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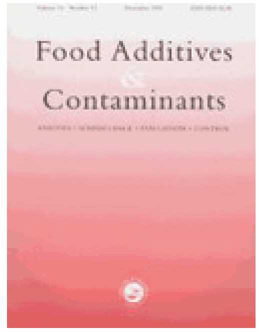

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Transfer of chemicals from feed to animal products - the use of transfer factors in risk assessment

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Abstract

The human risk assessment of feed contaminants has often been hampered by a lack of knowledge concerning their behavior when consumed by livestock. To gain a better understanding of the transfer of contaminants from animal feed to animal products, a meta-analysis of published literature was made. Data concerning feed contaminant concentrations, feeding periods, residue levels in animal products, and other parameters, were gathered and recorded. For each case a "transfer factor", defined as the ratio of the concentration of a chemical in an animal product to the concentration of the chemical in animal feed, was calculated. Scientifically founded transfer factors were calculated and analyzed for groups of chemicals based on their contaminant classes or physico-chemical properties. These database-derived transfer factors enable a more accurate risk assessment in the case of a feed contamination, and enable rapid risk management decision-making and/or intervention.

Keywords: Transfer factor; carry-over; contaminants; residues; risk assessment; risk management

Introduction

In recent years increasing attention has been paid to the risk to consumers posed by chemical contaminants or residues in animal feed. This was caused by various cases of milk, eggs or other animal products contaminated with environmental chemicals. The best-known examples include contamination of milk with dioxins and PCBs as a result of industrial activities (e.g. emission of dioxins and PCBs by waste incinerators). In addition, animal feed has been found adulterated with hormones, antibiotics, dioxins, and other chemicals either deliberately, or from malpractice, or from sloppy manufacturing practices. The current use of pesticides for crop protection is an example of controlled "contamination" of crops which may become available for human consumption via animal feed. Also, contamination of animal feed can occur in a more or less biological way as is the case with mycotoxins due to improper storage of feed or feed ingredients. Cases like the Belgian PCB incident, as described by Bernard *et al.* (2002), demonstrated that adequate risk management is indispensable.

As various kinetic processes determine the qualitative and quantitative transfer of contaminants from feed to edible commodities, it is noted that without detailed information on a specific contaminant, a worst case approach is the only way to perform a risk assessment. For most of the contaminants this will lead to an excessive overestimation of residue levels in animal commodities. However, for some accumulating compounds a worst case estimation may still be an underestimation of the actual residue levels after prolonged exposure. This might be the case for highly lipophilic compounds like DDT or for some (heavy) metals which are known to accumulate in edible offal. A risk assessment of a possible feed contamination using a worst-case approach might therefore lead to wrong decisions, costing effort and money in the case of an erroneous overestimation, or health risk to consumers in the case of an erroneous underestimation of the contamination levels of the edible products under evaluation. In order to respond promptly to questions concerning risk assessment of contaminated livestock feed, the availability of a comprehensive data set on the transfer from feed to animal products of various classes of contaminants was considered useful. Therefore, a meta-analysis of the literature was performed to gather data on the transfer from livestock feed to animal products covering various classes of chemicals. This paper will enable risk assessors to gain a better understanding on the transfer of feed contaminants to edible commodities. Furthermore, the data presented can be used to perform a rapid and founded estimation of feed contaminant transfer if needed.

Methods

Data on the transfer of contaminants from animal feed to animal products included in the database were mainly collected from the open literature. The literature databases AGRIS, AGRICOLA, Food & Human Nutrition, and Toxline, were searched covering the period of 1970 to 2005. The data on the transfer of pesticides were also obtained from publicly available evaluations by the FAO/JMPR, the Advisory Committee on Pesticides of the UK-PSD, and from pesticide dossiers filed in the archives of the TNO Quality of Life.

Several studies were published in languages other than English, including Czech, Dutch, German, Italian, Polish, Korean, and Japanese. Publications in other languages than English, Dutch and German were taken into account as far as data could be derived from English abstracts or are available in the tables provided in these publications. Only studies were selected in which the compound was administered via the feed or by alternative oral exposure (e.g. via capsules). Exposure via drinking water was not taken into account. Results from radio-labeled studies were only used in case individual residues were identified and analyzed. A database was generated using the Microsoft Corporation Excel 2003 (SP-2) software program for Windows XP. For each study the following data were recorded: chemical name, CAS number., molecular weight, log Po/w, water solubility, animal species name, concentration in the feed, amount of residue per commodity (e.g. eggs, whole milk, meat, fat, and edible offal's (e.g. kidney or liver)), feeding period, and remarks. CAS numbers or physico-chemical properties were retrieved online using Chemfinder.com or ChemIDplus (http://chem.sis.nlm.nih.gov/chemidplus/), whereas lacking log Po/w data were retrieved online using the interactive analysis logP predictor website: http://www.logp.com (Interactive analysis, Bedford, MA, USA). Not only the transfer of the compound itself, but also transfer of possible metabolites to the animal products were included if present. Within the remarks, information on residue differences between kidney and liver, periods to reach plateau levels in whole milk or egg, correction factors used, amongst other remarks, are specified.

The following defined classes of chemicals were selected for inclusion in the database.

Pesticides ("new"), mainly pesticides which are currently used within the EC; *pesticides ("old")*, as examples of lipophilic organochlorine compounds prohibited for use in the EC; *dioxins and furans*; *polychlorobiphenyls (PCBs) and polybrominated biphenyls (PBBs)*; *(heavy) metals,* both as unspecified metals in the matrix as well as specific metal containing compounds; *mycotoxins*; *hormones*; *veterinary medicines*; *nitrosamines*; and other compounds not belonging to one of the previous classes. A detailed list of chemicals present in the respective classes (public data only) is provided in table I.

<Insert table I>

Establishment of transfer factors

The term *transfer factor* is used throughout this paper to define the transfer of chemical compounds from animal feed to animal products as determined in animal feeding studies. The transfer factor is expressed as the concentration of the compound in animal products (mg/kg) divided by the concentration of the compound in animal feed (mg/kg), in which the concentration in animal products is on a wet weight basis, and in feed on a dry weight basis.

For most of the transfer factors, the compound itself is analyzed both in the feed and in the animal commodity. However, for (heavy) metals, most of the analytical methods used are specific for the metal in the respective commodity (e.g. Ni), but not for the compound as present in the feed (e.g. $NiCl_2$). The transfer factors calculated are therefore based on the metal ion and included in the database as such. Furthermore, several studies are included in the database based on sludge contaminated feed where no specific compound is known apart from the total metal concentration. For several other compounds, the parent compound is metabolized after becoming systemically available. An example is the metabolism of the pesticide 2,4-D to 2,4-dichlorophenol, where the metabolite may be present at concentrations exceeding that of the parent compound in sheep with a factor of 35. For metabolites, the metabolite concentration in the animal commodity is divided by the parent compound concentration in feed to calculate the respective transfer factor. In case the transfer factor is based on a metabolite, its identity is indicated in the database.

In case data are reported which are not in the appropriate format (e.g. residues in milk fat instead of whole milk, or residue in animal products based on a dry weight basis), standardized factors are used to convert these data accordingly. The following conversion factors were used in order to unify the data from the various available studies. An average multiplication factor of 4.0 was used for all matrices to convert dry animal product weight into wet tissue weight (Boyer, 1981). Milk data were often found to be expressed on the basis of milk fat, especially dioxin and PCB data. Since dietary risk assessment procedures take whole milk into account, all milk data in the database are expressed on the basis of whole milk. On the assumption that whole milk may contain up to 4.3% fat (Bluethgen, 1995), milk fat concentrations were multiplied by 0.043 to derive values for whole milk. Some egg data were expressed on the basis of egg fat or egg fatty acids. For the same reasons as for whole milk, the various egg data were converted to the whole egg using a conversion factor of 0.088, derived from the data of Schuler (1997). Data in egg white and yolk are converted to whole egg assuming a ratio of 65:35 (egg white: egg yolk). It is noted that in case actual data (e.g. percentage of milk fat) are specified in the publication, these data are used for the conversion.

In studies where the daily body dose, but not the feed concentration was specified, it was assumed that the dry weight feed consumption of dairy cattle was 20 kg/day, of pigs 3 kg/day, and of chickens 0.12 kg/day (EC working document 7031/VI/95, rev. 4).

If commodity levels are determined below the limit of determination (LOD), the LOD value was used for the calculation of the transfer factor. Transfer factors based on LOD values are marked in the database in case a compound specific analysis has to be performed. As a consequence, the calculated means are an overestimation of the means when calculated using the actual commodity concentrations (<LOD).

Statistics

The SAS/STAT software V8.2, 1999-2001 (Cary, NC. SAS Institute Inc.), statistical package was used to determine the distribution pattern of the transfer factors. The

Microsoft Office Excel 2003-SP2, including the Analysis ToolPak add-in was used to calculate the mean, median, 95th percentiles, and maximum values of the transfer factors.

Results

The meta-analysis of the literature evaluated up to 2005, covering about 250 references, resulted in a total of 3624 transfer factors, most of which were found on edible offal's (31%) and meat (25%), followed in about equal numbers by eggs (12%), whole milk (15%) and fat (17%). Animals included are cattle, poultry, pig, sheep, goat, rabbit and several birds like pheasant, turkey, duck and quail. An overview of the amounts of transfer factors found in each animal commodity, as well as for each of the various contaminant classes are given in table II.

<Insert table II>

Statistical parameters covering the geometric mean, geometric standard deviation, median, 95th percentile and maximum transfer factors were calculated using all transfer factors for each commodity, and are listed in table III. It appears that the highest transfer factors are found for fat and edible offal's. The transfer factors for eggs, meat and whole milk are generally lower compared with fat and edible offal's.

<Insert table III>

A further analysis of the values in table III was achieved for each animal product by calculating the statistical parameters also for each contaminant class. These values are given in table IV (meat, fat and edible offal's), and table V (eggs and whole milk).

<Insert table IV>

<Insert table V>

In general, the distribution of the transfer factors displayed a log-normal distribution for each contaminant class. The main exception was the population of transfer factors for the PCBs/PBBs in fat, for which a bimodal distribution pattern was found. Overall, it is noted that (as was to be expected) the transfer factor is depending on the lipophilicity of the compound (determined by the octanol-water partition coefficient; log Po/w), the potential accumulation of the compound in animal matrices, and/or the feeding level and feeding period. The highest transfer factors determined in the animal matrices were in the order fat > edible offal's > meat > eggs > whole milk. The highest transfer factors found in animal fat are indeed found to be related to lipophilic compounds which tend to accumulate in the body fat ("old" pesticides, dioxins, furans, PCBs, and PBBs). It is noted that these fat accumulating contaminants also showed a higher potential for egg and edible offal's, but less for whole milk. Metal compounds with potential accumulation in edible offal's are cadmium, copper, mercury, selenium, and zinc. Time related accumulation of metals was observed in edible offal's, but not in meat, fat, whole milk or fat, considering the concurrent P_{95} values.

The inclusion of feeding levels and feeding periods in the database are of importance to refine the selection of relevant data within the dataset before a transfer factor is elaborated in case of e.g. accumulating compounds. As can be seen in figure I, the transfer factors of edible offal after intake of cadmium for ca. 50 days are rather comparable between the different feeding levels ranging from 0.09 to 48 mg/kg. After a further continuous exposure, the transfer factors will differentiate depending on the dose. If tissue levels become too high, saturation will become apparent showing lower increase of the transfer factors (see the slope of the feeding level of 48 mg/kg in figure I), although the actual tissue concentration is still rising. At feeding levels of 300 and 600 mg/kg, respective concentrations of 668 mg/kg (TF= 2.2) and 667 mg/kg (TF= 1.1) in edible offal's are found at 70 days exposure (Bokori, 1995), showing a ceiling cadmium level in edible offal at 70 days.

<Insert figure I>

The use of contaminant classes will not in each case be applicable or scientifically valid in case a contaminant in the feed is found. Therefore, the use of transfer factors related to the physico-chemical properties of the compound was examined. Statistical analysis was performed using the respective molecular weight (MW) and the respective experimentally established or estimated log Po/w. Considering the transfer factors based on the molecular weight, no clear discrimination could be made between the groups defined. Main reason is the non-homogeneous distribution of the compounds over the molecular weight groups. Furthermore, the presence of accumulating metal compounds is highly affecting the outcome of the transfer factors of meat and edible offal at a MW below 100, as a large amount of transfer factors of metal contaminants are present without information on the respective anion (only metal levels reported in the respective studies). For these reasons the transfer factors based on the MW were not considered a feasible discriminator based on the available dataset. Establishing log Po/w categories between 0 and 8, using an increment of 1 between each category, showed a rather homogeneous distribution of the transfer data per group. The respective transfer factors and the amount of data available at the 95 percentile for each of the matrices are given in table VI. As no log Po/w can be calculated for inorganic compounds, it was decided to form separate groups for the metal compounds. P_{95} transfer factors are calculated covering the whole group of metals, accumulating metals (cadmium, copper, mercury, selenium and zinc), and non-accumulating metals. These figures are also included in table VI.

<Insert table VI>

Based on the data in table VI, relative low transfer factors are found with compounds having a log Po/w below 3, and for whole milk. High transfer factors are found in the log Po/w categories of 3-4 and 5-8, with highest transfer factors in fat at a log Po/w between

6 and 7. It is remarkable that the group with a log Po/w of 4-5 has much lower transfer factors compared to the adjoining groups for all matrices. It is noted that this observation seems not to be biased due to a small number of observations.

Use of the transfer database in risk assessment

Based on the current dataset, transfer factors based on the 95th percentile (P_{95}) can be used as a first step for assessing the transfer of specific contaminants. These P_{95} values can be applied in a tiered approach of risk assessment. In case chemical specific transfer data are available in the dataset, the actual data can be used in the risk assessment. If no chemical specific transfer data are available, the P_{95} value of the respective log Po/w category or the respective chemical group may be used. It is noted that in case transfer factors of a specific chemical group are considered, one should think about the surplus value of the chemical group over the respective log Po/w data, since assigning chemical groups is in general relatively arbitrary taken the biological processes influencing the transfer factors into account. At last a generic approach, by using the overall transfer factors of the respective edible commodity (see table III), might be considered for components for which little to no information is present, e.g. unidentified components.

It is noted that without the use of database derived transfer factors, only a literature search, which should include the fate and behavior of the contaminant, or, in case no compound specific information could be retrieved from the public literature, a worst case scenario can be used in the risk assessment. This approach is not only time consuming, but also limited to the contaminant, whereas information on comparable chemicals may be of value to estimate the transfer of the respective contaminant from the feed to the edible commodities. The use of database derived transfer factors in risk assessment, including a comparison using worst case assumptions, is illustrated in 3 case studies below.

Case 1: Nickel contamination.

To illustrate the value of the database, we used a case of a possible metal contamination of a raw material to be used in the production of animal feed. The question was raised about the consumer risks upon a possible presence of nickel in dairy cattle feed. The feed's contamination level was expected to be maximally 1.5 mg/kg feed (dry weight basis).

In order to perform a risk assessment, the maximum transfer factors of nickel were retrieved from the database for each commodity. As comparison, also the P_{95} transfer factor of the contaminant class of metals (and the subgroup of non-accumulating metals), the maximum metal transfer factor, and the transfer factors based on the overall P_{95} transfer factor were retrieved from the database to simulate an increasing level of uncertainty in case insufficient information on nickel would be present in the database. A comparison to a traditional risk assessment was made using worst case assumptions. For this we assumed complete absorption and retention of nickel by livestock animals and complete distribution towards (one of the) edible commodities. To bring some nuance into the worst case approach, we assumed a steady state after feeding for about 1 week (> 5 times the plasma half life). This would mean that only the cumulative nickel intake for 1 week would add to the ultimate residue levels in edible commodities. The respective transfer factors are given in table VII, in order of the assumed highest to lowest uncertainty.

<Insert table VII>

We used the figures of table VII as a basis for the risk assessment. For health risk assessment, a Tolerable Daily Intake (TDI) for nickel of 0.05 mg nickel per kg body weight per day (or 3 mg/person/day, assuming a body weight of 60 kg) can be used, as proposed by the Dutch National Institute of Public Health and the Environment (Baars *et al.*, 2001). Furthermore, a human consumption pattern is used, as assumed in the health risk assessment for residues of Veterinary Medicinal Products (EC, 2003) i.e. daily consumption of 1.5 kg of milk and milk products, 100 g eggs and egg products, 300 g meat, 50 g fat, 100 g liver, and 50 g kidney. On the basis of these figures and the presumed worst case assumptions, consumption of the cattle commodities would lead to intake estimates which can be compared to its respective TDI.

Based on these transfer factors, the intake by the consumption of the respective commodities was calculated as a percentage of the TDI for each commodity (see table VIII).

<Insert table VIII>

The results presented in table VIII indicate that in general with a growing level of uncertainty, an increased consumer risk is indicated. One should keep in mind that the nickel data are based upon actual (experimental) data, and as such can serve as comparison for the other evaluations. Looking at the P_{95} transfer factors for nickel it is noted that not kidney or liver, as estimated by the worst case approach or the maximum metal transfer factor, but meat may be the major source of nickel residue intake by consumers. The nickel intake via meat is in fact rather comparable to the calculations based on worst-case assumptions, the overall P_{95}, and the metal P_{95} transfer factors. Yet, it appears that the intake by whole milk and fat is expected to be much lower than assumed on the basis of the worst case assessment. Although differences in the intake calculations exist between the evaluations, it is noted that in case of lacking data for a specific metal, the P_{95} transfer factor of the contaminant class of (non-) accumulating metals is a better alternative over the worst case approach, showing intake estimations rather near the actual data.

Case 2: Contamination based on physical chemical properties (log Po/w <3).

To demonstrate the use of transfer factors based on physical chemical properties of a compound, experimental transfer data of a veterinary medicinal product were compared to database derived transfer factors based on the 95^{th}-percentile of the respective log Po/w class. Oikawa *et al.* (1977) exposed chicken for 5 successive days to 2000 and 4000 mg/kg of sulfamethoxazole (SMX) via feed. The log Po/w of SMX is 0.89 (chemfinder.com; experimental data of Hansch, 1995). Residue levels of free SMX in meat, fat, kidney, and egg including their respective calculated transfer factors, and the database derived transfer factors (P_{95}) are given in table IX. It is noted that SMX was not included in the database.

<Insert table IX>

When comparing the calculated and databases derived transfer factors after exposure to SMX, it is noted that the database derived transfer factors are about 10 times higher than calculated using the experimental data. This might be expected considering the short (5 day) exposure period to SMX. Although the database derived transfer factors are higher than might be expected form the experimental data, it is noted that when using worst case assumptions, considerable higher transfer factors are indicated (e.g. egg; 3.2, meat; 1.1, fat; 2.9, and kidney; 76). The worst case assumptions considered were a full absorption of SMX, followed by a complete distribution towards the matrix under consideration, no excretion of SMX, whereas an accumulation of SMX during 7 days is assumed for meat, fat, and kidney, taking into account a bodyweight of 1.9 kg, comprised of meat, fat and kidney, for 40%, 15%, and 0.6% of the bodyweight, respectively. An egg weight is considered of 0.053 kg (size S) with an egg production of 0.7 eggs/day. The database derived transfer factors is therefore considered to be of value for a more refined estimation of transfer compared to worst case assumptions.

Case 3: Contamination based on physical chemical properties (log Po/w ≥ 3).

Equivalent to case 2, a comparison is made based on the physical chemical properties of compounds with a relative high log Po/w, for which accumulation might be suspected in one or more edible matrices. Experimental data on the transfer of 3 dioxins and 1 furan from feed to fat are compared to the database derived transfer factor based on the 95th-percentile of the respective log Po/w class. The compounds used for the comparison were not (yet) included in the database when the comparison was made. Thorpe *et al.* (2001) exposed cattle for 4 weeks to a defined mixture of PCDD/F congeners, corresponding to feed levels of 7.5 ng/kg of each congener. After a recovery period of 1 week the animals were slaughtered. Analysis of the individual congeners was performed in fat, and the fat fraction of liver and meat. As no information was provided on the fat fraction of liver and meat, only the transfer of feed to fat was considered (see table X). It is noted that because of the one week recovery period, the highest residue reported was used for the calculations, instead of an average.

<Insert table X>

When calculating the actual transfer factors of the respective compounds based on the analytical data by dividing the concentration in fat by the concentration in feed, rather comparable transfer factors were elaborated for fat ranging from 5.7 to 7.6. Comparing these transfer factors to the database derived transfer factor based on the contaminant class of dioxins/furans (9, see table IV), the elaborated transfer factor to fat is about a factor 1.5 times higher than might be expected from the actual data. When elaborating the transfer factor based on the log Po/w class of 6-7 (table VI), the database derived transfer factor to fat is 30, which is about a factor 4.5 times higher than the calculated transfer factor based on the actual data. Considering the fat accumulating potential of the compounds present in the respective dioxins/furans class or the log Po/w class of 6-7, the P_{95} value is highly related to long term (> 1 Year) exposure. In case a longer exposure period is considered, it is expected that an increase in the actual transfer factor will be apparent. It is noted that when worst case assumptions were made, a transfer factor of 20 for fat was calculated. The worst case assumptions considered were a full absorption of each congener, followed by a complete distribution towards the fat, no excretion of the congeners, whereas an accumulation during 7 days is assumed, taking into account a bodyweight of 550 kg and a slaughter weight of 7 kg of fat. A limited accumulation period was chosen taking the recovery period of 1 week into account. Again a refinement can be made by restriction of data to be included for the calculation of the database derived transfer factor, by selecting the respective feeding periods or exposure concentrations. The database derived transfer factors showed an approximate 1.5 to 4.5 fold higher transfer compared to the actual data. It is however noted that for the actual data, a one week recovery period is included, whereas the transfer database is based on a continuous exposure until slaughter which may indicate somewhat higher levels in the animal matrices. As the compounds considered in this case are stable and have a high affinity for fat, the one week recovery is not considered to have a major effect on the decline of the compounds during the recovery period. Furthermore, the highest residue levels reported were used for the calculation of the actual transfer which is considered to compensate for a possible decline of the mean contamination values in fat. Taking these data into account, the database derived transfer factors showed a somewhat higher prediction of the actual transfer, but are regarded to give a more accurate prediction than when considering the transfer using worst case assumptions. Therefore, also in this case the use of database derived transfer factors is considered favorable over calculations using worst case assumptions.

Conclusion

It is not feasible to generate chemical-specific information for every compound for every situation at any moment, especially considering possible (differences in) metabolism, feed concentrations and exposure periods for each livestock animal. In this respect, the use of database derived transfer factors showed to be a powerful tool for the evaluation of contaminants and enables rapid risk management decision making and/or intervention.

Three cases of repeated exposure showed that the use of database derived transfer factors, based on the P_{95} values of contaminant or log Po/w classes, results in a rather accurate prediction of the presence of the respective contaminant in the edible commodity when compared to the actual experimental transfer factors. A slight overestimation of the transfer, as observed in most of the cases, is most likely related to the limited contaminant feeding period. Deriving transfer factors from the database restricted to actual feeding periods, feeding levels and/or relevant animals, will provide a more accurate prediction of the transfer than when all data in the respective group, including long term feeding periods, are used. Future studies with the database will be aimed at this refinement.

When the risk assessment using database derived transfer factors is compared to the risk assessment using worst case assumptions, the database derived transfer factors provide a far more accurate indication of the contaminant levels and its concurrent risk estimation, than when using the traditional worst-case approach. Further studies will also be aimed at a further validation of this approach. Great care should be taken when worst-case assumptions are used for assumed accumulating contaminants like highly lipophilic compounds (log Po/w of 5 to 8) or cadmium, copper, mercury, selenium or zinc containing compounds. Especially for these compounds, database derived transfer factors based on physical chemical properties or structural related compounds may provide a more rapid and accurate prediction than in case of using worst case assumptions.

Using database derived transfer factors, an evaluation can be performed using data of the specific compound, structural related compounds, compounds with comparable physico-chemical properties, or contaminant classes, if needed at specified feeding levels and/or feeding periods. Furthermore, the relative vulnerability of animal matrices to a feed contaminant can be evaluated. Instead of using worst-case assumptions, a generic approach in risk assessment, by using the overall transfer factors of the respective edible commodity, is preferable in case limited data on the identity or properties of the contaminant involved are available. When compared to a risk assessment using worst-case assumptions, a better understanding of the transfer of feed contaminants and residues to animal products resulting in a more refined risk assessment is possible using data base derived transfer factors.

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Table I List of chemicals present in the chemical classes

Pesticides (new)	CAS no.	(Heavy) metals	CAS no.
2,4-D	94-75-7	Aluminum	
2-Aminobutane	13952-84-6	Aluminum chloride	16603-84-2
Acephate	30560-19-1	Antimony	
Anilazine	101-05-31	Arsenic	
Atrazin	1912-24-9	Arsenic trioxide	
Azinfos-methyl	86-50-0	Cadmium	
Benomyl	17804-35-2	Cadmium chloride	10108-64-2
Chlorpyrifos	2921-88-2	Cadmium acetate	543-90-8
Cryomazine	66215-27-8	Cadmium sulphate	10124-36-4
Cyfluthrin	68359-37-5	Cadmium (Metallothionein)	
Deltamethrin	52918-63-5	Chromium	
Dimethoate	60-51-5	Chromium picolineate	
Famoxadone	131807-57-3	Chromium chloride	10025-73-7
Fenbuconazole	114369-43-6	Chromium 3+ (potassium chromate)	39322-04-8
Fenthion	55-38-9	Chromium 6+ (potassium chromate)	7789-00-6
Fluquinconazole	136426-54-5	Chromium 3+ (chromium sulphate)	10101-53-8
Imidacloprid	105827-78-9	Chromium rutile	
Kresoxim-methyl	143390-89-0	Sodium chromate	7775-11-3
Lambda-cyhalothrin	91465-08-6	Iron	
Methamidophos	10265-91-6	Ferric chloride	7705-08-0
Pirimicarb	023103-98-2	Cobalt	
Pirimiphos-methyl	29232-93-7	Cobalt carbonate	7542-09-8
Tebuconazole	107534-96-3	Cobalt (II) chloride	7646-79-9
		Copper	
		Copper sulphate	7758-98-7

Pesticides (old)	CAS no.
Aldrin	309-00-2
a-BHC	319-84-6
Chlordane	57-74-9
DDE	3547-04-4
DDT	50-29-3
Dieldrin	60-57-1
Endrin	72-20-8
HCB	118-74-1
a-HCH	319-84-6
b-HCH	319-85-7
b-Hepo	
Heptachlor	76-44-8
Lindane (g-BHC)	58-89-9
Methoxychlor	72-43-5
Mirex	2385-85-5
PCP	87-86-5

Mercury	
Mercury actetate	1600-27-7
Methyl-mercury dicyandiamide	502-39-6
Phenylmercuric acetate	62-38-4
Phenylmercuric hydroxide	100-57-2
Methoxyethyl mercury hydroxide	
Methylmercuric hydroxide	1184-57-2
Mercury nitrate	10045-94-0
Methylmercury	
Phenylmercury	
Ethylmercury chloride	107-27-7
Acetato fenylmercury	62-38-4
Lead	
Lead acetate	301-04-2
Lead oxide	1317-36-8
Lead sulphate	15739-80-7
Manganese	
Manganese chloride	7773-01-5
Molybdene	
Nickel	
Nickel chloride	7718-54-9
Nickel rutile	
Rubidium	
Sodium selenite	26970-82-1
Selenium	
Tin	
Vanadium	
Zinc	

Zinc sulphate	7733-02-0
Zinc lysine	

Mycotoxins	**CAS no.**
Aflatoxin B1	1162-65-8
Aflatoxin B2	7220-81-7
Aflatoxin G1	1165-39-5
Aflatoxin G2	7241-98-7
Deoxynivalenol	51481-10-8
Ochratoxine A	303-47-9
T-2 toxin	21259-20-1
Zearalenone	17924-92-4

Dioxins/Furans	**CAS no.**
OCDF	39001-02-0
OCDD	3268-87-9
2,3,7,8-TCDF	51207-31-9
2,3,7,8-TCDD	1746-01-6
2,3,4,7,8-PCDF	57117-31-4
2,3,4,6,7,8-HCDF	55684-94-1
1,2,4,6,8,9-HCDD	34465-46-8
1,2,3,7,8-PCDF	57117-41-6
1,2,3,7,8-PCDD	40321-76-4
1,2,3,7,8,9-HCDF	72918-21-9
1,2,3,7,8,9-HCDD	19408-74-3
1,2,3,6,8,9-HCDD	58200-69-4
1,2,3,6,7,8-HCDF	57117-44-9

PCB's/PBB's	**CAS no.**
Aroclor 1254	11097-69-1
PCB	608-93-5
PBB	67774-32-7
Firemaster BP-6	59536-65-1
2,2',4,4',5,5'-PBB	59080-40-9
2,2',3,4,4',5,5'-PBB	
PCB1	2051-60-7
PCB7	
PCB15	2050-68-2
PCB18	37680-65-2
PCB28	7012-37-5
PCB47	2437-79-8
PCB52	35693-99-3
PCB66	32598-10-0
PCB74	32690-93-0
PCB77	32598-13-3
PCB95	38379-99-6
PCB101	37680-73-2
PCB101	37680-73-2
PCB105	32598-14-4
PCB110	38380-03-9
PCB114	74472-37-0
PCB118	31508-00-6
PCB126	57465-28-8

1,2,3,6,7,8-HCDD	57653-85-7	PCB128	38380-07-3
1,2,3,4,7,8-HCDF	70648-26-9	PCB138	35065-28-2
1,2,3,4,7,8-HCDD	39227-28-6	PCB141	52712-04-6
1,2,3,4,7,8,9-HpCDF	55673-89-7	PCB149	38380-04-0
1,2,3,4,6,8-HCDD		PCB151	52663-63-5
1,2,3,4,6,7,9-HpCDD	58200-70-7	PCB153	35065-27-1
1,2,3,4,6,7,8-HpCDF	67562-39-4	PCB156	38380-08-4
1,2,3,4,6,7,8-HpCDD	35822-46-9	PCB157	69782-90-7
		PCB167	52663-72-6
		PCB169	32774-16-6
		PCB170	35065-30-6
		PCB180	35065-39-3
		PCB183	52663-69-1
		PCB187	52663-68-0
		PCB189	39635-31-9
		PCB194	35694-08-7
		PCB198	
		PCB206	40186-72-9
Veterinary medicines	**CAS no.**	**Nitrosamins**	**CAS no.**
Aminosidine	7542-37-2	N-nitrosodiethylamine (DENA)	55-18-5
Amprolium	121-25-5	N-nitrosodimethylamine (DMNA)	62-75-9
Avermectin B1a	71751-41-2	N-nitrosodipropylamine (DPNA)	621-54-7
Avilamycin	11051-71-1		
Bacitracin	1405-87-4		
Chloroamphenicol	56-75-7	**Hormones**	**CAS no.**
Chlorotetracycline	57-62-5	Melengestrol acetate	2919-66-6
Diclazuril	101831-37-2	Estradiol	50-28-2

Decoquinate	18507-89-6
Dimetridazole	551-92-8
Dinitolmide	148-01-6
Doxycycline	564-25-0
Erythromycin thiocyanate	114-07-8
Flubendazole	31430-15-6
Flumequin	42835-25-6
Furaltadone	139-91-3
Furazolidone	67-45-8
Halofuginone	55837-20-2
Lasalocid	11054-70-9
Monensin	17090-79-8
Narasin	55134-13-9
Neomycin	1404-04-2
Nicarbazin	330-95-0
Nifursol	16915-70-1
Nitrofurazone	59-87-0
Olaquindox	23696-28-8
Ormetoprim	6981-18-6
Oxolinic acid	14698-29-4
Oxytetracycline	79-57-2
Pyrimethamine	58-14-0
Robenidine	25875-51-8
Salinomycin	53003-10-4
Salinomycin sodium salt	55721-31-8
Spiramycin	8025-81-8
Spiramycin embonate	67724-08-7
Sulfachlorpyrazine	1672-91-9

Other	**CAS no.**
Citrinin	518-75-2
Sodium chlorate	7775-09-9
Acrylamide	79-06-1
Linoleic acid (Conjugated)	60-33-3
Fattyacid 20:4 n-6	
Fattyacid 20:5 n-3	
Fattyacid 22:6 n-3	
Eicosapentaenoic acid (20:5 n-3)	10417-94-4
Docosahexaenoic acid (22:6 n-3)	6217-54-5

Sulfadiazine	68-35-9
Sulfadimidine	57-68-1
Sulfadimethoxine	122-11-2
Sulfamethazine	57-68-1
Sulfaguanidine	57-67-0
Sulfamerazine	127-79-7
Sulfamethoxazole	723-46-6
Sulfamonomethoxine	1220-83-3
Sulfanilamide	63-74-1
Sulfaquinoxaline	59-40-5
Sulfisoxazole	127-69-5
Tetracycline	60-54-8
Trimethoprim	738-70-5
Tylosin	1401-69-0

Table II Contents of the database on transfer factors in animal commodities

Contaminant class	Number of transfer factors in each animal commodity					
	Eggs	Whole milk	Meat	Fat	Edible offal's	Total
All	433	532	920	632	1107	3624
Pesticides ("new")	85	133	222	210	227	877
Pesticides ("old")	44	66	5	146	12	273
(Heavy) metals	34	113	409	17	519	1092
Mycotoxins	66	20	126	62	184	458
Dioxins/Furans	46	88	34	91	37	296
PCBs/PBBs	1	77	32	56	35	201
Nitrosamines	2	15	2	0	2	21
Hormones	1	0	3	9	0	13
Vet. medicines	142	5	81	38	86	352
Other	12	15	6	3	5	41

Table III Overall transfer of all contaminants from feed to eggs, whole milk, meat, fat and edible offal's

Animal product	Overall transfer factor				
	GM	GSD	Median	P_{95}	Max
Eggs	0.18	0.49	0.007	1.14	5.5
Whole milk	0.10	0.18	0.013	0.50	1.4
Meat	0.09	0.34	0.008	0.33	6
Fat	3.0	10	0.046	15	180
Edible offal's	0.77	2.5	0.04	3.7	52

GM = geometric mean,

GSD = geometric standard deviation,

P_{95} = 95 percentile value,

Max = maximum value

Table IV Transfer factors for various contaminants into meat, edible offal's and fat

Commodity	Contaminant class	N	Transfer factor GM	GSD	Median	P_{95}	Max
Meat	Pesticides ("new")	222	0.006	0.013	0.0024	0.02	0.17
	Pesticides ("old")	5	0.032	0.026	0.029	0.07	0.07
	(Heavy) metals	409	0.17	0.50	0.023	0.8	6.1
	Mycotoxins	126	0.0060	0.023	0.0004	0.021	0.24
	Dioxins/Furans	34	0.11	0.10	0.08	0.33	0.33
	PCBs/PBBs	32	0.14	0.10	0.12	0.32	0.36
	Nitrosamines	2	0.022	0.004	0.022	0.024	0.025
	Hormones	3	0.01	0.0041	0.0090	0.012	0.012
	Vet. medicines	81	0.009	0.026	0.0022	0.027	0.18
	Other	6	0.018	0.040	0.001	0.077	0.10
Fat	Pesticides ("new")	210	0.025	0.067	0.0033	0.13	0.50
	Pesticides ("old")	146	10	19	5	30	180
	(Heavy) metals	17	0.10	0.30	0.011	0.35	1.3
	Mycotoxins	62	0.0051	0.0081	0.0020	0.021	0.042
	Dioxins/Furans	91	1.5	3.1	0.39	9	18
	PCBs/PBBs	56	3.9	5.2	1.7	16	18
	Hormones	9	0.53	0.31	0.55	1.0	1.2
	Vet. medicines	38	0.022	0.054	0.0021	0.15	0.22
	Other	3	0.00011	0.00006	0.00013	0.00014	0.00014
Edible offal's	Pesticides ("new")	227	0.017	0.04	0.005	0.08	0.25
	Pesticides ("old")	12	0.76	0.98	0.38	2.7	3.0
	(Heavy) metals	519	1.5	3.4	0.33	6.6	52
	Mycotoxins	184	0.024	0.20	0.0022	0.047	2.76

Commodity	Contaminant class		Transfer factor					
		N	GM	GSD	Median	P_{95}	Max
	Dioxins/Furans	37	1.3	4.0	0.070	6.5	18
	PCBs/PBBs	35	0.7	1.0	0.2	2.7	3.9
	Nitrosamines	2	0.023	0.00028	0.023	0.023	0.023
	Vet. medicines	86	0.048	0.12	0.0091	0.19	0.99
	Other	5	0.001	0.001	0.001	0.001	0.001

N = total amount of transfer factors, GM = geometric mean, GSD = geometric standard deviation, P_{95} *= 95 percentile value*

Table V Transfer factors for various contaminants into eggs and whole milk

Commodity	Contaminant class	N	Transfer factor				
			GM	GSD	Median	P_{95}	Max
Eggs	Pesticides ("new")	85	0.010	0.020	0.0049	0.03	0.17
	Pesticides ("old")	44	1.2	0.96	1.2	2.5	5.5
	(Heavy) metals	34	0.038	0.050	0.016	0.17	0.17
	Mycotoxins	66	0.0068	0.021	0.0006	0.018	0.11
	Dioxins/Furans	46	0.28	0.27	0.17	0.84	1.0
	PCBs/PBBs	1	0.92		0.92		0.92
	Nitrosamines	2	0.051	0.0155	0.051	0.061	0.062
	Vet. medicines	142	0.028	0.082	0.0050	0.12	0.81
	Other	12	0.09	0.071	0.11	0.17	0.18
Whole milk	Pesticides ("new")	133	0.0052	0.0080	0.0020	0.020	0.044
	Pesticides ("old")	66	0.25	0.16	0.25	0.52	0.62
	(Heavy) metals	113	0.027	0.062	0.0050	0.12	0.50
	Mycotoxins	20	0.0018	0.0015	0.0016	0.0046	0.005
	Dioxins/Furans	88	0.12	0.14	0.079	0.42	0.57
	PCBs/PBBs	77	0.26	0.32	0.13	0.87	1.4
	Nitrosamines	15	0.012	0.013	0.008	0.034	0.042
	Vet. medicines	5	0.006	0.008	0.005	0.017	0.020
	Other	15	0.17	0.20	0.041	0.51	0.53

N = total amount of transfer factors, GM = geometric mean, GSD = geometric standard deviation, P_{95} = 95 percentile value

Table VI Transfer factors categorized by log Po/w

Log Po/w	Transfer factor					
	Egg P$_{95}$ (N)	Whole milk P$_{95}$ (N)	Meat P$_{95}$ (N)	Fat P$_{95}$ (N)	Edible Offal's [1] P$_{95}$ (N)	All Matrices P$_{95}$ (N)
<0	0.03 (66)	0.02 (25)	0.02 (80)	0.01 (57)	0.02 (94)	0.02 (322)
0 to 1	0.05 (37)	0.03 (15)	0.04 (18)	0.01 (13)	0.30 (18)	0.04 (101)
1 to 2	0.04 (96)	0.02 (30)	0.01 (117)	0.01 (64)	0.02 (144)	0.02 (451)
2 to 3	0.13 (38)	0.01 (29)	0.02 (71)	0.02 (45)	0.04 (81)	0.03 (264)
3 to 4	0.92 (38)	0.33 (48)	0.01 (51)	**14.1** (77)	0.21 (65)	**2.00** (279)
4 to 5	0.11 (16)	0.03 (19)	0.05 (69)	0.58 (58)	0.08 (68)	0.25 (230)
5 to 6	**2.43** (26)	0.43 (45)	0.03 (35)	**17.0** (81)	**1.50** (36)	**14.0** (223)
6 to 7	**1.60** (44)	0.52 (108)	0.33 (32)	**30.0** (137)	**2.62** (39)	**14.0** (360)
7 to 8	0.75 (23)	0.90 (51)	0.33 (28)	**16.3** (48)	**2.79** (28)	**2.73** (178)
>8	0.21 (13)	0.32 (30)	0.04 (8)	0.74 (27)	0.08 (8)	0.38 (86)
Metals total	0.17 (34)	0.12 (112)	0.82 (408)	0.35 (17)	**6.61** (516)	**3.54** (1087)
Accumulating metals	0.17 (30)	0.15 (54)	**1.47** (219)	0.74 (10)	**9.62** (290)	**5.03** (603)
Non-accumulating metals	0.00 (4)	0.06 (58)	0.30 (189)	0.11 (7)	0.72 (226)	0.52 (484)

P$_{95}$ = 95 percentile value, N = total amount of transfer factors in the respective subgroup

[1] Edible offal's = liver and kidney

Table VII Case study of nickel contamination, transfer factors

	Transfer factor				
	Worst case	P_{95} overall	Max. metal	P_{95} metal (non-acc[a])	P_{95} Nickel
Whole milk	0.80	0.50	0.50	0.12 (0.06)	0.024 (0.025)
Meat	0.60	0.33	6.1	0.82 (0.30)	0.58 (0.66)
Fat	20	15	1.3	0.35 (0.11)	0.12 (0.13)
Liver	20	3.7	52	6.6 (0.72)	0.70 (0.72)
Kidney	74	3.7	52	6.6 (0.72)	0.70 (0.72)

[a] *P_{95} of non-accumulating metals*

Table VIII Case study of nickel contamination: percentage of the tolerable daily intake (TDI)

	% TDI				
	Worst case	P_{95} overall	Max. metal	P_{95} metal (non- acc[a])	P_{95} Nickel
Whole milk	60	38	38	9.0 (4.5)	1.8
Meat	9.0	5.0	92	12 (4.4)	8.7
Fat	50	38	3.3	0.88 (0.28)	0.30
Liver	100	19	259	33 (3.6)	3.5
Kidney	185	9.3	129	17 (1.8)	1.8

[a] *P_{95} of non-accumulating metals*

Table IX Transfer data on sulfamethoxazole in poultry

	Free SMX (mg/kg)		Calculated Transfer Factor		Worst case Transfer Factor	Database derived Transfer Factor (P_{95})[b]
	2000 mg/kg in feed	4000 mg/kg in feed	2000 mg/kg in feed	4000 mg/kg in feed		
Egg[a]	13.6	26.3	0.007	0.007	3.2	0.05
Meat	9.74	34.9	0.005	0.009	1.1	0.04
Fat	1.50	4.95	0.001	0.001	2.9	0.01
Kidney	51.7	118	0.026	0.029	76	0.30

[a] *Egg data are derived using an egg white:yolk ratio of 65:35*

[b] *Log Po/w class: 0-1*

Table X Transfer data of PCDD and PCDF in cattle

	Log Po/w	Levels in fat (mg/kg)	Calculated Transfer Factor	Database derived Transfer Factor (P_{95})
2,3,7,8-TCDD	6.08	5.6×10^{-5}	7.5	9[a] 30[b]
1,2,3,7,8-PeCDD	6.05	5.7×10^{-5}	7.6	
1,2,3,6,7,8-HxCDD	6.77	4.3×10^{-5}	5.7	
2,3,4,7,8-PeCDF	6.92	4.5×10^{-5}	6.7	

[a] *Contaminant class of dioxins/furans in fat*

[b] *Log Po/w class: 6-7*

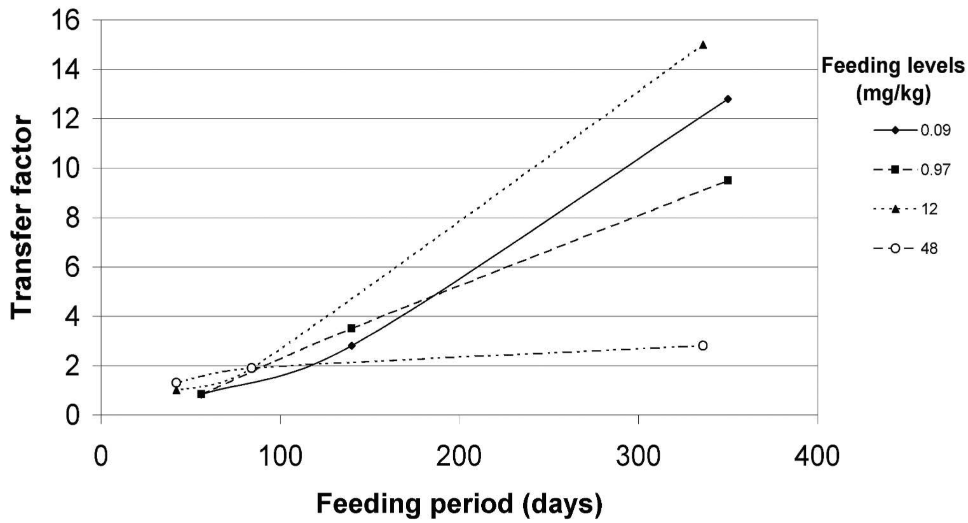

Figure I Transfer factor curves of cadmium in poultry edible offal's
199x121mm (600 x 600 DPI)