FSANZ Risk Assessment

Oxytetracycline in Tasmanian Salmon and Wild Fish

Executive summary

The Tasmanian Public and Environmental Health Service (Department of Health and Human Services) contacted FSANZ to request a risk assessment for oxytetracycline (OTC) in farmed salmon in southern Tasmania. It has been noted that considerable quantities of the antibiotic are being used "off label" in the salmon industry to treat certain diseases in their fish. OTC is used within the salmon industry in Australia and many countries in the world as an antibiotic to treat bacterial diseases in salmon which occur during the warmer months of the year.

There is concern that these treated fish may escape and be caught by recreational fishers. Also wild fish surrounding the farm areas are known to consume the medicated food and may be caught recreationally. The Tasmanian Public and Environmental Health Service is concerned about the potential public health issues of consumption of these fish shortly after exposure, as they may not be fit for human consumption due to residual levels of OTC.

FSANZ has conducted a risk assessment of consumption of recreationally caught wild fish and escaped farmed fish following treatment with OTC. This risk assessment does not consider the commercial harvest of salmon, as salmon destined for sale must comply with the Australian New Zealand Food Standards Code temporary MRL of 0.2 mg/kg for OTC in salmonids.

The current acceptable daily intake (ADI) set for OTC for all Australians is 0.03 mg/kg bw/day established by the Therapeutic Goods Administration (TGA) in 2003 (Department of Health & Ageing 2006).

To assess any potential risk, a dietary exposure assessment was conducted based on analytical concentrations of OTC supplied by the Public and Environmental Health Service in Tasmania and food consumption data from the 1995 Australian National Nutrition Survey (NNS), and was calculated using the FSANZ dietary modelling program, DIAMOND. The Australian population 2 years and above and the subgroup, Australian children 2-6 years were assessed for baseline OTC dietary exposure and for two scenarios when Tasmanian fish were consumed; one including all foods with OTC permissions and one for consumers of Tasmanian fish only, with dietary exposure estimates then compared to the ADI.

The concentration of OTC in farmed salmon based on the data supplied from the Public and Environmental Health Service ranged from <0.01 mg/kg to 2.7 mg/kg with four not detected results. Wild fish species included mackerel with OTC concentrations from <0.002 mg/kg to 1.3 mg/kg. Due to results including composite samples of three fish, a conservative estimate of 3.9 mg/kg was used for the dietary exposure assessment to allow for a "worst case scenario" assessment. This assumed that all of the residue in the composite sample was from one fish. Similarly, for flathead samples where concentrations ranged from 0.01 mg/kg to 0.082 mg/kg, a worst case scenario estimate of 0.42 mg/kg concentration level was taken. The highest OTC concentrations were used in the dietary modelling for each fish assessed.

Australian's overall mean dietary exposure to OTC from all foods with OTC permissions at their current MRL limits (Baseline) was 5% of the ADI with high OTC consumers at 13% of their ADI. Children 2-6 years were also well below the ADI with mean dietary exposure for 95th percentile consumers of 27% of the ADI.

In the first scenario, Australians' dietary exposure estimates for OTC were based on consumers of the specified Tasmanian fish species and fish not identified as a specific type (as reported in the Australian 1995 NNS) plus consumers of all other foods with OTC permissions. The 'fish not specified' were included in the dietary exposure estimate with the higher OTC concentrations assigned to the Tasmanian fish to ensure a conservative estimate. The estimated mean dietary exposure to OTC for Australians 2 years and above from all foods (at MRL) and the specified fish at reported Tasmanian OTC concentrations was 5% of the ADI, and 17% of the ADI for 95th percentile OTC consumers. Australian children 2-6 years had higher OTC mean dietary exposure estimates than the general population of 14% of the ADI and 29% of the ADI for 95th percentile consumers of OTC.

In the second scenario, Australians' dietary exposure estimates for OTC were based on consumers of the specified Tasmanian fish species and fish not identified as a specific type only. Mean dietary exposure for all Australians was 15% of the ADI and 48% of the ADI for 95th percentile OTC consumers. For children 2-6 years the mean dietary exposures for fish consumers was 39% of the ADI and 145% of the ADI for 95th percentile OTC consumers. Only two out of 989 respondents in this age group exceeded the ADI, in these cases due to reported consumption of 'fish not specified'.

Based on the concentration data from Tasmania and the dietary exposure calculations conducted by FSANZ, it was estimated that 6 serves or more per week for any population group of salmon, mackerel and flathead may be consumed before exceeding the ADI, taking background dietary exposure from all other foods into account. This is based on the results for children 2-6 years where 8 serves of salmon, 6 serves of mackerel or 55 serves of flathead may be consumed per week before the ADI is exceeded (for serves per day, see Section 5), assuming a standard 150 gram serve size. For the whole Australian population 2 years and above, more fish can be consumed per week, such that 33 serves of salmon, 22 serves of mackerel or 212 serves of flathead may be consumed per week before the ADI is exceeded.

The findings of this risk assessment indicate that there are no public health risks associated with the consumption of Tasmanian farmed salmon and wild fish living in the waters surrounding their cages based on concentrations of OTC supplied by the Tasmanian Public and Environmental Health Service.

1. Background

The Public and Environmental Health Service in Tasmania requested FSANZ to conduct a risk assessment for oxytetracycline (OTC) in farmed salmon in southern Tasmania. OTC is used within the salmon industry as an antibiotic to treat bacterial diseases in salmon that occur during the warmer months of the year. It was noted that considerable quantities of the antibiotic are being used "off label". In 2005, approximately 4 tonnes of OTC was used to treat farmed salmon in Tasmania.

This has been raised as a concern due to the possibility of OTC entering the human food supply via a number of avenues including fish escaping from farms and wild fish swimming near farms where treatment is taking place and being caught and consumed by recreational fisherman soon after treatment. Furthermore, withholding times of fish after treatment may be insufficient and further work may be needed to determine an appropriate length of time prior to safe human consumption.

FSANZ was asked to advise on possible public health risks arising from the consumption of farmed salmon and wild fish (particularly flathead and mackerel) captured in a similar area to farms treating their salmon with OTC, as well as potential strategies for risk management and communication.

2. Hazard identification and characterisation

Tetracycline antibiotics are broad spectrum antimicrobial agents with applications in human therapy, animal husbandry, aquaculture and apiculture. Tetracyclines exert their bacteriostatic effect by disrupting protein synthesis and thus cell multiplication. They reversibly bind to 30S subunits of bacterial ribosomes, thus blocking attachment of aminoacyl-tRNA to the ribosome. The inhibitory effect is normally reversed when the drug is removed.

The tetracyclines oxytetracycline, chlortetracycline and tetracycline have similar microbiological activity and microorganisms that are resistant to one are often resistant to other members of this class.

The tetracyclines are incompletely absorbed from the human gastrointestinal tract, with approximately 60-80% of oxytetracycline being absorbed from an empty stomach. This incomplete absorption allows high concentrations to develop in the intestine, which perturb intestinal microflora by selecting for resistant strains; altering metabolic activity and allowing overgrowth of pathogenic, opportunistic or resistant microorganisms. This alteration in the balance of the microflora often has no identified deleterious effect. In general, the normal intestinal flora balance is restored within days of withdrawing treatment.

The therapeutic uses of tetracyclines are limited by their common side-effects including gastrointestinal irritation and superinfections. Gastrointestinal effects include nausea, vomiting and diarrhoea, attributed to irritation of the mucosa. Tetracyclines inhibit the growth of faecal coliforms, which can lead to overgrowth of tetracycline-resistant organisms, particularly yeasts and the enterococci *Proteus* and *Psuedomonas*. The most clinically important superinfection that can occur as a result of tetracycline therapy is that of

Clostridium difficile, which can lead to antibiotic-induced diarrhoea and pseudomembranous colitis due to production of a cytotoxic toxin (WHO, 1999).

Long term therapy may produce changes in the blood, including leukocytosis, atypical lymphocytes and toxic granulation of granulocytes, as well as liver injury. Prolonged exposure can discolour the teeth of children and of infants of mothers treated with OTC during pregnancy. OTC can also depress bone growth in foetuses and children, although this effect is readily reversed when exposure is of short duration.

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) re-evaluated the safety of tetracyclines at its 50th meeting in 1998 (WHO, 1999). The Committee concluded that the selection of resistant bacterial strains in human intestinal microflora is the most sensitive end-point for evaluating the effect of tetracyclines. The Committee established an acceptable daily intake (ADI) of 0 - 0.03 mg/kg bw for oxytetracycline, tetracycline and chlortetracycline, separately or in combination, because of their similar antimicrobial activity (WHO, 1999).

The Committee had previously noted (at its 54th meeting in 1995) that the lowest NOEL for toxicological effects was 100 mg/kg bw/day for chlortetracycline in dogs (WHO, 1996). Thus, the ADI appears to provide an adequate margin of safety when compared with the lowest NOEL for toxicological effects.

The current ADI set for OTC for all Australians is 0.03 mg/kg bw/day established by the Therapeutic Goods Administration (TGA) in 2003 (Department of Health & Ageing 2006). This ADI was used for this dietary exposure assessment.

The TGA has not set an acute reference dose (ARfD) for OTC and there are no established short term toxicity issues.

3. Dietary exposure assessment

A dietary exposure assessment was conducted by FSANZ in the following ways:

- Baseline - an estimate of the dietary exposure for the general population as a result of eating foods permitted to contain OTC based on their current MRLs in the Code (see Section 4.1)[1];
- All foods including Tasmanian seafood (scenario 1)- an estimate of the dietary exposure for the general population as a result of eating foods permitted to contain OTC based on their current MRLs in the Code (see Section 4.2) apart from specified fish where the reported concentrations from Tasmania were used; and
- Tasmanian seafood only (scenario 2)- an estimate of the dietary exposure for consumers of salmon, flathead and mackerel and 'fish not specified as to type' only based on the levels of OTC reported in these species in Tasmania (see Section 4.3).

Each dietary exposure assessment was conducted for the Australian population 2 years and above and for Australian children 2-6 years. Children 2-6 years were included in this

[1] This is likely to overestimate baseline exposure as the 20th Australian Total Diet Survey (FSANZ 2003) included tests for OTC in a range of meats, dairy products, eggs, offal meat and infant formula and OTC was not detected in any of these foods.

assessment as a separate subgroup as a precautionary measure to determine their overall exposure to OTC and are also included in the overall Australian population estimate.

The FSANZ dietary modelling computer program, DIAMOND, was used for the exposure assessment calculations. The estimated dietary exposure was calculated for each individual to get an exposure distribution for the population. Summary statistics such as mean and 95th percentile exposures from the population groups assessed were then derived. Results were reported as mg/d, mg/kg bw/d and as %ADI.

Calculations were also conducted to determine how much of each type of fish could be consumed before the ADI is exceeded based on the OTC concentrations determined in Tasmania, taking account of the background dietary exposure from all foods other than fish.

3.1 Concentration data

3.1.1 Maximum residue limits in the Food Standards Code

FSANZ, and the Australian Pesticides and Veterinary Medicines Authority (APVMA), have allocated OTC a temporary MRL of 0.2 mg/kg for all salmonids. Salmonids were assumed to be salmon and trout for the purpose of this assessment. This value was used in this assessment.

The foods with MRLs included in the exposure assessment included honey, kidney and liver (cattle, goats, pigs and sheep), mammalian meat, milks, offal of poultry, poultry meat and salmonids (salmon and trout) (see Table 1). Mammalian fat and poultry fat were included in this assessment as a conservative measure and were allocated the current MRL for mammalian meat and poultry meat of 0.1 mg/kg bw/day.

Table 1. Current MRL permissions as stated in Australia New Zealand Food Standards Code

OXYTETRACYCLINE INHIBITORY SUBSTANCE, IDENTIFIED AS OXYTETRACYCLINE	MRL (MG/KG)
HONEY	T0.3
KIDNEY OF CATTLE, GOATS, PIGS AND SHEEP	0.6
LIVER OF CATTLE, GOATS, PIGS AND SHEEP	0.3
MEAT (MAMMALIAN)	0.1
MILKS	0.1
POULTRY, EDIBLE OFFAL OF	0.6
POULTRY MEAT	0.1
SALMONIDS	T*0.2

T – refers to a temporary MRL.
* - The MRL is at the limit of quantification for the analytical method.

3.1.2 Concentration of OTC in Tasmanian fish

Sixteen samples of farmed salmon were collected for analysis. One sample of pooled flesh and two samples of pooled serum were also used for analysis totalling 19 samples. All salmon samples were collected from marine farm cages in south eastern Tasmania and analysed either 10 to 15 days post treatment or 70 days post treatment. The concentration range of OTC in farmed salmon was < 0.01 mg/kg to 2.7 mg/kg with a median value of 0.25 mg/kg. Four samples showed a not detect (nd) result. The highest concentration reported in farmed salmon was 2.7 mg/kg which used for the exposure assessment as a conservative measure. As this figure is for pooled serum rather than flesh, it is likely to be an overestimate of the concentration in salmon as consumed.

Slimy mackerel and flathead were the two species of wild fish captured for analysis from a close vicinity to salmon farm cages. Fifteen samples of slimy mackerel were assessed, with nine fish being pooled samples (three pooled samples of three fish) and six individual samples. The concentration range of OTC found in slimy mackerel was <0.002 mg/kg to 1.3 mg/kg with a median value of 0.34 mg/kg. Due to the composite samples being assessed, a conservative estimate of 3.9 mg/kg was used to allow for any fluctuations in concentrations among fish in the sample. This was calculated based on a maximum concentration of 1.3 mg/kg in a composite sample of three, assuming one fish contained all of the chemical (1.3 x 3 = 3.9 mg/kg).

Twenty nine samples of flathead were assessed for concentrations of OTC, comprising of one individual sample of flathead and seven pooled samples of four fish per sample. Four samples returned a not detect result. OTC concentrations ranged from 0.01 mg/kg to 0.082 mg/kg with a median value of 0.03 mg/kg. A worst case scenario was also assumed for composite samples of flathead. The highest concentration of OTC in flathead reported by the Public and Environmental Health Service, 0.42 mg/kg, was used for the dietary exposure assessment.

All data and worst case scenarios for individual fish samples are shown in Table 2.

Table 2. OTC concentrations in Tasmanian salmon and wild fish (mackerel and flathead)

	Sample Time	Sample Type	Location	Result mg/kg
Farmed Salmon	Immediately post treatment	Medicated fish and controls	Medicated cage at Tassal Bruny MF	
	t = ?	Pooled Flesh from untreated fish		nd
	Day 10	Pooled Serum		**2.7**
	Day 15	Sample 1		0.3
	Day 15	Sample 2		nd
	Day 15	Sample 3		0.72
	Day 15	Sample 4		nd
	Day 15	Sample 5		0.3
Farmed Salmon	Immediately post treatment	Medicated fish and controls	Medicated Cage at Flathead Bay MF	
	Day 10	Pooled Serum		1.4
	Day 15	Sample 1		0.091
	Day 15	Sample 2		0.25
	Day 15	Sample 3		0.31
	Day 15	Sample 4		nd
	Day 15	Sample 5		0.3
Farmed Salmon	70 days post treatment	Samples of fish flesh from medicated cage	Tassal Cage (unknown location)	
		Sample 1		< 0.01
		Sample 2		0.08
		Sample 3		0.04
		Sample 4		0.03
		Sample 5		0.02
		Sample 6		0.04
Wild Fish	1 day post treatment	Pooled Fish Samples	Roberts Point MF	
		Sample 1 Slimy Mackerel (n = 3)	Inside Cage	1.2 (3.6)*
		Sample 2 Slimy Mackerel (n = 3)	Inside Cage	1.3 (**3.9**)*
		Sample 3 Slimy Mackerel (n = 3)	Outside Cage	0.55
		Sample 4 Flathead (n = 4)	Outside Cage	nd
		Sample 5 Flathead (n = 4)	Outside Cage	0.014 (**0.42**)*
		Sample 6 Flathead (n = 4)	Outside Cage	nd
		Sample 7 Flathead (n = 4)	Outside Cage	nd
		Sample 8 Flathead (n = 4)	Outside Cage	0.01 (0.04)*
		Sample 9 Flathead (n = 4)	Outside Cage	0.082 (0.33)*
		Sample 10 Flathead (n = 4)	Outside Cage	nd
Wild Fish	5 weeks post treatment	Individual Fish Samples	Roberts Point MF (unspecified location)	
		Sample 1		0.002
		Sample 2		0.002
		Sample 3		0.002
		Sample 4		0.19
		Sample 5		0.34
		Sample 6		0.44
		Sample 7		0.046

* Shows the worst case scenario for each pooled sample.
nd – not detected.
Bolded concentrations were used for the dietary exposure assessment.
Samples in brackets represent where the analytical result of the composite has been multiplied by the number of individual samples in the composite.

3.2 Food consumption data

DIAMOND contains dietary survey data for Australia from the 1995 Australian National Nutrition Survey (NNS) that surveyed 13 858 people aged 2 years and above. The NNS used a 24-hour food recall methodology.

Estimated exposures to salmon and wild fish were based on a single 24-hour recall for all Australian survey respondents. The individual dietary records for each respondent were used for exposure calculations.

The NNS data used for the dietary exposure assessments from 1995 is currently the best, most comprehensive data available on an individual record basis. Therefore, conducting dietary exposure assessments based on these data provides the best estimate of actual consumption of a food and the resulting estimated dietary exposure to a food chemical. However, it should be noted that limitations exist within the NNS data. These limitations relate to the age of the data and the changes in eating patterns that may have occurred since the data were collected. Generally, consumption of staple foods such as fruit, vegetables, meat, dairy products and cereal products, which make up the majority of most people's diet, is unlikely to have changed markedly since the NNS was conducted (Cook, Rutishauser, and Allsopp, 2001; Cook, Rutishauser, and Seelig, 2001). However, there is an increasing level of uncertainty associated with the consumption of other foods where these may have changed in consumption since 1995, or where new foods on the market were not available in 1995.

According to the 1995 Australian NNS, 1.7% (230 consumers from 13858 surveyed) of people consumed salmon, with a mean consumption of salmon in Australia of 99 g/day with 95th percentile consumers having 285 g/day.

Ten consumers (0.1%) had a mean consumption of flathead at 142 g/day with 95th percentile consumption at 541 g/day. A similar amount of people consumed mackerel (9 people, 0.1%), however, at a slightly lower amount of 116 g/day and 95th percentile at 257 g/day.

Fish which was unspecified as to type (i.e. the NNS respondent was not sure of what specific type of fish they consumed) was included in the dietary exposure estimate as a conservative measure for this estimate. Consumption for fish not further specified was 73 g/day and 95th percentile at 233 g/day with 568 (4.1%) consumers.

The frequency of consumption of various foods was also collected by NNS respondents 12 years and over via a Food Frequency Questionnaire (FFQ). Generally, fish is considered an 'occasionally consumed' food as <25% population consumed more than once a week. Twenty three percent of those surveyed consumed canned tuna, salmon or sardines at least once a week, 23% consumed steamed, baked or grilled fish at least once a week and fried fish was consumed by 14% respondents at least once a week.

3.3 Assumptions

The aim of the dietary exposure assessment was to make as realistic an estimate of dietary exposure as possible. However, where significant uncertainties in the data existed, conservative assumptions were generally used to ensure that the dietary exposure assessment did not underestimate exposure.

The assumptions made in the dietary modelling are listed below:

- OTC was present in the fat of meat and therefore allocated a concentration equivalent to the MRL of 0.1 mg/kg which was assigned to meat (mammalian) and poultry meat;
- where a food or food group has a zero concentration of OTC, it was not included in the exposure assessment;
- where a food was not included in the exposure assessment, it was assumed to contain a zero concentration of OTC;
- consumption of foods as recorded in the NNS represent current food consumption patterns;
- where a food has a specified OTC concentration, this concentration is carried over to mixed foods where the food has been used as an ingredient e.g. salmon with pasta in white sauce;
- there are no reductions in OTC concentrations from food preparation or due to cooking;
- the consumption of fish, in particular salmon, mackerel and flathead has not changed since the Australian 1995 NNS was conducted;
- salmon, mackerel and flathead consumed and reported on were from Tasmania;
- fish that weren't identified as a specific type in the Australian NNS were included in the dietary exposure assessment for Tasmanian salmon and wild fish (see Section 4.3) and were given the highest concentration to assume a worst case scenario; and
- OTC concentration data provided are all treated as concentrations in flesh, although the highest value for treated salmon is from pooled serum.

These assumptions are likely to lead to a conservative estimate for OTC dietary exposure.

4. Dietary exposure results

4.1 Estimated dietary exposure from all foods permitted to contain OTC at the MRL (Baseline)

The estimated baseline dietary exposures to OTC are shown in Table 3.

The estimated mean dietary exposure to OTC from all foods with OTC MRL permissions for the Australian population 2 years and above was 0.0014 mg/kg bw/day. The estimated 95th percentile exposure for this group was 0.0040 mg/kg bw/day.

The estimated mean dietary exposure to OTC for all foods with permissions for children aged 2-6 years in the Australian population was 0.0038 mg/kg bw/day with 95th percentile exposure to OTC at 0.0081 mg/kg bw/day.

Table 3. Estimated dietary exposure to OTC from all foods with MRL permissions for the Australian population 2 years and above and 2-6 years (Baseline)

OTC exposure	2 Years & Above All Foods with MRL Permission* (mg/kg bw/day)	2-6 Years All Foods with MRL Permission* (mg/kg bw/day)
Mean	0.0014	0.0038
95th Percentile	0.0040	0.0081

* consumers of foods assumed to contain OTC only.

4.2 Estimated dietary exposure from all foods permitted to contain OTC at the MRL except specific fish, with reported Tasmanian OTC concentrations (scenario 1)

The dietary exposure estimate from all foods permitted to contain OTC with salmon, mackerel, flathead and 'fish not specified' included with concentrations from Tasmanian data (Table 4), was slightly higher than baseline estimates. Estimated mean exposures for the population 2 years and above were 0.0016 mg/kg bw/day with 95th percentile consumption at 0.0051 mg/kg bw/day.

Children's mean exposure to OTC from all foods with OTC permissions including salmon, mackerel, flathead and 'fish not specified' at Tasmanian OTC concentrations was estimated to be 0.0041 mg/kg bw/day and for 95th percentile OTC consumers 0.0087 mg/kg bw/day.

Table 4. Estimated dietary exposure to OTC from all foods with MRL permissions including Tasmanian fish data

OTC Exposure	2 Years & Above All Foods with MRL Permission* (mg/kg bw/day)	2-6 Years All Foods with MRL Permission* (mg/kg bw/day)
Mean	0.0016	0.0041
95th Percentile	0.0051	0.0087

* consumers of foods assumed to contain OTC only.

4.3 Estimated dietary exposure from Tasmanian salmon and wild fish only (scenario 2)

When the exposure assessment was conducted for consumers of salmon, mackerel, flathead and 'fish not specified' only using the Tasmanian concentration data, the estimated mean dietary exposure for the Australian population 2 years and above was 0.0045 mg/kg bw/day. The estimated 95th percentile OTC exposure was 0.0143 mg/kg bw/day.

Children 2-6 years had a higher mean exposure of 0.0113 mg/kg bw/day which is to be expected as children consume more food per kilogram of body weight compared to adults. The 95th percentile exposure for consumers of OTC was 0.0435 mg/kg bw/day.

The estimated dietary exposures for Tasmanian fish only are shown in Table 5.

Table 5. Estimated dietary exposure to OTC from salmon and wild fish only*

OTC Exposure	All Australians 2 Years & Above (mg/kg bw/day)	Australians 2-6 Years (mg/kg bw/day)
Mean	0.0045	0.0113
95th Percentile	0.0143	0.0435

* 'fish not specified' were also included in the dietary exposure estimate and assigned the highest OTC concentration for Tasmanian fish.

5. Risk characterisation

The estimated daily exposures to OTC for the Australian population 2 years and above and 2-6 years were calculated as a percentage of the ADI of 0.03 mg/kg bw/day, in order to determine whether the exposures posed a risk to public health and safety. The total number of people surveyed for the Australian 1995 NNS was 13 858, the total numbers of consumers for each scenario are also reported here.

5.1 Dietary exposure as a percent of the ADI from all foods at MRLs (Baseline)

The baseline dietary exposure for all Australians 2 years and above included 13 810 consumers of OTC. Mean dietary exposure for this group was 5% of the ADI. The 95th percentile exposure was also well below the ADI at 13%.

Children 2-6 years baseline exposure to OTC from all foods was estimated at 13% of the ADI with 95th percentile exposure at 27% of the ADI. There were 987 consumers of OTC in this scenario for this age group.

5.2 Dietary exposure as a percent of the ADI from all foods at MRL with fish assigned Tasmanian concentration data (scenario 1)

The estimated mean daily exposure from all foods with MRL permissions and salmon, mackerel, flathead and 'fish not specified' with reported Tasmanian concentrations for consumers of OTC 2 years and above was 5% of the ADI and 17% of the ADI at the 95th percentile dietary exposure. There were 13 816 consumers of OTC in this scenario.

Australian children 2-6 years had estimated mean dietary exposures at 14% of the ADI for OTC and 29% of the ADI for 95th percentile exposures to OTC. There were 988 consumers of OTC in this scenario.

5.3 Dietary exposure as a percent of the ADI for Tasmanian salmon and wild fish only (scenario 2)

The estimated dietary exposure to OTC for the Australian population 2 years and above from the consumption of Tasmanian salmon, mackerel, flathead and 'fish not specified' only was 15% of the ADI. Estimated exposures at the 95th percentile were 48% of the ADI. There were 804 consumers of OTC in this scenario.

Australian children 2-6 years had higher dietary exposure estimates compared to the general population. Mean dietary exposure from Tasmanian fish species only was 38% of the ADI and the 95th percentile exposure to OTC was 145% of the ADI.

The dietary exposure assessment for Australian 2-6 year olds reported that 26 children (from 989 respondents in this age group) had consumed fish. Of these 26 children, 2 were estimated to have dietary exposures that exceeded the ADI (7.7% of fish consumers), in these cases due to reported consumption of 'fish not specified'.

5.4 Estimation of maximum exposure before ADI exceeded

Further calculations were done to estimate the number of serves of Tasmanian fish that could be consumed, based on the concentration data provided, before the ADI would be exceeded, taking account of background exposure from all other foods. This information assists in characterising the risk of consuming Tasmanian fish treated with OTC.

5.4.1 Background exposure from all foods apart from fish

The following estimations of background exposure from all foods apart from fish were used as the basis for all calculations following in this section.

5.4.1.1 Background exposure for Australians 2 years and above

The background dietary exposure to OTC was estimated by FSANZ by hand and included all foods with current MRL permissions except for fish.

The background exposure to OTC from food was 0.0014 mg/kg bw/day as determined from all non-seafood food sources at the MRL. Therefore, an individual can consume a quantity of fish equivalent to an OTC exposure of 0.0286 mg/kg bw/day before the ADI of 0.03 mg/kg bw is exceeded (i.e. 0.03 – 0.0014 = 0.0286). For an individual with a mean body weight of 67 kg (as derived from the 1995 NNS aged 2 years and above), this equates to an OTC exposure of 1.9 mg/day.

5.4.1.2 Background exposure for Australian Children 2-6 years

The background exposure to OTC from food was 0.0038 mg/kg bw/day as determined from all non-seafood food sources at the MRL. Therefore, an individual child can consume a quantity of fish equivalent to an OTC exposure of 0.0262 mg/kg bw/day before the ADI of 0.03 mg/kg bw is exceeded (i.e. 0.03 – 0.0038 = 0.0262). For an individual with a mean body weight of 19 kg (as derived from the 1995 NNS aged 2-6 years), this equates to an OTC exposure of 0.5 mg/day.

5.5 Estimation of the maximum amount of salmon and wild fish that can be consumed before exceeding the ADI

The following calculations are for the Australian population 2 years and above and Australian children 2-6 years. The number of serves is calculated based on the following equation:

The estimated dietary exposure must be below the ADI such that:

$$\text{ADI} - \text{background exposure} > \frac{\text{food consumption x chemical concentration}}{\text{mean body weight}}$$

The equation needs to be re-arranged to estimate the consumption amount:

$$\text{Food consumption kg/d} < \frac{(\text{ADI mg/kg bw/d} - \text{background exposure mg/kg bw/d}) \text{ x kg bw}}{\text{concentration mg/kg}}$$

The estimated consumption amounts are then expressed as a number of 150 gram serves of fish per week.

Results for these calculations can be found in Table 5 for the Australian population aged 2 years and above and Table 6 for children aged 2-6 years.

5.5.1 Salmon

Based on a maximum concentration of OTC of 2.7 mg/kg for farmed salmon, Australians 2 years and above may consume 710 grams of Tasmanian fish per day before the ADI is exceeded.

Children 2-6 years may consume 185 grams of Tasmanian fish per day before the ADI is exceeded.

5.5.2 Wild Fish

Two species of wild fish were sampled in the waters surrounding the salmon farms and assessed for OTC concentrations.

5.5.2.1 Mackerel

Based on a maximum OTC concentration of 3.9 mg/kg for wild mackerel, Australians 2 years and above may consume 490 g/day before the ADI is exceeded. Children 2-6 years may consume 130 g/day before they will exceed the ADI.

5.5.2.2 Flathead

Based on a maximum concentration of OTC of 0.42 mg/kg for wild flathead, an individual may consume 4560 g/day or 4.6 kg/day before the ADI is exceeded. Children 2-6 years may consume 1185 g/day or 1.2 kg/day before they will exceed the ADI.

5.5.3 Amount of Tasmanian fish containing OTC that can be consumed per week

The amount of Tasmanian fish containing OTC per day that can be consumed before the ADI is exceeded has been converted to standard serve sizes, assuming 150 g fish/serve.

Table 5. Estimated amount of fish that can be consumed by the Australian population 2 years and above before the ADI is exceeded

		OTC Concentration mg/kg	Amount Of Fish Per Day Before ADI# Exceeded (grams)	Serves of Fish Per Week*
Salmon		2.7	710	33
Wild Fish	**Mackerel**	3.9	490	22
	Flathead	0.42	4560	212

* Based on a standard serve of 150 grams.
# ADI of 0.03 mg/kg bw/day.

Table 6. Estimated amount of fish that can be consumed by Australian children 2-6 years before the ADI is exceeded

		OTC Concentration mg/kg	Amount of Fish Per Day Before ADI# Exceeded (grams)	Serves of Fish Per Week*
Salmon		2.7	185	8
Wild Fish	**Mackerel**	3.9	130	6
	Flathead	0.42	1185	55

* Based on a standard serve of 150 grams.
# ADI of 0.03 mg/kg bw/day.

Based on the estimated number of serves that can be consumed per week of Tasmanian fish, any population group can have six standard serves or more per week. Based on the food frequency data collected in the NNS, this is likely to be more than the majority of the population would be consuming in reality.

6. Conclusion

On the whole, the findings of this risk assessment indicate that the consumption of Tasmanian farmed salmon and wild fish living in the waters surrounding their cages does not raise health concerns for any Australian population groups. The current treatment procedures using OTC as a measure to control bacterial diseases among farmed fish are shown to be at a level which is safe for recreational fisherman eating their own catch to consume.

Overall dietary exposures do not exceed the ADI for all scenarios assessed with the exception of children 2-6 years at 95th percentile OTC dietary exposure. This exceedance of the ADI was due to the inclusion of "fish, not specified" in FSANZ's exposure assessment as a precautionary measure to ensure a conservative estimate. It is considered that children in the 2-6 year age bracket will not consume this larger amount of fish everyday, as a result FSANZ has not identified this as a public health risk. In addition, the ADI is the amount which is estimated can be safely consumed daily over a lifetime. As the ADI for oxytetracycline is based on a very sensitive measure of changes in gut microflora, and as it is known that these effects usually reverse quickly (WHO 1999), a short term exceedance of the ADI is not expected to have a negative impact on health.

All scenarios assessed showed that any population group can have six standard serves or more per week before the ADI for OTC is likely to be exceeded, based on results for children. The Australian population as a whole, 2 years and above can consume 33 standard (150 gram) serves per week before the ADI is exceeded. This equates to approximately 4.5 150 gram serves per day. It is unlikely that it would an individual would consume this amount on a daily basis.

There are a number of limitations in this risk assessment which impact on the degree of confidence that can be placed on the dietary exposure assessment. The assumptions made are described in Section 3.3. In addition, the data provided are for salmon 10, 15 and 70 days post treatment and no data have been provided on OTC levels in salmon immediately after treatment. No information has been provided about frequency of OTC treatments to indicate whether the concentrations measured follow a single bolus or may represent steady state concentrations. It is possible that fish caught recreationally immediately after OTC treatment may have higher levels of OTC.

Based on the sample times and OTC concentrations supplied for this risk assessment, it appears that consumption of fish at the concentrations reported does not raise public health concerns, even if it is assumed that the highest concentration of OTC reported in farmed salmon or wild fish post treatment is consumed. However, the OTC fish concentration data provided illustrate that OTC concentrations decreased as time post treatment increased indicating that a longer withholding period is preferred.

7. Potential impact of OTC in sediment and water discharge

The Tasmanian Public and Environmental Health Service also sought advice from FSANZ on the possible public health risks resulting from OTC in sediment below farm cages and in water discharged from commercial hatcheries. Some data was provided on OTC concentrations in sediment indicating that OTC is present as an environmental contaminant in sediment below and up to 500 metres from farm cages. It is possible that this OTC may enter the food chain. There are reports of detectable levels of OTC in mussels, crabs and other scavengers around fish farms following use of medicated feed (Coyne et al, 2001).

As there are so many unknowns and site-specific influences, such as water flows, site geography, sediment quality and the range of aquatic species present, an assessment of the risks from this route of OTC exposure was not possible.

Research elsewhere indicates that the concentrations of OTC in the sediments under farm cages is highly variable (Coyne et al, 2001). High OTC concentrations have been associated with significant accumulation of medicated feed due to over-supply. The persistence of OTC in sediment also varies widely, with reports of half-lives ranging from 9 to 419 days (Coyne et al, 2001). Persistence of OTC in sediment has been associated with significant accumulation of organic deposits resulting in anoxic sediment. This indicates that concentration and persistence of OTC in sediment can be impacted by husbandry practices that influence sediment quality.

8. References

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