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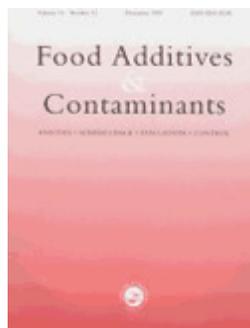
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**Modelling consumer exposures to nutrients and additives in animal products.**

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**Abstract**

Current guidelines for assessing human exposures to nutrients and other substances used in animal feed are based on methods used for veterinary pharmaceuticals. These methods assume high level daily consumption of animal products and do not take account of differences between species or between consuming humans. A more detailed dietary modelling approach is described, which takes these factors into account as well as high level consumption by different age groups. The proposed approach is evaluated in three case studies, iodine, selenium and astaxanthin, which have previously undergone thorough evaluation by EU authorities. When applied in a tiered approach the proposed model provides results that are consistent with previous assessments and with results obtained using other modelling techniques. The results indicate that the method has the potential to provide a conservative, reliable and flexible alternative to existing approaches to intake estimation.

**Keywords:-** Feed additives; risk assessment; intakes; dietary exposure modelling

## Introduction

In Europe the addition of feed additives to animal feed is governed by Regulation (EC) No 1831/2003 on the placing on the market and use of feed additives in animal nutrition (European Commission, 2003a). The Regulation includes provisions to ensure that residual amounts of these additives remaining in animal products have no adverse effects on the health of the consumer. Consumer exposure to nutrients are controlled through the setting of tolerable upper intake levels (ULs) for different age groups by the European Food Safety Authority (EFSA, 2006a). Exposure to other additive residues/metabolites are controlled by determining acceptable daily intakes (ADIs), which are usually expressed as mg/kg bodyweight/day.

Current guidelines for the assessment of additives in animal nutrition set out in Commission Regulation 429/2008 provide a method for establishing maximum residue levels (MRLs) for marker residues of feed additives based on food consumption data (Table 1) (European Commission, 2008). This method was originally developed for the assessment of MRLs for veterinary pharmaceutical residues, which can be administered orally or by injection and may have acute effects. At the time that the method was developed (during the 1980s), accurate information about the consumption of foods of animal origin was difficult to obtain and so “high arbitrary daily consumption data were applied in order to assure protection of consumers” (European Commission, 2005). The method was adopted for feed additives several years later. When using this method, MRLs and withdrawal periods are proposed in such a way that the total amount of toxicologically significant residue ingested daily should be lower than the ADI. An arbitrary body weight of 60 kg was also adopted.

The actual quantities proposed for individual food items in the daily diet in the Regulation 429/2008 model may not appear excessive for large portion sizes. However, they assume that these amounts are eaten by every individual every day whereas in reality many of these foods, particularly offal, may be eaten less

1 frequently and so average consumption over the longer term will be much lower,  
2 even for high level consumers. Furthermore they do not take interspecies differences  
3 into account. For example, particular products may be authorised only in certain  
4 species and the consumption of beef, pork or lamb will be significantly lower than the  
5 total for mammalian meat. The method also does not take account of variations  
6 related to the consumer's age. In particular, infants tend to consume more milk than  
7 adults when expressed on a body weight basis. Finally the method assumes that an  
8 individual can be a high level consumer of all of these food commodities  
9 simultaneously, whereas in reality a high-level consumer of one food is not  
10 necessarily a high-level consumer of all others.

11  
12 The values used in the Regulation 429/2008 model to represent concentration of  
13 nutrients or feed additives in animal products also warrant consideration. The feed  
14 additive guidelines relate to the use of tissue concentrations identified in efficacy  
15 trials but not all products from treated animals will contain the maximum recorded  
16 amount and not all animals in the food chain will have received supplements or feed  
17 additives. As a consequence, most consumers will be exposed to average  
18 concentrations much lower than the maximum values used in this model over the  
19 longer term. Only in certain exceptional circumstances, for example where meat is  
20 always obtained from the same source, could it be assumed that the entire supply  
21 contains the supplement or additive at the maximum level.

22  
23 The present Regulation 429/2008 model therefore represents a worst case and could  
24 be used in situations where there are concerns about acute exposure (amount  
25 consumed in any single day) to a substance of particular toxicological concern or in  
26 other exceptional circumstances as a maximum estimate of short-term intake  
27 (MESTI). However, in the majority of cases, where concern is related to exposures  
28 averaged over the longer term a more detailed model might produce more relevant  
29 results. This paper will review some simple approaches to intakes modelling and  
30 proposes a structure where they can be applied in a tiered approach so that the best  
31 use can be made of available data. Conservative estimates of high level intake can  
32 then be compared with Upper tolerable Limits (ULs) or with Acceptable Daily Intakes  
33 (ADIs).

34

## 1 **Materials and methods**

### 2 Methods for modelling intakes of substances from the diet

3 Intakes of substances from the diet can be estimated using the general formula:

$$4 \quad \text{Daily intake} = \frac{\text{mass of food (per day)} \times \text{concentration of substance}}{5 \quad \text{body weight}}$$

6  
7 Each of the variables used to estimate intake (food mass, substance concentration,  
8 body weight) is subject to variability. Methods that assign one value to each variable  
9 (such as the average or maximum) are described as 'deterministic', whilst methods  
10 that take account of some aspects of variability (usually food consumption and body  
11 weight in original survey data) are 'distributional'. 'Probabilistic' models aim to take  
12 account of all sources of variability using more sophisticated models (see Lambe  
13 2002, for example). Distributional and probabilistic models require access to raw data  
14 from food consumption surveys so that intakes for each individual can be estimated  
15 and the population statistics calculated. Because of this they are more time-  
16 consuming and expensive to perform and are usually applied after completing a  
17 tiered assessment scheme, which uses simple yet conservative deterministic models  
18 to eliminate substances where there is no cause for concern about intakes.  
19 Resources can then be concentrated on those substances where there is real  
20 potential to exceed ULs or ADIs.

21  
22 A reliable screening method is therefore required that can effectively identify  
23 substances that have the potential to exceed ULs or ADIs, whilst applying a simple,  
24 deterministic approach. Furthermore, this type of method is very useful for the safety  
25 assessment of substances in case of pre-marketing authorisation. Therefore, the  
26 method should be shown to maintain conservatism so that it does not fail to identify  
27 substances where high intakes might be of concern. To achieve this, the model must  
28 take account of multiple exposure routes, high level consumption by individuals and  
29 differences related to age. To maintain a conservative approach the model should  
30 use high-end estimates, where a range of values is available.

31  
32 Where a substance can be present in a number of different food items it is possible  
33 to calculate average or high level intake associated with each item using the formula

1  
2 1 above. High level consumption is usually taken to be an upper percentile (usually 95<sup>th</sup>  
3 or 97.5<sup>th</sup>) of the distribution of consumption data for consumers of the food (note that  
4 2  
5 3 non-consumers should not be included in this statistic). Upper percentiles are used to  
6 4  
7 5 represent maximum levels of consumption because it is unlikely that consumption  
8 6  
9 7 over the period of the survey (4 or 7 days) is unlikely to be sustained in the longer  
10 8  
11 9 term. The use of the 97.5<sup>th</sup> percentile to represent high food consumption therefore  
12 10  
13 11 effectively represents the entire population. Estimation of total average intake is  
14 12  
15 13 straightforward since average *per capita* intakes from each source can be simply  
16 14  
17 15 summed. High level intakes from each source cannot be summed because a high  
18 16  
19 17 level consumer of one food is not necessarily a high level consumer of all foods.  
20 18  
21 19 Several methods for overcoming this problem, without resorting to a distributional  
22 20  
23 21 model, have been proposed and three will be considered here.  
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14 Intakes of high level consumers of an individual food can be estimated by taking the  
15 97.5th percentile intake for consumers of this food and adding this to the population  
16 average intake from all other foods in the diet ('highest plus mean' – model 1)  
17 (Verger, 1995). An alternative method has been developed by the UK Pesticides  
18 Safety Directorate in which total high level intake is based on taking the two highest  
19 97.5th percentiles for consumers of individual foods and adding this to the population  
20 average from the rest of the diet ('two-highest plus mean' – model 2) (UK PSD,  
21 1995). This method is also recommended in the Guidelines to the European Food  
22 Safety Authority's 'concise diet' (EFSA, 2008). However, the Guidelines state that it is  
23 very unlikely that there exist individuals being high-level consumers of more than one  
24 food category, unless the number of food categories is very high. The Guidelines  
25 also warn against the use of these approaches (models 1 and 2) where the diet is  
26 broken down into many sub-categories of food.  
27

28 A third approach, which is sometimes used in the absence of high level consumption  
29 data, is to use three times the population mean to estimate total high level intake  
30 ('three-times mean' – model 3) (Bernier *et al*, 1994). The aim of each model is to  
31 provide a reliable estimate of total high level intake, such as would be produced by a  
32 distributional model.  
33

1  
2 1 All three models for estimating high level intakes have been compared with results  
3  
4 2 produced by distributional modelling of intakes of 40 examples of nutrients,  
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6 3 contaminants, food additives and novel food ingredients conducted in recent years  
7  
8 4 for UK consumers (examples include mineral hydrocarbons (Tennant, 2004) and  
9  
10 5 food colours (Tennant *et al* 2004 and Tennant and O'Callaghan, 2005)). The original  
11  
12 6 intake estimates were based on consumption by UK consumers (Gregory et al 1995,  
13  
14 7 Gregory 2000 and Henderson et al 2002) and included 5 to 25 food groups,  
15  
16 8 depending on the application. Each of the three models was used to estimate total  
17  
18 9 high level intake for the population and this was compared to the 97.5<sup>th</sup> intake  
19  
20 10 calculated using the distributional model, based on the same concentration data  
21  
22 11 (usually maximum levels). Minimum, average, median, interquartile range and  
23  
24 12 maximum estimates of total high level intake generated by each model have been  
25  
26 13 expressed as a percentage of the same estimate generated by the distributional  
27  
28 14 model (Table 2). No systematic differences between the methods regarding age  
29  
30 15 groups or number of food groups or the type of substance were observed.  
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32 16

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34 17 The results indicate that the 'three-times mean' model (model 3) tends to under-  
35  
36 18 estimate high level intake, in some cases by 80% and so should be used only in the  
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38 19 absence of better data. The 'highest plus mean' model (model 1) provides the most  
39  
40 20 accurate estimates but can under-estimate by 20%. This under-estimation is  
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42 21 relatively minor in the context of other uncertainties associated with risk assessment  
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44 22 and so the model can be used where there are other sources of conservatism in the  
45  
46 23 overall approach. The 'two-highest plus mean' model (model 2) almost always over-  
47  
48 24 estimates the true value, sometimes by a factor of up to three. This model would be  
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50 25 suited to situations where there are no other sources of conservatism in the overall  
51  
52 26 approach. However, the method is likely to produce a much higher proportion of false  
53  
54 27 positive results, which could undermine the screening strategy. The EU SCOOP 4.2  
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56 28 project investigated this method (model 2) and found that it over-estimated food  
57  
58 29 additive intakes by 2 – 70% (European Commission 1997). Overall the 'highest plus  
59  
60 30 mean' model (model 1) produces the most useful results. If results are close to but  
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32 still below the UL or ADI some further investigation may be required.  
33  
34

## Development of a screening model for additives in animal products

A tiered approach to intake modelling has been developed that can be applied according to the level of detail available about the distribution and levels of additive substances in food (Figure 1). Both tiers of the proposed approach use per capita average and 97.5th percentile food consumption data based on individual data in UK food consumption surveys of pre-school children (1½ - 4½ yrs) , schoolchildren (5 – 18 yrs) and adults (19 – 65 yrs) plus published data on food consumption by infants (6-12 months) (Gregory et al 1995; Gregory 2000; Henderson et al 2002; Mills & Tyler 1992). The UK database provides the opportunity for detailed assessment of the consumption of specific food categories by particular age groups, not available from more aggregated data sets such as that used in the EU SCOOP 3.2 project (European Commission, 2003b). This allows different levels of detail to be built into a tiered approach. The data are expressed as daily intakes averaged over the duration of the surveys (7 or 4 days)

The Regulation 429/2008 MRL model will be used as the basis for an initial (Tier 1) screen and for cases where there are concerns about acute exposures to determine maximum estimates of short-term intake (MESTI) (Table 1). The first tier of the proposed approach (Tier 2) will generate an estimate of theoretical maximum daily intake (TMDI) based on actual consumption of food groups used in the Regulation 429/2008 MRL model averaged over several days (Table 3). TMDI food consumption data differ from the Regulation 429/2008 MRL model because all dairy products are included, not just milk. In some cases there were too few consumers to make reliable estimates of consumption of certain minor products or data were not separately reported. In these cases it was assumed that the fat:muscle ratio for mammals was 0.167 and the liver:muscle ratio was 0.33, the kidney:muscle ratios was 0.033 and the fat:muscle ratio was 0.3 for birds, as in the Regulation 429/2008 MRL model. At Tier 2 total high level intakes are estimated by taking the highest two 97.5<sup>th</sup> percentiles and adding them to average intakes from all other foods (model 2), in order to maintain a high level of conservatism.

The second tier of the proposed approach (Tier 3) will generate an estimate of theoretical estimated daily intake (TEDI). It uses the same raw data as the Tier 2 model but sub-divided by animal species (Table 4). 'Other meat' is included to allow

1  
2 1 for species such as rabbits and 'other poultry' and for minor species such as duck  
3  
4 2 and game. Only fish species suitable for aquaculture are included and 'other farmed'  
5  
6 3 uses halibut as a surrogate because this species is being developed for aquaculture.  
7  
8 4 Food consumption data for infants could not be subdivided because the original data  
9  
10 5 are not accessible. Consumption data were unavailable for poultry kidney and fat and  
11  
12 6 fat in all species and so estimates were taken from Tier 2.  
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14 7

15  
16 8 At Tier 3 total high level intakes are estimated by taking the highest 97.5th percentile  
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18 9 and adding this to average intakes from all other foods (model 1). Conservatism is  
19  
20 10 maintained because the intake assessment is based on the maximum levels reported  
21  
22 11 in efficacy studies and not longer-term averages (including levels in foods not  
23  
24 12 treated) to which consumers are actually exposed. Average bodyweights for each  
25  
26 13 age group are available to convert intakes from mg/person/day to mg/kg bw/day for  
27  
28 14 comparison with ADIs (Table 5.)  
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30 15

## 31 16 **Results**

32  
33 17 Evaluation of intake models is difficult in the absence of a 'true' answer. The model  
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35 18 developed here for estimating high level intakes of additives (including nutritional  
36  
37 19 additives) from animal products will be evaluated using two approaches. Firstly by  
38  
39 20 comparison of results produced by the method with the conclusions of recent  
40  
41 21 opinions considering intake estimates produced by the EFSA panel on additives and  
42  
43 22 products or substances used in animal feed (FEEDAP). The second approach will  
44  
45 23 assess the outputs of the model in comparison with using the same concentration  
46  
47 24 data in a distributional model. The distributional model will use the same tissue  
48  
49 25 concentration values as the TEDI model but the values will be applied to the  
50  
51 26 consumption values of each individual in the original surveys to calculate his or her  
52  
53 27 total intake and the high level intake value will be the 97.5<sup>th</sup> percentile of the entire  
54  
55 28 population distribution.  
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### 58 30 Case study 1 - Iodine

59 31 In January 2005 the EFSA FEEDAP panel reviewed the possible detrimental effect  
60 32 on human and animal health or the environment of iodine, used at the current levels  
33 33 authorised under Directive 70/524/EC (4, 20 and 10 mg/kg feed for horses, fish and

1 all other species, respectively) (EFSA, 2005a). They concluded from worst case  
2 estimations, that iodine intake from beef, pork or poultry would not exceed 0.1  
3 mg/day for an adult person and was probably nearer to 0.05 mg/day, which was well  
4 below SCF ULs. Further estimates were therefore limited to model calculations  
5 primarily with milk and eggs. Fish was not considered by the FEEDAP panel because  
6 the iodine content of farmed fish was below the iodine in marine fish.

7  
8 The panel considered theoretical milk and egg consumption patterns appropriate to  
9 different age groups. They concluded that with a concentration of 4 mg iodine/kg in  
10 complete feed for dairy cows and laying hens, the intake levels would be 0.3 mg/day  
11 for adults and adolescents and 0.055 – 0.109 mg/day for children 4-6 yrs.

12  
13 The screening method, using the same levels of iodine in beef, pork and poultry  
14 muscle, liver and kidney and in milk and egg as well as levels in fish, resulted in a  
15 total Tier 1 MESTI estimate of 16.7 mg/day. The Tier 2 TMDI estimate, using the  
16 same food concentrations gave total high level iodine intakes of 3.9, 2.4, 2.0 and 1.0  
17 mg/day for adults, schoolchildren, pre-school children and infants respectively (Table  
18 6). The main contributor to MESTI and TMDI estimates was wild sea-caught fish.

19  
20 The Tier 3 TEDI estimate, based on species tissue concentrations, gave total high  
21 level of iodine intake estimates of 0.45, 0.40 and 0.54 mg/day for adults,  
22 schoolchildren and pre-school children (including intake from other sources). The  
23 validation of Tier 3 estimates for iodine intake was investigated using the  
24 distributional model. This model gave high level (97.5<sup>th</sup> percentile) estimates of iodine  
25 intakes of 0.44, 0.39 and 0.51 mg/day adults, schoolchildren and pre-school children.  
26 The principal source of intake was milk.

27  
28 The proposed model produced iodine TEDI intake estimates that were close to  
29 estimates provided by the FEEDAP panel based on modelled milk and egg  
30 consumption. The TEDI intake estimates were about 0.1 mg/day higher because they  
31 also included intakes from meat, fish and other animal products and the results were  
32 confirmed in the distributional model.

1  
2 1  
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4 2 Case study 2 - Selenium  
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7 3 The FEEDAP panel estimated maximum daily intakes of selenium from animal  
8  
9 4 products in terms of a worst case scenario, using maximum levels in beef and pork  
10  
11 5 muscle, liver and kidney and in milk and egg with the theoretical daily consumption of  
12  
13 6 food commodities of animal origin provided in Commission Regulation 429/2008 (see  
14  
15 7 Table 1) (EFSA, 2006b). The total exposure was 0.428 mg/day, which exceeded the  
16  
17 8 ULs established for the different age-based populations.

18 9  
19  
20 10 A refinement of the figures was achieved using consumption data obtained from  
21  
22 11 twelve EU countries using pig tissue levels as a worst case, average meat, liver and  
23  
24 12 kidney consumption (calculated in same ratio as in Regulation 429/2008), average  
25  
26 13 milk consumption and high level egg consumption data obtained from the SCOOP  
27  
28 14 3.2 project (European Commission 2003b). This gave a maximum daily Se intake of  
29  
30 15 0.105 mg/day, which was below the UL set by the SCF for adults. Intakes for children  
31  
32 16 aged 4-6 years were estimated to be 0.039 mg/day.

33 17  
34  
35 18 The proposed new screening method, using the same levels of selenium in beef and  
36  
37 19 pork muscle, liver and kidney and in milk and egg resulted in an identical Tier 1  
38  
39 20 MESTI estimate, of 0.43 mg/day. The Tier 2 TMDI estimate, gave total high level  
40  
41 21 selenium intakes of 0.16, 0.10, 0.10 and 0.07 mg/day for adults, schoolchildren, pre-  
42  
43 22 school children and infants, respectively. The Tier 3 TEDI estimate, based on species  
44  
45 23 tissue concentrations, gave total high level selenium intake estimates of 0.10, 0.09  
46  
47 24 and 0.06 mg/day for adults, schoolchildren and pre-school children.

48 25  
49  
50 26 As a validation of the Tier 3 TEDI model estimates of selenium intake by consumers  
51  
52 27 of animal products were estimated in a distributional model. This model gave high  
53  
54 28 level selenium intake estimates of 0.10, 0.07 and 0.06 mg/day for adults,  
55  
56 29 schoolchildren and pre-school children.

57  
58 30 The results obtained with the proposed new tiered approach produced intake  
59  
60 31 estimates that were close to those provided by FEEDAP (Table 7). Though slightly

1  
2 1 more conservative, the Tier 3 TEDI results were also close approximations to the  
3  
4 2 results obtained by distributional modelling based on the same input data.  
5  
6 3

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8  
9 4 Case study 3 - Astaxanthin

10 5 In their 2005 assessment of potential consumer exposures to astaxanthin the  
11 6 FEEDAP panel used three models because they felt that data on the consumption of  
12 7 salmon and trout were insufficient (EFSA, 2005b). In the first model, based on  
13 8 salmon and trout production in Europe, the Panel concluded that with maximum  
14 9 astaxanthin levels in salmon of 10 mg/kg and in trout of 25 mg/kg, daily average  
15 10 astaxanthin intake would be 0.045 mg. The second model used WHO GEMS  
16 11 average consumption data for all fish European consumers, of 34g per day. This  
17 12 would result in astaxanthin intakes of 0.34 – 0.85 mg/day.  
18  
19 13

20 14 The final scenario was based on the SCOOP 3.2 project (European Commission  
21 15 2003b), in which average fish consumption ranged from 13 to 80 g/day and high level  
22 16 fish consumption 103 to 165 g/day for adults. Assuming that all fish are salmon or  
23 17 trout and that all salmon and trout are fed with astaxanthin at the highest level  
24 18 approved resulted in astaxanthin intakes of 0.8 - 2.0 mg astaxanthin/day for average  
25 19 consumers and of 1.6 - 4.1 mg astaxanthin/day for high consumers. This was  
26 20 regarded as a considerable over-estimate because the consumption figure included  
27 21 all sea-food, including the wild catch.  
28  
29 22

30 23 Using the same levels of astaxanthin in salmon and trout flesh resulted in a Tier 1  
31 24 MESTI estimate, using the proposed screening method, of 7.5 mg/day. The Tier 2  
32 25 TMDI estimate, based on total fish consumption, gave high level astaxanthin intakes  
33 26 of 2.7, 1.5, 1.2 and 0.4 mg/day for adults, schoolchildren, pre-school children and  
34 27 infants, respectively (Table 8). The Tier 3 TEDI estimate, based solely on salmon and  
35 28 trout consumption, gave high level astaxanthin intake estimates of 1.2, 1.5 and 0.6  
36 29 mg/day for adults, schoolchildren and pre-school children.  
37  
38 30

39 31 As a validation of the Tier 3 TEDI model estimates of astaxanthin intakes by  
40 32 consumers of salmon and trout were estimated in a distributional model. This model

1  
2 1 gave high level astaxanthin intake estimates of 1.06, 0.53 and 0.45 mg/day for  
3  
4 2 adults, schoolchildren and pre-school children.  
5  
6 3

7  
8 4 The TMDI model gave similar intake estimates to the most conservative model used  
9 5 by FEEDAP, which is to be expected since both are based on total fish consumption.  
10 6 The TEDI model gave lower estimates and these were similar to the results of  
11 7 distributional modeling using the same data, which were based on salmon and trout  
12 8 consumption only.  
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## 20 10 Discussion

21  
22 11 An effective risk assessment scheme, based on tiered default methods, should have  
23 12 two important properties:

- 24 13 1 The system should be sufficiently conservative that it always identifies  
25 14 compounds which could exceed toxicological safety limits; and
- 26 15 2 The system should keep to a minimum compounds which require costly,  
27 16 detailed evaluations on a case-by-case basis.  
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37 18 The proposed modelling approach is designed to fit between very simple, highly  
38 19 conservative methods and highly sophisticated distributional and probabilistic  
39 20 methods. Comparison with the results of FEEDAP evaluations of potential intakes of  
40 21 nutrients and feed additives have shown that the proposed method provides  
41 22 consistent results that would form the basis of similar risk assessments. The results  
42 23 of the top tier TEDI estimate were compared with results obtained using distributional  
43 24 modelling using the same input data and found to produce very similar results.  
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52 26 The present model is based on UK food consumption data that are available for  
53 27 adults and children at *per capita* average levels and for high level consumers. The  
54 28 model could be extended using data from other national food consumption surveys  
55 29 provided that they were statistically consistent. National variations in food  
56 30 consumption patterns are likely to result in differences in the proportion of people  
57 31 consuming a particular food and the frequency of their consumption. This could result  
58 32 in differences in *per capita* average consumption. However, differences in individual  
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1 high level consumption are less likely to be affected by national variations because  
2 there are physiological limits to the amount that any one individual can consume. The  
3 proposed model, although based on consumption data from one EU country, has  
4 shown its relevance even when compared with more international database used by  
5 the FEEDAP Panel.

6  
7 Intake estimates produced by all of the models under consideration provide  
8 conservative estimates because they assume maximum concentrations of nutrients  
9 or additives in all tissues at all times. In reality, consumers are exposed to a range of  
10 possible concentrations, including from animals fed with feeds not containing the  
11 additive, which may be zero. If appropriate for further monitoring, intake methods  
12 could therefore be further improved by refining data used to represent long term  
13 average concentrations in tissues (unless there are concerns about acute  
14 exposures).

15  
16 The MESTI would be considered as the final exposure assessment in cases of  
17 significant toxicological concern, such as coccidiostats and histomonostats, to  
18 provide an additional margin of safety or where there are concerns about short-term  
19 toxicity. In all other cases the exposure assessment would be refined down to the  
20 TMDI or TEDI depending on the availability of data.

## 21 22 **Conclusion**

23 Overall the proposed method provides a refinement of the existing Regulation  
24 429/2008 method because it takes account of longer term average consumption,  
25 allows for different concentrations in different animal species and takes account in  
26 differences in age of consumer, including bodyweight. It is consistent with risk  
27 modeling in use in comparable areas (pesticides, etc.), while the model in Regulation  
28 429/2008 is not. Comparison with recent FEEDAP evaluations has shown that the  
29 proposed method successfully meets the need for a more refined approach. The  
30 method has the additional advantage that it is much easier to identify sources of high  
31 exposure and so tailor risk management actions more precisely. It is therefore  
32 concluded that the proposed MESTI/TMDI/TEDI method will provide a useful  
33 alternative to existing intake modeling approaches.

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## References

Bernier JJ, Causeret J, Hoellinger H and Sushett M. 1994. Méthode pour assurer, au sein d'une population, le non dépassement de la dose journalière admissible des additifs alimentaires. *Médecine et Nutrition* 1: 9-117.

EFSA. 2005a. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on the request from the Commission on the use of iodine in feedingstuffs (Question N°EFSA-Q-2003-058). Adopted on 25 January 2005. *The EFSA Journal* (2005) 168, 1-42.

EFSA. 2005b. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on the request from the European Commission on the safety of use of colouring agents in animal nutrition PART I. General Principles and Astaxanthin (Question No. EFSA-2003-060). Adopted on 30<sup>th</sup> November 2005. *The EFSA Journal* (2005) 291, 1-40.

EFSA. 2006a. Opinion of the Scientific Committee on Food Scientific Panel on Dietetic Products, Nutrition and Allergies. Tolerable Upper Intake Levels for Vitamins and Minerals. ISBN: 92-9199-014-0.

EFSA. 2006b. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on the safety and efficacy of the product Sel-Plex®2000 as a feed additive according to Regulation (EC) No 1831/2003 (Question No EFSA-Q-2005-071). Adopted on 19 of April 2006. *The EFSA Journal* (2006) 348, 1-40.

EFSA. 2008. European Food Safety Authority. Guidance Document for the use of the Concise European Food Consumption Database in Exposure Assessment. EFSA/DATEX/2008/01. Parma, 17 March 2008.

European Commission. 1997. Reports on Tasks for Scientific Cooperation. Report on Methodologies for the Monitoring of Food Additive Intake across the European Union. Directorate General Industry.

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- 1  
2 1 European Commission. 2008. Commission Regulation (EC) No 429/2008 of 25 April 2008 on  
3 detailed rules for the implementation of Regulation (EC) No 1831/2003 of the European  
4 Parliament and of the Council as regards the preparation and the presentation of applications  
5 and the assessment and the authorisation of feed additives. OJ L133/1; 22.5.08.  
6  
7  
8  
9  
10  
11 6 European Commission. 2003a. Regulation (EC) No 1831/2003 of the European Parliament  
12 and of the Council of 22 September 2003 on additives for use in animal nutrition. OJ L  
13 268/29, 18.10.2003  
14  
15  
16  
17 9  
18  
19 10 European Commission. 2003b. Draft Report from Task 3.2.11: Assessment of the dietary  
20 exposure to arsenic, cadmium, lead and mercury of the population of the EU Member States.  
21 European Commission, Directorate-General Health and Consumer Protection, Reports on  
22 tasks for scientific co-operation, Final draft, 5 December 2003.  
23  
24  
25  
26 14  
27  
28 15 European Commission. 2005. Notice to applicants and note for guidance. Establishment of  
29 maximum residue limits (MRLs) for residues of veterinary medicinal products in foodstuffs of  
30 animal origin.  
31  
32  
33 18  
34  
35 19 Gregory J R, Collins D L, Davies PSW, Hughes JM, and Clarke PC. 1995. National Diet and  
36 Nutrition Survey; Children aged 1½ to 4½ years. HMSO, London.  
37  
38  
39 21  
40  
41 22 Gregory J. 2000. National Diet and Nutrition Survey: young people aged 4 to 18 years.  
42 Findings: Volume 1. London: The Stationery Office.  
43  
44  
45 24  
46  
47 25 Henderson L, Gregory J and Swan G. 2002. The National Diet and Nutrition Survey:  
48 adults aged 19 to 64 years. Types and quantities of foods consumed. Her Majesty's  
49 Stationery Office (HMSO). ISBN 0 11 621566 6.  
50  
51 27  
52  
53 28  
54  
55 29 Mills A and Tyler H. 1992. Food and nutrient intakes of British infants aged 6 – 12 months.  
56 HMSO, London.  
57  
58  
59 31  
60

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Food Additives & Contaminants

- 1  
2 1 Lambe, J. 2002. The use of food consumption data in assessments of exposure to food  
3 2 chemicals including the application of probabilistic modelling. Proceedings of the Nutrition  
4 3 Society, 61, 11–18  
5 4  
6 5  
7 6  
8 7  
9 8  
10 9 Tennant DR, Gedrich K, Godfrey D and Davidson J. 2004. Intakes of beta-carotene from its  
11 6 use as a food additive, fortificant and dietary supplement in France, Germany and the UK.  
12 7 *British Food Journal* 106(6):436-456.  
13 8  
14 9  
15 10 Tennant DR. 2004. The usage, occurrence and dietary intakes of white mineral oils and  
16 11 waxes in Europe. *Food and Chemical Toxicology*. 42(3):481-492.  
17 12  
18 13  
19 14  
20 15  
21 16  
22 17  
23 18 Tennant DR and O'Callaghan M. 2005. Survey of usage and estimated intakes of annatto  
24 13 extracts. *Food Research International* 38:911-917.  
25 14  
26 15  
27 16  
28 17  
29 18 UK PSD. 1995. Methods for the Estimation of Dietary Intakes of Pesticide Residues. UK  
30 16 Pesticides Safety Directorate, Ministry of Agriculture, Fisheries and Food.  
31 17  
32 18  
33 19  
34 20  
35 18 Verger P. 1995. One example of utilisation of the 'French Approach'. Paper presented at the  
36 19 ILSI Europe Workshop on Food Additive Intake, 29-30 March, Brussels, Belgium.  
37  
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Table 1. Daily human food consumption values recommended in Regulation 429/2008

Food product	Mammals	Birds	Fish
Muscle	300 g	300 g	300 g(*)
Liver	100 g	100 g	
Kidney	50 g	10 g	
Fat	50 g(**)	90 g(***)	
+ Milk	1,500 g		
+ Egg		100 g	

(\*) Muscle and skin in natural proportions.  
(\*\*) For pigs 50g of fat and skin in natural proportions.  
(\*\*\*) Fat and skin in natural proportions.

**Table 2.** Performance of three deterministic intake modelling methods compared to distributional model.

<b>Deterministic model</b>	<b>Minimum</b>	<b>Average</b>	<b>Median</b>	<b>IQ range</b>	<b>Maximum</b>
Highest plus mean (1)	78%	108%	98%	89 - 117%	194%
Two-highest plus mean (2)	97%	152%	139%	124 - 163%	292%
Three-times mean (3)	18%	79%	73%	49 - 99%	234%

Note: Figures represent percentage of the distributional model estimate predicted by each deterministic model.

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Table 3. Food consumption data used in TMDI (Tier 2) model (g/day)

	Tissue	Adults		Schoolchildren		Pre-school children		Infants	
		Mean	97.5th %ile	Mean	97.5th %ile	Mean	97.5th %ile	Mean	97.5th %ile
<b>Mammals</b>	Muscle	47.77	138.34	28.54	103.63	18.45	61.25	12.10	38.50
	Liver	1.25	42.06	0.26	18.89	0.24	24.29	0.80	18.50
	Kidney	0.26	30.94	0.08	15.38	0.09	16.90	0.20	3.70
	Fat	0.21	1.15	1.72	10.37	1.72	10.37	0.07	0.23
<b>Dairy</b>	All dairy	261.74	671.75	204.90	620.35	317.42	839.13	337.75	871.90
<b>Poultry</b>	Muscle	29.88	104.30	16.67	77.24	7.27	42.00	3.40	15.50
	Liver	0.08	34.67	0.02	22.12	0.03	18.93	1.13	5.17
	Kidney	0.99	3.44	0.55	2.55	0.00	2.73	0.01	0.05
	Fat	8.96	31.29	5.00	23.17	2.18	12.60	1.02	4.65
<b>Egg</b>	All egg	23.82	78.18	15.23	52.80	13.07	48.24	12.10	45.80
<b>Fish</b>	All fish	26.27	107.93	11.66	61.73	8.03	47.02	3.40	15.50

Table 4. Food consumption data used in TEDI (Tier 3) model (g/day)

	Tissue	Adults		Schoolchildren		Pre-school children	
		Mean	97.5th %ile	Mean	97.5th %ile	Mean	97.5th %ile
<b>Bovine</b>	Muscle	20.92	87.69	11.68	65.81	9.27	46.82
	Liver	0.12	40.5	0.00	4.86	0.02	11.75
	Kidney	0.22	28.06	0.08	15.74	0.07	13.95
<b>Porcine</b>	Muscle	22.9	88.97	13.65	61.71	7.95	36.48
	Liver	0.56	26.42	0.19	17.50	0.11	21.02
	Kidney	0.01	17.14	0.00	6.53	0.00	0.19
<b>Ovine</b>	Muscle	3.07	68.93	2.66	39.29	0.88	25.35
	Liver	0.5	44.99	0.05	28.93	0.08	23.10
	Kidney	0.03	34.64	0.44	6.56	0.02	18.94
<b>Other meat</b>	Muscle	0.88	19.29	0.55	12.30	0.36	18.72
	Fat	0.209	1.15	1.72	10.37	1.72	10.37
<b>Dairy</b>	Milk	242.29	653.15	194.91	598.40	310.10	834.00
	Butter	3.23	14.8	1.36	19.61	1.21	13.63
	Cheese	14.8	61.34	8.19	48.95	5.76	30.65
	Other dairy	1.42	32.49	0.45	16.06	0.34	22.88
<b>Poultry</b>	Broilers	26.27	99.57	14.09	72.77	6.63	42.04
	Turkeys	3.42	55.74	2.49	36.38	0.64	27.04
	Other poultry	0.38	47.22	0.09	32.41	0.01	6.57
	Liver	0.08	34.67	0.02	22.12	0.03	18.93
	Kidney	0.99	3.44	0.46	2.40	0.00	2.73
	Fat	8.96	31.29	4.23	21.83	1.99	12.61
<b>Egg</b>	All egg	23.82	78.18	15.23	52.80	13.07	48.24
<b>Fish</b>	Salmon	3.4	58.68	0.46	41.82	0.28	25.74
	Trout	0.64	47.53	0.12	60.62	0.06	22.98
	Prawns	2.41	48.88	0.50	30.51	0.12	17.31
	Other farmed	0.03	20.6	0.12	60.62	0.01	12.85

Table 5. Average bodyweight data.

Population group	Adults	Schoolchildren	Pre-school children	Infants
Age (yrs)	19 - 65	4 – 18	1.5 – 4.5	0.5 – 1.0
Weight (kg)	70.1	43.3	14.5	8.7

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**Table 6.** Results of iodine intake estimation using FEEDAP methods, proposed new tiered approach and distributional modelling, in comparison to SCF ULs

<b>Age group:</b>	<b>Adult</b>	<b>15 – 17</b>	<b>11 – 14</b>	<b>7 – 10</b>	<b>4 – 6</b>	<b>1 – 3 yrs</b>	
<b>SCF UL:</b>	600	500	450	300	250	200	mg/day
<b>FEEDAP (beef, Pork, poultry)</b>	0.05-0.1	-	-	-	-	-	mg/day
<b>FEEDAP (eggs, milk)</b>	0.3	0.3	0.3	-	0.06 – 0.11	-	mg/day
<b>New MESTI (entire diet)</b>	16.7	-	-	-	-	-	mg/day
<b>New TMDI (entire diet)</b>	3.86	2.35	2.35	2.35	2.35	2.01	mg/day
<b>New TEDI (entire diet)</b>	0.45	0.40	0.40	0.40	0.40	0.54	mg/day
<b>Distributional model</b>	0.44	0.39	0.39	0.39	0.39	0.51	mg/day

Table 7. Results of selenium intake estimation using FEEDAP methods, proposed new tiered approach and distributional modelling, in comparison to SCF ULs

Age group:	Adult	15 – 17	11 – 14	7 – 10	4 – 6	1 – 3 yrs	
<b>SCF UL:</b>	0.30	0.25	0.20	0.13	0.09	0.06	mg/day
<b>FEEDAP (conservative)</b>	0.428	-	-	-	-	-	mg/day
<b>FEEDAP (refined)</b>	0.105	-	-	-	0.039	-	mg/day
<b>New MESTI</b>	0.43	-	-	-	-	-	mg/day
<b>New TMDI</b>	0.16	0.10	0.10	0.10	0.10	0.07	mg/day
<b>New TEDI</b>	0.10	0.09	0.09	0.09	0.09	0.06	mg/day
<b>Distributional model</b>	0.10	0.07	0.07	0.07	0.07	0.06	mg/day

Table 8. Results of astaxanthin intake estimation using FEEDAP methods, proposed new tiered approach and distributional modelling.

Age group:	Adult	Schoolchild	Pre-school Infant		yrs
	19 - 65	4 - 18	1½ - 4½	½ - 1	
FEEDAP (initial)	0.45	-	-	-	mg/day
FEEDAP (refined)	0.34-0.85	-	-	-	mg/day
FEEDAP (final)	0.8-4.1	-	-	-	mg/day
New MESTI	7.5	-	-	-	mg/day
New TMDI	2.70	1.54	1.18	0.39	mg/day
New TEDI	1.22	1.52	0.58	-	mg/day
Distributional model	1.06	0.53	0.45	-	mg/day

**Figure caption:**

Figure 1. Tiered approach to estimating consumer intakes of feed additives and nutrients

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