

2000



COUNCIL OF EUROPE CONSEIL DE L'EUROPE

DIOXIN CONTAMINATION IN FOODSTUFFS

**Report prepared by Jean-François Narbonne,
rapporteur for the Committee of Experts on
nutrition, food safety and consumer health**

Health protection of the consumer

Council of Europe Publishing

Partial Agreement Division in the Social and
Public Health Field
Directorate General III – Social Cohesion
F – 67075 STRASBOURG Cedex
Web site: <http://www.coe.fr/soc-sp>

CONTENTS

	<i>Page</i>
PREFACE	5
1. INTRODUCTION	9
2. HAZARD CHARACTERISATION.....	10
3. EXPOSURE EVALUATION.....	14
4. RISK MANAGEMENT AND RECOMMENDATIONS.....	16

PREFACE

THE COUNCIL OF EUROPE

The Council of Europe is a political organisation which was founded on 5 May 1949 by ten European countries in order to promote greater unity between its members. It now numbers 41 member States¹.

The main aims of the Organisation are to reinforce democracy, human rights and the rule of law and to develop common responses to political, social, cultural and legal challenges in its member States. Since 1989 the Council of Europe has integrated most of the countries of central and eastern Europe into its structures and supported them in their efforts to implement and consolidate their political, legal and administrative reforms.

The work of the Council of Europe has led, to date, to the adoption of over 170 European conventions and agreements, which create the basis for a "common legal space" in Europe. They include the European Convention on Human Rights (1950), the European Cultural Convention (1954), the European Social Charter (1961), the European Convention on the Prevention of Torture (1987) and the Convention on Human Rights and Bioethics (1997). Numerous recommendations and resolutions of the Committee of Ministers propose policy guidelines for national governments.

The Council of Europe has its permanent headquarters in Strasbourg (France). By Statute, it has two constituent organs: the Committee of Ministers, composed of the Ministers of Foreign Affairs of the 41 member States, and the Parliamentary Assembly, comprising delegations from the 41 national parliaments. The Congress of Local and Regional Authorities of Europe represents the entities of local and regional self-government within the member States. These bodies and the intergovernmental committees are served by a multinational European Secretariat.

¹ Albania, Andorra, Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Moldova, The Netherlands, Norway, Poland, Portugal, Romania, Russian Federation, San Marino, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, "the former Yugoslav Republic of Macedonia", Turkey, Ukraine, United Kingdom of Great Britain and Northern Ireland.

PARTIAL AGREEMENT IN THE SOCIAL AND PUBLIC HEALTH FIELD

The Council of Europe has a vast range of activities since only questions of defence are excluded from its competence.

Where a lesser number of member states of the Council of Europe wish to engage in some action in which not all their European partners desire to join, they can conclude a 'Partial Agreement' which is binding on themselves alone.

The Partial Agreement in the social and public health field was concluded on this basis in 1959. At present, the Partial Agreement in the public health field has 18 member states².

The principal areas of activity include:

- protection of public health and especially the health of the consumer
- rehabilitation and integration of people with disabilities.

The activities are entrusted to Committees of experts, which are responsible to a Steering committee for each area.

The work of these Partial Agreement committees occasionally results in the elaboration of conventions or agreements, but the more usual outcome is the drawing-up of recommendations to member states in the form of resolutions adopted by the Committee of Ministers. The resolutions should be considered as statements of policy for national policy-makers. Governments have actively participated in their formulation: the delegates to the Partial Agreement committees are both experts in the field in question and responsible for the implementation of government policy in their national ministries.

² Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Ireland, Italy, Luxembourg, The Netherlands, Norway, Portugal, Slovenia, Spain, Sweden, Switzerland, United Kingdom of Great Britain and Northern Ireland.

This procedure provides for considerable flexibility in that any state may reserve its position on a given point without thereby preventing the others from going ahead with what they consider appropriate. Another advantage is that the resolutions are readily susceptible to amendment should the need arise. Governments are furthermore called upon periodically to report on the implementation of the recommended measures.

A less formal procedure is the publication of general guidelines intended to serve as a model for member States. Each government can interpret these guidelines in accordance with its own law and practice in the matter.

Furthermore, scientific reports aimed at informing both governments and experts in the field are published on specific questions of current concern.

Bodies of the Partial Agreement in the social and public health field enjoy close co-operation with equivalent bodies in other international institutions. Contact is also maintained with international non-governmental organisations (INGOs) and industry, working in similar or related fields.

DIOXIN CONTAMINATION IN FOODSTUFFS

Dioxins can be found as contaminants in almost every part of the environment and therefore present an obvious public health concern. The present report outlines the health hazards posed by dioxins and evaluates human exposure to and intake of dioxins from foodstuffs. It also sets out recommendations for relevant source-directed measures for reducing the contamination of food by dioxins and gives guidance on risk management in foods.

1. INTRODUCTION

Polychlorinated dibenzo-*p*-dioxins (PCDDs) and dibenzofurans (PCDFs) are halogenated aromatics compounds that have been identified as contaminants in almost every component of the global ecosystem including the air, aquatic and marine sediments, fish, wildlife and human adipose tissue, milk and blood. PCDDs and PCDFs are industrial by-products that are formed during the production of chlorinated phenols and their derived products and other chlorinated compounds. These contaminants have also been identified as by-products from the combustion of municipal and industrial waste, petrol, wood, coal and numerous other combustion processes. Lastly, PCDDs and PCDFs are formed during the bleaching of wood and pulp paper, and during metal-producing and metal-recycling processes. The structures of individual PCDD and PCDF congeners differ by their degree of chlorination and the ring substitution patterns. There are 135 individual PCDFs and 75 individual PCDDs. The composition of the PCDD and PCDF by-products are highly variable dependent on their source. However, quantitative analysis of PCDDs/PCDFs in environmental matrix requires a number of different procedures in order to prepare concentrated and cleaned extracts before analysis by gas chromatography combined with mass spectrometry technique. Such analysis is expensive and is a limiting factor for monitoring programmes.

2. HAZARD CHARACTERISATION

Concern over dioxins arose initially because one particular congener, 2,3,7,8-TCDD, was found to be extremely toxic to some types of laboratory animals. Toxic potency has been demonstrated to be associated with the number and position of chlorine atoms, since congeners lacking chlorines in the four lateral positions, as well as those having chlorines in addition to those in the 2,3,7 and 8 positions, have been shown to be less toxic than TCDD. In addition, congeners chlorinated in the lateral positions have been found to accumulate preferentially in animal tissues and have been implicated in the human poisoning incidents. As a result of toxic potency, widespread distribution, persistency and potential for bioaccumulation of congener mixtures available for human exposure, dioxin risk assessment requires a number of analytical, toxicological and epidemiological data.

2.1. Toxicokinetics

The toxicokinetic of PCDDs/PCDFs is related to their characteristics in terms of lipophilicity and susceptibility to CYP dependent metabolism. Absorption of PCDDs and PCDFs after oral administration is dependent on the vehicle used but remains very high (ranging from 60 to 90%), both in experimental animals and humans. However, elimination is much slower in man (T_{1/2} about 7 years for TCDD in man compared to a few weeks in rodents). Congeners with few chlorine atoms are usually metabolised and eliminated faster than higher chlorinated ones. The body burden in animals and humans can be easily estimated by measurements in tissues and plasma lipids.

2.2. Toxicity in experimental animals

The acute LD₅₀ of TCDD varies over 5000-fold range between Guinea pig (most sensitive) and Hamster. Among PCDDs and PCDFs, 2,3,7,8-TCDD exhibits the higher toxic potency. Toxicological effects of PCDDs have been found dose-related and thus are relevant to risk assessment for man:

- 1) induction of hepatic monooxygenases,
- 2) effects on components and functions of the immune system,
- 3) reproductive and developmental toxicity,
- 4) organ toxicity,
- 5) effects on hormone systems,
- 6) effects on the central nervous system
- 7) carcinogenicity.

For carcinogenicity, TCDD is regarded as a promotor and is not genotoxic. Therefore, a classic approach via NOAEL and safety factors seems adequate for risk assessment.

2.3. Tolerable Daily Intake (TDI)

European governments have developed a range of TDIs depending on the toxicological endpoints observed and the safety factors applied at the endpoint. In 1990 the WHO recommended a TDI of 10 pg I-TEQ/kg bw/day. This TDI was based on carcinogenic effect in rat (NOAEL 10 ng I-TEQ/kg/day and safety factor of 1000) and on primate reproductive performance (NOAEL of 1 ng I-TEQ/kg/day and safety factor of 100). The UK and Belgium have adopted the WHO recommendation of 10 pg I-TEQ/kg/day. Sweden, Norway and Finland have adopted a TDI of 5 pg I-TEQ/kg/day using a safety factor of 200. The Netherlands adopted, in 1982, a TDI of 4 pg I-TEQ/kg/day with a safety factor of 250 and recommended recently to reduce the TDI to 1 pg I-TEQ/kg/day. In France, safety factors of 50-1000 have been applied to obtain TDIs in the range of 1-10 pg I-TEQ/kg/day. In Germany, a similar range of TDIs was obtained using safety factors of 100-1000, 1 pg I-TEQ/kg/day being regarded as a non-statutory precautionary TDI, and 10 pg I-TEQ/kg/day as a preventive or intervention TDI. The American Environmental Protection Agency (EPA) has proposed a virtual safe dose of 0.006 pg/kg/day, corresponding to an acceptable lifetime tumour risk of 10^{-6} . In Japan, the TDI was recently reduced to 5 pg I-TEQ/kg/day. In the light of current scientific knowledge, it can be generally assumed that an exposure lower than 1 pg I-TEQ/kg/day does not present adverse human health implications. The 1998 WHO-consultation recommended that every effort should be made to reduce exposure to the lower end of the advised range of 1-4 pg TEQ/kg bw/day.

2.4. Effects on Humans

Health effects such as chloracne have been identified as an effect of dioxins in humans. Epidemiological data on dioxins have been collected through studies on victims of accidents, occupational exposure and on veterans who were engaged in herbicide scattering operations in the Vietnam war. Records

of poisoning of humans by furans include cases of cooking oil contamination in Japan and Taiwan.

In February 1997 the IARC classified 2,3,7,8-TCDD as a «known» human carcinogen, but continues to regard other PCDDs/PCDFs as «not classifiable» despite a similar mode of action to 2,3,7,8-TCDD. Other effects than carcinogenicity have been studied in humans as discussed in a recent Toxicology Forum in Berlin (1996). The following acute effects have been observed: chloracne, porphyria cutanea, liver dysfunctions, respiratory and neurological disorders, increased diabetes susceptibility, and changes in lipids parameters in blood. Recent epidemiological studies have focused on the anti-oestrogenic effect and subtle developmental effects in infants and children. However, since confounding factors may have been present, any or all of the effects observed cannot be ascribed specifically to dioxine exposure.

Most of the comparisons between human and animal dioxin toxicity refer to the mechanism of action based on binding to Ah receptor. Activation of the Ah receptor can result in endocrine and paracrine disturbances and alterations in cell functions, including growth and differentiation. Some of these effects have been observed both in humans and animals, indicating the existence of common mechanisms of action. However, the human Ah receptor has a lower affinity for TCDD binding than rodents, suggesting that humans may be one order of magnitude less sensitive to TCDD than mice and rats. It has been demonstrated that the induction of CYP1A1 in human lymphocytes by TCDD falls into a bimodal distribution with high responders and low responders. A high inducibility phenotype for CYP1A1 induction may be associated with increased susceptibility to lung cancer. Moreover, Ah receptor mediated CYP1A induction can be obtained without ligand binding. These points are very important for the choice of safety factor in TDI calculation.

2.5. Toxic Equivalent Factors

Although there are extensive data on the toxicity of 2,3,7,8-TCDD, toxicological information on the other 209 compounds in the family is much more sparse. In order to help in the toxicological evaluation of complex mixtures, a concept of toxic equivalent factors (TEFs) has been developed, taking in account the mechanism of action of PCDDs and PCDFs. Although 2,3,7,8- TCDD is the most potent congener able to bind Ah receptor, other

compounds that interact with this receptor result in similar effects, albeit at higher doses. These relative potencies are expressed as TEFs. After examining the relative potency of different PCDDs and PCDFs for a variety of end points both *in vitro* and *in vivo*, such as cancer, reproductive effects, body weight loss, cell transformation, immunotoxicity and Ah receptor binding, a set of TEFs has been developed. In 1988 a NATO/CCMS sub-committee proposed a new set called International TEFs adopted by several regulatory agencies in North America and Europe. The TEF models contain many sources of uncertainties related to a lack of scientific data on congeners, differences in toxicokinetics and metabolism, the interaction between congeners, and to variations between species and individuals. TEF values for human beings and mammals were revised by the WHO in 1997. At the present time, the TEFs can be regarded as an interim procedure to be improved.

2.6. Coplanar PCBs

The toxicity of coplanar PCBs follows a similar mechanism to that of dioxins and attention must be given to their risks to human health. While some correlation can be found between the presence of PCDDs/PCDFs and PCBs in animal fat, coplanar congeners are minors in PCBs mixtures and non coplanar PCBs exhibit higher toxicity than coplanar congeners in some toxicological end points (effects on thyroxin transport and on brain development). If coplanar PCBs can be associated to PCDDs/PCDFs for AhR dependent toxicological effects, these congeners should not be only considered for risk evaluation of PCBs. Moreover, differences in the origin of the contamination between PCBs and PCDDs/PCDFs lead to differences in risk management.

3. EXPOSURE EVALUATION

3.1. Analytical aspects

Over the past three decades the analytical technology involved in the determination of chlorinated PCDDs and PCDFs has evolved following advances in the science of both isolating the analyses as well as identifying and measuring them. In the course of this evolution, the techniques of mass spectrometry have been the primary driving force. However, analytical

methodology for dioxin samples from the environment and foodstuffs remain difficult and costly, limiting the quantity and significance of the data available.

PCDDs and PCDFs have been identified in extracts of samples from the environment and the composition of these analyses depend on their origins and inputs from nearby sources. The congener distribution for most atmospheric samples resembles the typical combustion pattern for these compounds. Octa and hepta-CDDs are dominant in PCDD profiles, and tetra and penta-CDFs are dominant among PCDFs. Similar patterns have been detected in plant extracts. In contrast, only 2,3,7,8 substituted PCDDs and PCDFs are currently detected in animal samples, while OCDD often remains the dominant congener. In 1990, municipal incinerators appeared to be the major source of dioxins in the atmosphere (from 47% in Germany to 82% in the Netherlands). In the past decades, the manufacture of polychlorinated aromatic chemicals has probably been the major source. Maximum air emission from combustion sources was evaluated from 926 g I-TEQ/year in West Germany (1990) to 3870 g I-TEQ/year in the U.K. (1989). Dioxins and furans are almost insoluble in water and therefore strongly adsorbed to soil and organic matter where they persist for many years due to their chemical stability and resistance to biodegradation. These compounds are thus available for biological absorption, and first of all for organisms containing significant amounts of fat. Therefore, PCDDs and PCDFs can contaminate food destined to human consumption and they are more likely to be present in fatty foods such as meat, fish and dairy products, rather than fruit, vegetables and drinking water.

3.2. Intake data

Human exposure to PCDDs and PCDFs is possible by several routes. Intake by inhalation and by ingestion of contaminated particles is minor compared to the contribution from contaminated foodstuffs. The data used here for food intake calculations are from various surveys carried out by official bodies from different countries. The majority of the studies has been conducted on cow's milk and dairy products, fish and meat products. Other foodstuffs investigated in some countries yield the relative contributions of major food types for the estimation of the total dietary intake of dioxins and furans. The major route of food contamination seems to be the ingestion of contaminated

herbage (with any adhering soil) and feed by cattle leading to the contamination of milk, meat and derivative products. The concentrations in milk and dairy products range from 0.4 to 27 pg I-TEQ/g fat. The mean level of contamination in milk from retail samples is situated between 0.4 and 2 pg I-TEQ/g fat. The mean content in samples from contaminated farms ranges from 3 to 27 pg TEQ/g fat. PCDD and PCDF intake from milk and dairy products is between 25 and 45% of the total intake. Similarly, meat and meat products (including eggs and fat) provide nearly 25% of the total intake. Fish has been reported in the literature to be a major dietary source of dioxins and furans for the populations around the Baltic (up to 60%). As indicated previously, PCDD and PCDF contents in vegetables, cereals and fruit are very low as can be expected for non-fatty foodstuffs. However, cereal products containing significant quantities of added fat may contain appreciable levels of PCDDs and PCDFs. Thus the contribution of vegetables is nearly 5% to the total intake, while in countries which usually consume significant quantities of biscuits and cakes cereal products can contribute up to 15% of the total intake. Thus the total intake in European countries is in the range of 70 to 350 pg I-TEQ/person/day. A total diet study in the UK reported a mean estimated dietary intake of 125 pg I-TEQ/day, and a calculation from the Netherlands showed that the 99 percentile of the adult population had a dioxin intake below 150 pg TEQ/day. Based on the intake data available from European countries, it can be estimated that the intake of PCDDs/PCDFs in pg I-TEQ/kg/day ranges from 1 to 5 for adults (70 kg) and from 3 to 12 for infants (13 kg).

Levels of PCDDs and PCDFs in human milk have been reported from different countries. In Europe, the values range from 9 to 67 pg I-TEQ/g fat. Accordingly, the intake of PCDDs and PCDFs by breast-fed infants has been estimated to vary from 27 to 418 pg I-TEQ/kg /day.

4. RISK MANAGEMENT AND RECOMMENDATIONS

4.1. Recommendations for emission-reducing measures

The currently estimated food intake of TCDD equivalents by adults is lower than the WHO TDI, but higher than the guideline level. Since PCDDs and PCDFs are known to be persistent in the environment, their levels tend to increase as a result of continuous release. Therefore, the introduction of

these compounds into the environment should be reduced. Accordingly, the following emission-reducing measures are recommended.

Incinerators: Emission of PCDDs and PCDFs by all kinds of incinerators (including municipal solid waste incinerators) should be limited to a maximum of 0.1 ng I-TEQ/Nm³

Metal industry: Emission from metal-producing and metal-recycling industries should be minimised by optimisation of technical procedures and equipment.

Motor vehicles: The use of halogenated scavengers in petrol should be phased out as soon as possible.

Chlorine-containing chemicals: Production and use of chlorine-containing chemicals such as certain pesticides and wood preservatives should be reduced in combination with the reduction of the contamination of these products by dioxins and PCBs.

Pulp and paper industries: Bleaching processes other than involving chlorine treatment should be adopted to minimise the presence of PCDDs and PCDFs in pulp and paper products and effluent waste. For materials in contact with food the maximum level should be reduced as much as possible.

Fireproofing substances: The use of PCB as fireproofing substances should be re-examined

Other sources: Since the origin of a large fraction of PCDDs and PCDFs is not known, every effort should be made to identify other sources of contamination pathways, in order to take appropriate measures.

4.2. Recommendations for risk management in foods

- 1) Emission-reducing measures are recommended as the best way for risk-management.
- 2) Main dietary intake of PCDDs and PCDFs is from milk and dairy products due to the considerable consumption of these foodstuffs,

particularly by children. Thus standards in milk and dairy products should be recommended:

- Levels lower than 1 pg I-TEQ/g fat are a desirable target achievable after reduction of PCDD pollution in the environment.
 - Levels higher than 5 pg I-TEQ/g fat must lead to the consideration of a ban on trade of affected milk and dairy products (fat content higher than 2%).
- 3) National and international monitoring of the levels of contamination in both milk and dairy products as well as in fat from meat, fish, seafood and eggs is recommended.
 - 4) Monitoring of dioxins in human milk and blood is recommended as a way of obtaining information on the level of human intake of these contaminants from foodstuffs.

4.3. General recommendation on further data

Generally, further epidemiological and toxicological data are expected to contribute to the clarification of the effects of dioxines on consumer health.

SELECTED LIST OF PUBLICATIONS

Nitrates and nitrites in foodstuffs (1993) ISBN 92-871-2425-6

Contaminants in food (Resolution AP (93) 3)

Lead in food (1994) ISBN 92-871-2573-2

Cadmium in food (1995) ISBN 92-871-2878-2

Mercury in food (1995) ISBN 92-871-2880-4

Lead, cadmium and mercury in food: Assessment of dietary intakes and summary of heavy metals in foodstuffs (1994) ISBN 92-871-2620-8

Health aspects of nitrates and its metabolites (particularly nitrite)
Proceedings of International Workshop, Bilthoven (NL) 8-10 November 1994,
ISBN 92-871-2792-1