is equivalent to 7.0 mg neomycin base/kg body weight. The following dose ranges are expressed as neomycin sulfate.

Cattle:	10-22 mg/kg
Cows (Intramammary):	150 to 350 mg/infusion
Sheep:	10 mg/kg
Swine:	10-22 mg/kg
Poultry:	10-30 mg/kg (chickens, turkeys, ducks)

The duration of administration of neomycin sulfate is 3-7 days for poultry and up to 14 days for larger animals. Typical durations for dairy cows and swine are 5 and 10-14 days, respectively.

METABOLISM

Pharmacokinetics

Neomycin is poorly absorbed from the intestinal tract in man and animals (3 to 10%) and has low absorption from the udder. Absorbed neomycin collects in the kidney and, to a lesser extent, in the liver. It is not metabolized except by phosphorylation, adenylation, and acetylation in the digestive tract: absorbed neomycin remains as parent compound. Orally administered neomycin is excreted primarily in the feces (>90%). Absorbed neomycin is excreted via the kidneys by glomerular filtration. After intramammary administration, neomycin is "flushed" from the udder by milking (in the dry cow after freshening).

Rat

In studies with rats given ^{14}C-neomycin in their feed, biliary and urinary excretion of radioactivity were both very low (0.27 $\pm$ 0.01 and 0.83 $\pm$ 0.07%) of the ^{14}C in the dose, respectively, n = 3). This excretion data along with data on the ^{14}C-residues of tissues from calves indicates that urinary excretion is an approximation of the absorption of neomycin. (Aschbacher, 1994)

Cattle

Eleven calves of various ages were dosed with ^{14}C-labeled neomycin in a study to examine the influences of age, diet, and method of administration on the disposition of neomycin. All calves were killed 96 h after a single oral dose of approximately 30 mg/kg body weight. As indicated by urinary excretion, absorption of neomycin was greater in 3 day old calves (11.1%) than in 54- to 64-day old non-ruminating calves (1.5%) dosed similarly. Absorption of neomycin was similar in non ruminating (0.58%) and ruminating (2.13%) calves when the doses were administered in solution via a nippled bottle. In ruminating calves, absorption was somewhat less when the dose was administered on feed via a gelatin capsule (0.5%) than when given in solution via a nippled bottle (2.13%). Concerning the level of absorption of neomycin, this study indicates that the age of the calves is more important than whether the calves are ruminating or not. The concentrations of neomycin in muscle, liver and kidney are given in Table 1. (Aschbacher, 1994)

Table 1. ^{14}C Concentrations (expressed as equivalents of neomycin on a fresh tissue basis) in tissues 96 hours after oral dosing of calves with ^{14}C-neomycin

	Neomycin equivalent, μg/g		
Age at dosing, d	Kidney	Liver	Muscle
3 (n = 2)[a]	55.0 ± 14.9	1.93 ± 0.49	0.091 ± 0.007
12 (n = 1)[a]	24.0	0.67	0.044
54-64 (n = 3)[a]	4.9 ± 2.85	0.17 ± 0.06	0.016 ± 0.007
53-63 (n = 3)[ab]	7.4 ± 3.40	0.33 ± 0.11	0.064 ± 0.070
59-60 (n = 2)[bc]	0.77 ± .73	0.11 ± 0.08	0.024 ± 0.002

[a]Dose administered in solution via a nippled bottle.
[b]Calves had fully developed rumen at time of dosing.
[c]Dose administered on ground grain via a gelatin capsule.

Six ruminating dairy calves, approximately 30 months old, were given neomycin sulfate orally (overdosed at 96 mg/kg, b.i.d.) for fifteen and one half days. The mean absorption was small (0.45%) with a wide range (0.01-1.27%). (Pedersoli, 1994).

Poultry

Neomycin, in a single dose of 30 mg/kg body weight, was given in drinking water to fasted broilers. Blood level reached 2.02 μg/ml 30 minutes after medication. Two hours after, levels in 1 g or 1 ml of tissues were 32.77 μg in the small intestine wall, 8.35 μg in kidney, 2.12 μg in the lung, 1.36 μg in plasma, 0.66 μg in the liver and 0.49 μg in the heart. (Ibayashi, 1994).

Metabolism in Food and Laboratory Animals

Cattle

Greater than 90% of the radioactivity extracted from the kidneys of calves dosed with ^{14}C-neomycin was estimated to be in the form of neomycin. A bioassay of the kidney yielded a value of 30 μg/g as compared to the radio assay of 45 μg/g neomycin equivalents. This is good agreement considering that the extraction procedure of the bioassay may not have removed all of the neomycin. This study confirms the fact that neomycin is not metabolized (Aschbacher, 1994).

TISSUE RESIDUE DEPLETION STUDIES

Cattle

Twenty cattle (10 steers and 10 heifers) approximately 6 months of age were placed on a 14-day treatment of medicated water calculated to provide approximately 10 mg neomycin sulfate per pound body weight (22 mg/kg) daily. Two untreated, negative control cattle (1 steer, 1 heifer) were housed in a separate pen for the treatment phase. After the medication period, 4 treated cattle (2 of each gender) were killed for tissue collection and drug residue analyses at each withdrawal interval of 0 hours and at 1, 3, 7 and 14 days (only 3 cattle, however, were sampled on withdrawal day 7 due to a bloat mortality of a heifer midway through the treatment phase). Both unmedicated control cattle were also killed on the last medication day and their tissues assayed for neomycin. Tissues were assayed for neomycin residues by using a cylinder-plate microbiological method.

No neomycin was detected in tissues from the 2 unmedicated control cattle. Neither were neomycin residues found in the muscle, liver or kidney fat tissues of any of the medicated cattle at any sampling point. Neomycin residues were only found in the kidneys of treated cattle. Kidney neomycin concentrations were similar at zero and 24 hours withdrawal, at 0 hours withdrawal the mean level was 2.791 μg/g and it was 2.899 μg/g at 24 hours withdrawal. At 3 days withdrawal, the mean kidney neomycin level was 1.685 μg/g. By 7 days withdrawal, 2 of the 3 treated cattle that were sampled had detectable kidney neomycin residues below the 0.5 μg/g limit of quantification (LOQ) and 1 animal had a level of 0.62 μg/g. One of the 4 treated cattle sampled at 14 days withdrawal had residues below the 0.5 μg/g LOQ and the other 3 treated cattle sampled at 14 days withdrawal did not have detectable residues. Concentrations of neomycin in kidneys of cattle are shown in Table 2 (Ronning, 1993).

Table 2. **Kidney tissue neomycin residue levels (μg/g) in cattle, sheep, goats and swine.**

Withdrawal	Assayed neomycin levels (μg/g)			
Time, d	Cattle	Sheep	Goats	Swine
0 (12 h for	2.912		1.752	1.464
0 goats)	3.436		0.503	1.806
0	2.607		1.324	1.602
0	2.209		<0.5	3.824
Mean	**2.791**		**1.020**	**2.174**
1	2.209	0.537	1.891	1.338
1	2.536	0.707	1.165	<0.5
1	4.169	1.802	3.313	2.833
1	2.680	0.881	2.041	3.008
Mean	**2.899**	**0.982**	**2.103**	**1.920**
3 (2 day for	1.723	ND	1.891	<0.5
3 goats)	1.272	ND	0.556	1.084
3	1.924	0.522	2.203	1.651
3	1.821	<0.5	2.203	0.595
Mean	**1.685**		**1.713**	**0.958**
7 (3 day for	0.620	ND	<0.5	ND
7 goats)	<0.5	ND	1.542	<0.5
7	**	ND	0.516	0.991
7	<0.5	ND	1.843	<0.5
Mean			**1.100**	**0.498**
14 (4 day for	ND***	ND	ND	ND
14 goats)	ND	ND	1.000	ND
14	ND	ND	1.290	ND
14	<0.5	ND	0.503	0.906
Mean			**0.698**	**0.227**
21		ND		
21		ND		
21		ND		
21		ND		

*Values reported of <0.5 are for results that were below the analytical lower limit of quantification of 0.5 μg/g.
**No sample available, animal died.
***None Detected; i. e., no measurable zone of inhibition.

Six calves (3 bulls, 3 heifers) weighing 275-400 lbs, approximately 4 months old, received an oral dose of 41.8 mg neomycin sulfate (29.3 mg neomycin base)/kg body weight/day for 14 days. Two calves (1 bull, 1 heifer) served as controls. At 12 hours past the last treatment, all calves were euthanized and the kidneys collected for analysis.

Kidney samples were analyzed by microbiological assay using the method of Barbiers and Neff. Standards were prepared in extracts of control tissue because of what the sponsor described as a positive bias when neomycin was combined with tissue. At zero withdrawal, the mean concentration of neomycin in the kidney was 16.6 μg/g, range 10.5-21.0 μg/g (Stahl, et. al., 1989).

Six non-ruminating calves, 2-4 days of age and average weight 43 kg, were dosed with neomycin sulfate to give 18.6 mg neomycin base/kg/day for 14 days. The calves were sacrificed at 12 hours following the final dose, and the kidneys were collected for neomycin analysis. Neomycin was not detected in the kidneys of the control calves at detection limits of 0.27 μg/g, but in medicated calves, the average concentration was 71.1 μg/g (Fagerberg, 1988).

The kidneys of the calves in the above study were analyzed for neomycin by both microbiological assays and an HPLC assay. The average of the total neomycin (neomycin B plus C) by the HPLC method was 303 μg/g. Average neomycin levels of 161 and 400 μg/g were determined using both a buffer-based and a spiked-tissue-based standard curves, respectively. A second laboratory determined the neomycin levels in one of the animals to be 296 μg/g (Shaikh, et. al., in press).

Sixteen, 3 day old, non-ruminating Holstein bull calves were given a dose of 10 mg neomycin sulfate /lb (15.4 mg neomycin base/kg) body weight, added to a milk replacer. The dose was administered once daily for fourteen days. Groups of four calves each were slaughtered at 7, 14, 21, and 28 days after the last dose, and the kidneys assayed for neomycin by microbiological methods (Arnold, 1990).

Cattle - Dairy

Five Holstein cows were orally dosed with 15.4 mg neomycin base/kg body weight/day for four days. Milk samples were collected beginning with an initial sample taken before treatment through 18 milkings (12 hour intervals for 9 days). The limit of detection for the assay was 0.2 μg/g. Neomycin was not detected in any of the milk samples during the first 6 days of the study and the analysis was concluded at that point (Van Buren, 1986).

Sheep

Twenty sheep (10 wethers and 10 ewes) were placed on a 14-day treatment program of neomycin drench solution administration s.i.d to provide approximately 10 mg neomycin sulfate per pound body weight. Two untreated, negative control sheep (l wether, 1 ewe) were housed in a separate pen during the treatment phase.

After the medication period, 4 treated sheep (2 of each gender) were killed for tissue collection and drug residue analyses at each withdrawal interval of 1, 3, 7, 14 and 21 days. Just prior to the first withdrawal phase tissue collection from medicated sheep, tissues were collected from 2 unmedicated control sheep that were also included in the study. Collected tissues were assayed for neomycin residues using a cylinder-plate microbiological method.

Neomycin was not detected in any tissue from the 2 unmedicated control sheep. Neither was neomycin found in muscle, liver or fat tissues of any medicated sheep at any sampling point. Neomycin was found only in kidneys of treated sheep. All 4 sheep sampled at 24 hr withdrawal were positive for kidney neomycin residues, levels ranged from 0.537 to 1.802 μg/g and averaged 0.982 μg/g. Of tissues collected at 3 days withdrawal, only 1 of 4 animals sampled had a quantifiable kidney neomycin concentration (0.522 μg/g). Another 3-day withdrawal sheep had detectable (<0.5 μg/g) kidney residues, and the remaining two 3-day withdrawal sheep had no detectable residues. Kidneys collected at withdrawal days 7, 14 and 21 did not have detectable neomycin. Concentrations of neomycin in kidneys of sheep are shown in Table 2 (Ronning, 1994).

Goats

Twenty goats, 10 castrated males and 10 females, were treated 14 days with neomycin drench solution administered orally s.i.d to provide approximately 10 mg neomycin sulfate per pound body weight. Two untreated, negative control goats (1 of each gender) were housed in a separate pen during the treatment phase.

After the medication period, 4 treated goats (2 of each gender) were killed for tissue collection and drug residue analyses at each withdrawal interval of 12, 24, 48, 72 and 96 hours. Tissues were collected from both unmedicated control goats just prior to initial tissue collections from medicated goats. Collected tissues were assayed for neomycin residues using a cylinder-plate microbiological method.

Neomycin was not detected in any tissue from either of the 2 unmedicated control goats. Neither was neomycin found in muscle, liver or fat tissues of any medicated goats at any sampling point. Neomycin was found only in kidneys of treated goats; levels averaged approximately 1.0 μg/g at 12 h withdrawal, 2.1 μg/g at 24 h withdrawal, 1.7 μg/g at 48 h withdrawal, 1.1 μg/g at 72 h withdrawal and 0.7 μg/g at 96 h withdrawal. Concentrations of neomycin in kidneys of goats are shown in Table 2 (Ronning, 1994b).

Swine

Twenty pigs, ten barrows and ten gilts, were treated 14 consecutive days with medicated water calculated to provide approximately 10 mg of neomycin sulfate per pound of body weight daily. The 20 treated pigs were housed in 5 groups of 4 pigs each, with each group of pigs in an individual, raised crate located in a climate-controlled indoor facility. Similarly, the two untreated control pigs, one barrow and one gilt, were housed in the same building in an individual, raised crate.

At the conclusion of the medication period, four treated pigs (two of each gender) were euthanatized for tissue collection and drug residue analyses at each of the withdrawal intervals of 0 hours and at 1, 3, 7 and 14 days. Both unmedicated control pigs were also killed on the last medication day (withdrawal interval 0), and their tissues assayed for neomycin. Tissues were assayed for neomycin residues by using a cylinder-plate microbiological method.

No neomycin was detected in muscle, fat or liver tissues from any treated or control pig. For the kidney tissues of the two non-medicated control pigs, one pig had no detectable neomycin residues and one pig had an assayed neomycin level below the limit of quantification (<0.5 μg/g). Mean assayed kidney neomycin level at 0 hours withdrawal was 2.174 μg/g; and it was 1.920 at 24 hour withdrawal. At three days withdrawal the mean level was 0.958 μg/g. By seven days withdrawal, one pig had no detectable neomycin residue in kidney tissue, two pigs had <0.5 μg/g and one pig had 0.991 μg/g. At 14 days withdrawal, three of the four pigs had no detectable neomycin residues in kidney tissue while one pig was assayed as having 0.906 μg/g neomycin in its kidney tissue. Concentrations of neomycin in kidneys of swine are shown in Table 2 (Fagerberg, 1993).

Twenty-four (21 treated and 3 controls) swine of both sexes fed an average of 18.5 mg neomycin base/kg live weight/day for 14 days. Neomycin was not detected in liver, muscle, heart, or fat, at 0, 5, 8, 10, or 14 days withdrawal but was found to be 1.95 μg/g (mean, $n=3$) in kidney at zero withdrawal and 0.84 μg/g at eight days post treatment. The agar diffusion microbiological assay of Barbier et al. was used for analysis of tissues, although the limits of sensitivity were not mentioned (Barbiers, et. al., 1984).

Poultry

Residues of neomycin were studied by giving 10 mg or 30 mg/kg/day of neomycin to 4-week-old broilers for 7 days (detectable level: 0.05 μg (activity) per ml or g using a microbioassay method with *Staphylococcus epidermidis* as test organism). At 10 mg/kg/day, residues were detected in the kidney at day 10 after withdrawal. At 30 mg/kg/day, neomycin was detected in kidney and liver at days 13 and 3 after withdrawal, respectively (Ibayashi, 1994).

Broilers (150) were given feed containing 319 mg neomycin base per kg feed, which resulted in the animals receiving an average of 36.7 mg neomycin base/kg bird/day for seven days. Ten birds, five males and five females, were slaughtered on the last day of the treatment and on the five consecutive days following. Neomycin was not detected at any withdrawal time in liver or muscle at the sensitivity of the method which was 0.45 μg/g for muscle and 0.75 μg/g for liver (Strass, et. al., 1987a).

Hens (150) were fed 33.2 to 40.25 mg neomycin base/kg live weight/day. The animals were only dosed for five to seven days instead of twelve days as is recommended for residue studies in eggs. Eggs from 50 hens were sampled throughout the dosing period and at one day intervals for four days post treatment. Eggs from the other 100 birds were sampled before treatment and daily for 14 days withdrawal. Neomycin was not detected in any of the eggs at the detection limit of 0.45 μg/g. (Strauss, et. al, 1987b)

Turkeys

In this study, eight turkeys (4 of each sex) were gavaged with neomycin sulfate solution with a dose equivalent to 18.6 mg neomycin base/kg/day for 14 days. Two control birds of each sex were gavaged with sterile water for the duration of the study period. The animals were sacrificed at zero withdrawal, six hours past the last treatment, and livers from the controls and three each of the males and females were collected for assay. Neomycin was not detected in livers from the controls or in the female birds at the lower limit of quantification, 0.045 μg/g. In males, neomycin concentrations in liver were 0.16, 2.3, and 5.0 μg/g (George, 1988).

METHODS OF ANALYSIS FOR RESIDUES IN TISSUES

Neomycin has six cationic sites. The binding of neomycin to macromolcules is primarily ionic in nature. This binding can be disrupted by low pH and high concentrations of other cations. Analysis of neomycin in edible tissues requires extraction procedures that disrupt this binding to macromolcules.

Neomycin levels in all tissues can be determined by cylinder plate microbiological assay methods, using *Staphylococcus epidermidis* with reported limits of detection between 0.15 and 1.25 μg/g. The specificity of the microbiological assay for neomycin is increased due to the the high extraction temperatures and the length of the extraction. Many antibiotic, particulary the β-lactams are destroyed using the vigorous extraction conditions. However, other aminoglycosides may interfere with the analysis of neomycin (Barbiers, et. al., 1967) (Food and Drug Administration, USA, 1968) (Official Methods of Analysis, 1984).

Recent microbiological methods have released neomycin from macromolecules by extraction with 0.1N HCl plus 0.06M $CaCl_2$. Recovery from spiked tissue from four species has been reported to be 85-103% (Fagerberg, 1993; Ronning, 1993a, 1993b, 1994).

Neomycin in milk can be determined by a high performance liquid chromatograph (HPLC). Milk is passed directly through an Amberlite CG-50 ion exchange resin column, and the neomycin which is retained on the column is derivatized with ortho-phthalaldehyde. The derivatized neomycin is eluted from the column with potassium borate buffer/methanol and analyzed by HPLC. A HISEP HPLC column with flurorometric detection is used. The detection limit is 50 ng/g (Agarwal, 1990).

An HPLC method using an ion-pairing mobile phase, a reverse phase ODS column, post-column derivatization with o-phthalaldehyde reagent and fluorometric detection can measure residues of both neomycin B and C. The method is specific for neomycin and has a limit of detection of 0.10 μg/ml in plasma. The detector sensitivity was 3.5 ng of neomycin with a signal-to-noise ratio of 5 (Shaikh, et. al., 1985).

A screening method for the determination by HPLC in muscle of cattle, sheep and pigs and in muscle, liver, kidney and fat of veal calves uses a trichloroacetic acid/ethylene diamino tetraacetic acid method of extraction to break the ionic bonds. The limit of quantification for neomycin is 50 ng/g for muscle (Heitzman, R. J., 1994).

Changing the mobile phase of the above liquid chromatographic method eliminated variable retention times and frequent regeneration of the columns when analyzing for neomycin. The detection limit for kidney tissue was reported to be 0.5 μg/g. The method is specific because it distinguishes other aminoglycosides and antibiotics commonly used in food-producing animals. The method was used to determine neomycin in control samples of liver, muscle, milk, plasma and urine (Shaikh, 1993).

Residues of neomycin in bovine kidney can be determined and confirmed by HPLC/MS/MS. This method uses a matrix solid-phase dispersion method for tissue extraction. The method recovered 46% of the neomycin and had a limit of detection of 0.25 μg/g (McLaughlin, L. G., 1994).

APPRAISAL

Neomycin is poorly absorbed from the intestinal tract in man and animals (3% to 10%) and has low absorption from the udder. Absorbed neomycin accumulates in the kidney and, to a lesser extent, in the liver. It is not metabolized except by phosphorylation, adenylation, and acetylation in the digestive tract: absorbed neomycin remains as the parent compound. A ^{14}C-radiolabeled study in calves supports these conclusions except for very young animals (3-5 days of age). Orally administered neomycin is excreted primarily in the feces (>90%). Absorbed neomycin is excreted via the kidneys by glomerular filtration. After intramammary administration, neomycin is absorbed to a small extent in the lactating cow as evidenced by the neomycin found in the kidney for up to 14 days.

Numerous studies have been reported where neomycin was administered to farm animals at various dose levels and dosing times using primarily the oral route of administration. Those studies using the water soluble products are considered likely to result in the highest concentrations of residues in the edible tissues.

Tissue residue studies with neomycin have established parent neomycin as the marker residue and kidney to have the highest concentration of neomycin. The residues of neomycin in the kidney also persist the longest. This is true of all species tested. For all mammalian species, kidney was considered to be the target tissue. In poultry, kidney is considered inedible. Therefore, liver, the only other tissue with detectable residues of neomycin, is the target tissue for poultry.

At zero withdrawal periods, residue levels in the kidney of cattle, swine, chickens and turkeys were 2.8, 2.2, 8.4 and 5.0 mg/kg, respectively. At zero withdrawal the neomycin levels in milk (after oral administration) and eggs were both <0.2 mg/kg. The neomycin levels in kidney of sheep (one day withdrawal) and goats (12 hour withdrawal) were both 1.0 mg/kg. The kidney level in ducks at 14 days withdrawal was 0.89 mg/kg. The levels in milk from intramammary infusion of neomycin were 0.22 and 0.07 mg/l at 48 hours and 72 hours withdrawal, respectively. The residues in kidney after intramammary infusion at 14 days withdrawal were less than 5 mg/kg.

Adequate microbiological methods with a limits of quantification of 0.5 mg/kg in tissues and 0.2 mg/l in milk are available. HPLC and mass spectrometric methods are also available with limits of quantification of 0.1 mg/kg.

Maximum Residue Limits

Based on the residue studies and the temporary ADI of 0-30 μg/kg, temporary MRLs were established for parent neomycin in cattle, sheep, goats, pigs, chickens, turkeys and ducks:

Muscle	500 μg/kg
Liver	500 μg/kg
Kidney	5000 μg/kg
Fat	500 μg/kg
Eggs (Chicken)	500 μg/kg
Milk (Cattle)	500 μg/l

The ADI of 0-30 μg/kg BW permits a daily intake of 1800 μg of neomycin for a 60-kg person. Using the above temporary MRL values, the theoretical maximum daily intake is muscle (300 g) 150 μg; liver (100 g) 50 μg; kidney (50 g) 250 μg; fat (50 g) 25 μg; eggs (100 g) 50 μg; and milk (1.5 l) 750 μg. The total is 1275 μg per day.

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