

codex alimentarius commission



FOOD AND AGRICULTURE
ORGANIZATION
OF THE UNITED NATIONS

WORLD
HEALTH
ORGANIZATION



JOINT OFFICE: Viale delle Terme di Caracalla 00100 ROME Tel: 39 06 57051 www.codexalimentarius.net Email: codex@fao.org Facsimile: 39 06 5705 4593

Agenda Item 9

CX/FAC 03/11
December 2002

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON FOOD ADDITIVES AND CONTAMINANTS

Thirty-fifth Session

Arusha, Tanzania, 17 - 21 March 2003

DISCUSSION PAPER ON THE USE OF ACTIVE CHLORINE

Governments and international organizations wishing to submit comments on the following subject matter are invited to do so **no later than 31 January 2003** as follows: Netherlands Codex Contact Point, Ministry of Agriculture, Nature Management and Fisheries, P.O. Box 20401, 2500 E.K., The Hague, The Netherlands (Telefax: +31.70.378.6141; E-mail: info@codexalimentarius.nl, with a copy to the Secretary, Codex Alimentarius Commission, Joint FAO/WHO Food Standards Programme, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy (Telefax: +39.06.5705.4593; E-mail: Codex@fao.org).

INTRODUCTION

1. At the thirty-third session of the Codex Committee on Food Additives and Contaminants (CCFAC), the question of safe use of active chlorine on foodstuffs was raised by Denmark.¹ Active chlorine components are chemical substances (used for water treatment or surface treatment of foodstuffs); consequently, they can be found as residues or reaction products in foodstuffs. However, the use of active chlorine in or on foodstuffs has not been assessed for safety by JECFA. Despite the lack of a safety evaluation, various uses of active chlorine components are being discussed in Codex Commodity Standards.
2. In the following text, the term *active chlorine* includes both active chlorine components and reaction products thereof.
3. The delegation of Denmark pointed out that active chlorine is widely used on food for decontaminating/disinfecting purposes yet safety of such chemicals has not been convincingly demonstrated until now.
4. The Committee discussed the issue and agreed that the delegation of Denmark, in cooperation with the delegations of Norway, Finland, Israel and WHO, should prepare a discussion paper for consideration by the thirty-fourth session of the CCFAC.
5. The Discussion Paper on the Use of Active Chlorine was presented and discussed at the 34th Session of the Codex Committee on Food Additives and Contaminants.² It was noted that active chlorine was commonly utilised for different purposes, including direct food contact uses. The Committee recognised the need to assess the use of active chlorine by JECFA taking into account the existence of different chlorine compounds, various possibilities of their use on foods, and possible by-products formed. In addition both microbiological and toxicological risks of active chlorine use should be considered in evaluation of its safety.

¹ ALINORM 01/12A, paras. 199-204

² ALINORM 03/12, paras. 69-73

6. The Committee agreed that the Discussion Paper should be revised in the light of the discussion and comments received in response to a Circular Letter. The Discussion Paper was circulated for comments but no comments were received and it is recommended, that the Committee re-opens the discussion taking into account the discussion at the 34th Session.

PURPOSE

7. The general purpose of the Codex Alimentarius (through the Codex Standards) is to protect consumers' health while ensuring fair practice in the food trade. The purpose of this paper is to form the background for a discussion at the Codex Committee on Food Additives and Contaminants on the use of active chlorine as a disinfecting/ decontaminating agent applied on food) and the safety aspects of such use.

BACKGROUND

8. Active chlorine in the hygiene standards of Codex is regarded as disinfectant, however there are different possible definitions under which chemicals (such as active chlorine) could be classified in the Codex system, as a function of their intended use. The definitions relevant to consider are quoted below:

DEFINITIONS³

9. *Disinfectants* are not defined in Codex. However, the term *disinfection* could be defined as follows: The destruction of pathogenic and other microorganisms by thermal or chemical means to eliminate a defined scope of microorganisms, but not necessarily all microorganisms. The term is normally used for the antimicrobial treatment of surfaces of food contact materials, tools etc. The normal requirement would be that after disinfection, the surface etc. is cleaned with potable water, or in some regions, a recommendation of "drainage" only (without rinsing) if the concentration of chlorine compounds does not exceed a certain level. This applies also to other disinfectants, at varying concentrations.

10. *Pesticide* means any substance intended for preventing, destroying, attracting, repelling, or controlling any pest including unwanted species of plants or animals during the production, storage, transport, distribution and processing of food, agricultural commodities, or animal feeds or which may be administered to animals for the control of ectoparasites. The term includes substances intended for use as a plant growth regulator, defoliant, desiccant, fruit thinning agent, or sprouting inhibitor and substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport. The term normally excludes fertilizers, plant and animal nutrients, food additives, and animal drugs.

11. *Contaminant* is defined as "any substance not intentionally added to food, which is present in such food as a result of the production (including operation carried out in crop husbandry, animal husbandry and veterinary medicine), manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food or as a result of environmental contamination. The term does not include insect fragments, rodent hair and other extraneous matter.

12. *Food additive* is defined as "any substance not normally consumed as a food by itself and not normally used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packing, transport or holding of such food results, or may be reasonably expected to result (directly or indirectly) in it or its by-products becoming a component of or otherwise affecting the characteristics of such food. The term does not include "contaminants" or substances added to food maintaining or improving nutritional qualities or maintaining nutritional qualities."

13. *Processing aid* is defined as "any substance or material, not including apparatus or utensils, and not consumed as a food ingredient by itself, intentionally used in the processing of raw materials, foods or its ingredients, to fulfil a certain technological purpose during treatment or processing and which may result in the non-intentional but unavoidable presence of residues in the final product."

³ Codex Procedural Manual, Eleventh Edition, FAO and WHO 2000.

14. These Codex definitions above are complex and sometimes open to interpretation. Confusion arises when a substance is used for various purposes, for instance as a food additive or a processing aid. In the case of active chlorine, it may at present be considered in any of the six above-mentioned categories. Part of this discussion was reflected in the discussion paper on processing aids, CX/FAC 01/10.

15. To ensure the protection of consumers is, however, one of the main purposes of Codex Alimentarius, and the safety aspects have to be taken into account in all cases.

CHLORINE STATUS AND CODEX STANDARDS

16. Chlorine was evaluated by JECFA as a food additive in 1963: there is INS 925 for chlorine and INS 926 for chlorine dioxide, both defined as flour treatment agents. Safety evaluation of active is furthermore included in some of the Codex Code of Practice or draft Code of Practice as well as in the WHO Guidelines for Drinking Water Quality. However, JECFA has not evaluated safety of active chlorine components when used in water for direct contact with food during industrial processes..

Codex Committee on Fish and Fishery Products (CCFFP).

17. CCFFP addressed the use of chlorinated water in fish and fishery production and had for consideration a document prepared by the WHO in collaboration with FAO, including a survey of current practices in member countries. This paper recalled that chlorinated water was widely used to prevent microbial contamination and concluded that additional work in the area was recommended, and current scientific evidence did not warrant the change of the Codex recommended level of 10 mg/l (Code of Practice for Frozen Shrimps and Prawns). The CCFFP concluded that no further action was necessary on this matter.⁴

Codex Committee on Food Hygiene (CCFH).

18. CCFH is currently elaborating a Proposed Draft⁵ Code of Practice for the Primary Production and Packing of Fresh Fruit and Vegetables. This Proposed Draft Code of Practice is forwarded to step 5, and includes a proposal for the use of active chlorine as a “disinfectant”.

19. Furthermore, CCFH has proposed draft Guidelines for the Hygienic Reuse of Processing Water in Food Plants⁶, which also mentions the use of chlorine

WHO guidelines concerning the use of chlorine in drinking water

20. The WHO Guidelines for Drinking Water Quality accept the use of active chlorine with the following guideline levels⁷

Chemical component	WHO guideline level	WHO comments
Monochloramine	3 mg/l	-
Di- and trichloramine	-	No adequate data to permit the recommendation of a health-based guideline value
Chlorine	5 mg/l	Concentrations of the substance at or below the health-based guideline value may affect the appearance, taste or odour of the water. For effective disinfection, there should be a residual concentration of free chlorine of ≥ 0.5 mg/litre after at least 30 minutes contact time at pH < 8.0.
Chlorine dioxide	-	A guideline value has not been established because of the rapid breakdown of chlorine dioxide and because the chlorine guideline value is adequately protective for potential toxicity from chlorine dioxide.

⁴ Alinorm 01/18, paragraphs 146-149

⁵ Alinorm 01/13A, paragraphs 31-82 and Appendix II.

⁶ CX/FH 00/8

⁷ Guidelines for drinking-water quality, second edition, volume 2. Health criteria and other supporting information, WHO, 1996

WHO Drinking Water Unit requested that JECFA evaluates in 2002 the use of NaDCC : Sodium dichloroisocyanurate . This is written in the JECFA Report: List of substances scheduled for evaluation and request for data, 59th meeting, June 2002.

CHEMICAL CONSIDERATIONS

21. The use of active chlorine includes both inorganic and organic compounds such as chlorine gas, liquid chlorine, chlorine dioxide, derivatives of hypochlorous acid, organic forms such as chloramines or derivatives of isocyanuric acid. The common antimicrobial principle of liquid chlorine or hypochlorites is hypochlorous acid. Concentrations of use of chlorine dioxide are much lower.

22. The active chlorine can react with organic materials in food or/and water. Among the reaction products, most frequently seen are trihalomethans. However, many other components may be found in food as a result of the active chlorine. Some of these by-products may be undefined at present and therefore not detected analytically.

Table 1. Reaction products from treatment with chlorine (Klein, 1990; LeBel et al., 1997; Lykins Jr. et al., 1986; Merlet et al., 1985; Richardson et al., 1996; Ventura et al., 1999 and Zimmerli et al., 1993).

Reaction products	
Trihalomethans	Trichloro-, bromodichloro-, dibromochloro- and tribromomethane
Halogenated alkanes	Chlorinated and bromated ethane, propane and butane
Halogenated alkenes	Chlorated and bromated ethylene, propene and butene
Halogenated acids	Monochloro-, dichloro- and trichloro acetic acid
Halogenated aldehydes	Trichloroethanal, chloropropanals
Halogenated ketones	Di-, tri- and tetrachlorosubstituted propanone
Halogenerated alcohols	Chloral hydrate
Haloacetonitrils	Trichloroaceto-, dichloroaceto-, dibromoaceto- and bromochloroacetonitrile
Haloamins	Chloramine
Trichloronitromethane	Chlorpicrine
Halogenated phenols	Mono-, di- and trichlorophenols
Halopropanols	3-chloropropanediol, dichloropropanol
Halohydroxy-furanons	3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone

Table 2. Concentrations of chlorinated reaction products in water for food processing, drinking water and different types of food and beverages. The concentrations are calculated in microgram/l for the liquids and for solid foodstuffs in nanogram/gram.

Source	Component	Concentration	Reference
Water for processing	Trichloromethane	4,6 – 57,0 µg/l	Uhler and Diachenko, 1987
	Monobromodichloromethane	2,2 – 14,1 µg/l	Uhler and Diachenko, 1987
	Trichlorethylene	3,0 – 7,8 µg/l	Uhler and Diachenko, 1987
	1,1,1-trichloroethane	2,0 – 4,3 µg/l	Uhler and Diachenko, 1987
	Tetrachloroethylene	1,3 µg/l	Uhler and Diachenko, 1987
Drinking water	Monochloroacetic acid	3,6 – 13,4 µg/l	Jolley, 1989
	Dichloroacetic acid	4,2 – 208 µg/l	Jolley, 1989
	Trichloroacetic acid	0,6 – 115 µg/l	Jolley, 1989
	Chloralhydrate (2,2,2-Trichlor-1,1-ethandiol)	<0,03 – 16,4 µg/l	Jolley, 1989
	Trichloropropanone	<0,5 – 2,4 µg/l	Jolley, 1989
	Trichloronitromethane	< 3 µg/l	Jolley, 1989
Cola type beverages	Trichloromethane	9 – 178 µg/l	Entz, Thomas and Diachenko, 1982, Uhler and Diachenko, 1987
	Monobromodichloromethane	1,2 – 3,8 µg/l	Entz, Thomas and Diachenko, 1982, Uhler and Diachenko, 1987
Other carbondioxide-containing beverages	Trichloromethane	14,5 – 32 µg/l	Entz, Thomas and Diachenko, 1982
	Trichloromethane	2,3 – 15,6 µg/l	Uhler and Diachenko, 1987
	Monobromodichloromethane	1,2 – 2,3 µg/l	Uhler and Diachenko, 1987
Pasteurized milk	Trichloromethane	17 µg/l	Entz, Thomas and Diachenko, 1982
	Trichloromethane	0 – 3,1 µg/l	Kroneld and Reunanen, 1990
	1,1,1-trichlorethane	0 – 0,03 µg/l	Kroneld and Reunanen, 1990
	Tetrabromomethane	0 – 0,02 µg/l	Kroneld and Reunanen, 1990
	Monobromodichloromethane	0 – 0,07 µg/l	Kroneld and Reunanen, 1990
	Monochlorodibromomethane	0 – 0,3 µg/l	Kroneld and Reunanen, 1990
Cheese	Trichloromethane	15 – 17 ng/g	Entz, Thomas and Diachenko, 1982
	Trichloromethane	2,4 – 10,9 ng/g	Uhler and Diachenko, 1987
	1,1,1-trichlorethane	1,2 – 6,4 ng/g	Uhler and Diachenko, 1987
Butter	Trichloromethane	56 ng/g	Entz, Thomas and Diachenko, 1982
	Monobromodichloromethane	7 ng/g	Entz, Thomas and Diachenko, 1982
Ice cream	Trichloromethane	4,6 – 31,2 ng/g	Entz, Thomas and Diachenko, 1982, Uhler and Diachenko, 1987
	1,1,1-trichlormethane	2,7 – 37,3 ng/g	Uhler and Diachenko, 1987
Mayonnaise	Trichloromethane	34 ng/g	Entz, Thomas and Diachenko, 1982

MICROBIOLOGICAL EFFECTS and risk analysis

23. In most cases, the use of active chlorine would be requested due to microbiological problems occurring in food or water. The concentration of use would be a balanced compromise between the benefits against the microbiological hazards and the danger of hazards from residues of chemicals. The use of active chlorine components has various different effects on the microflora. The efficiency of chlorine as a disinfecting or decontaminating agent is depending on pH and the temperature of use. Whenever the use is considered, it is essential to consider whether active chlorine indeed has the requested effect or not.

24. In general, the positive, microbiologically decontaminating effect of chlorine compounds should be compared with a possible negative effect of chlorine and its derivatives intake

Table 3 Some examples are given on the bactericide effect of active chlorine on various microorganisms (Block, 1991)⁸:

Organism	pH	Temperature (°C)	Exposure time (minutes)	Cl ₂ Concentration (mg/l)	Bactericide effect (% reduction)
<i>Bacillus anthracis</i>	7,2	22	120	2,3 – 2,4	100
<i>Escherichia coli</i>	7,0	20-25	1	0,055	100
<i>Listeria monocytogenes</i>	9,5	20	0,5	100	99-100
<i>Staphylococcus aureus</i>	7,2	25	0.5	0,8	100
<i>Endamoeba histolytica</i> cysts	7,0	25	150	0,08-0,12	99-100
<i>Adenovirus</i>	8,8-9,0	25	0,6-0,8	0,2	99,8
<i>Poliovirus</i>	7,0	25-28	2	0,11-0,2	99,9

TOXICOLOGICAL CONSIDERATIONS (of chlorine intake)

25. The guideline value (of what?) in the WHO guidelines for drinking water is based on a TDI for free chlorine of 150 microgram/kg body weight, and for monochloramine based on a TDI of 94 microgram/kg of body weight as a guideline value. The WHO maximum guideline value for chlorine residue in drinking water is 5 mg/l (3.2.3). In 1998, the American Environmental Protection Agency established a maximum residual disinfection level (MRDL) of 4 mg/l for chlorine in public water systems.

26. Results from animal studies with oral administration of chlorine or chlorine-treated food products showed no signs of teratogenicity, reproductive toxicity and carcinogenicity (Vetrano, K.M., 2001). There is conflicting evidence whether the administration of chlorine-bleached flour to rats has acute toxic effects.

27. Various halogenated by-products can be formed during chlorine disinfection, and their toxicological effects have likewise been investigated in animal and in vitro studies. The effects of high doses of these substances range from oxidative toxicity (e.g. chlorite) and mutagenicity (e.g. trichloronitromethane) to repro-

⁸ Comment: Might not be equivalent to effects on real foods, as the effect on microorganisms on food might be different (less bactericidal) by orders of magnitude.

ductive effects (e.g. chloroacetates), neurotoxicity (e.g. trihalomethanes) and carcinogenicity (e.g. trichloroacetaldehyde, dichloroacetat, trihalomethanes).

28. WHO has established guideline values in drinking water (WHO, 1996) for the following disinfection by-products: dibromochloromethane (100 µg/l), chloroform (200 µg/l), bromodichloromethane (60 µg/l), bromoform (100 µg/l), dichloroacetate (50 µg/l), trichloroacetate (100 µg/l), trichloroacetaldehyde (10 µg/l), dichloroacetonitrile (90 µg/l), dibromoacetonitrile (100 µg/l), trichloroacetonitrile (1 µg/l), 2,4,6-trichlorophenol (200 µg/l), cyanogen chloride (70 µg/l), chlorite (200 µg/l). No guideline values have been established for other by-products of potential concern, such as chloropropanols and chlorinated hydroxyfuranone (MX).

29. In 2000, the disinfectants and the disinfectant by-products were evaluated by IPCS (International Programme on Chemical Safety (WHO, 2000) and the main conclusions were:

1. No by-product studied to date is a potent carcinogen at concentrations normally found in drinking water.
2. Epidemiological studies do not provide convincing evidence that chlorinated water increases the risk for cardiovascular disease, cancers or adverse pregnancy outcomes.

30. Although the scientific evidence for potentially harmful effects of ingesting chlorine-treated food products is weak, the formation of toxic halogenated by-products is still an uncertain and relevant factor to be investigated and an updated risk assessment from an international expert committee on food and chemicals in food is needed.

SUMMARY

31. The paper describes different aspects of chlorine: its definitions, various reasons of use, and chemical, microbiological and toxicological aspects. The use of active chlorine in foodstuffs (and on foodstuffs) can be regarded as included in either of the above-mentioned definitions on disinfectants (decontaminants), pesticides, food additives, processing aids, or contaminants. Some Codex member countries regard active chlorine as a food additive, others exclusively as a processing aid, and in the Codex Code of Hygiene Practice, it is described as a disinfectant. Moreover, it could be argued that the reaction products in the food after the use of active chlorine are contaminants in the foodstuffs and the content of these reaction products should be evaluated for safety.

OPTIONS FOR DECISIONS

32. The use of active chlorine, and other chemicals or reaction products thereof on foodstuffs should not endanger human health.

33. If active chlorine is to be considered for the use on foodstuffs, the first priority must be to perform a proper risk assessment of such use. In Codex, chemicals used in food either as food additives or as processing aids or found in foodstuffs due to contamination should be evaluated by JECFA. The safety evaluation should be given main priority before a component is applied on foodstuffs.

: the priority of Codex, through Codex Standards is to protect consumer's health and facilitate free trade among member countries. All the elements of a Codex standard have one universal objective: insure consumption of safe food... The use of active chlorine may influence food safety, both from microbiological and chemical point of views. In order to ensure consumer safety and to facilitate free trade, the options for the use of active chlorine in foods include the following:

- i. Various active Chlorine compounds should be assessed by JECFA. Available material concerning active chlorine as a chemical used in contact with food should be forwarded to JECFA for chemical and toxicological risk assessment. Such assessment should be combined with microbiological efficiency of this group of chemicals.

- ii. The above-mentioned standards from CCFH and CCFFP should not include the use of chlorine as an agreed Codex treatment of vegetables or shrimps prior to a risk assessment. The proposed standard should be forwarded to CCFAC for endorsement of the use of chlorine in line with the procedure for food additives and contaminants in Codex standards.
 - iii. In cases where the active chlorine may be regarded as a *food additive*, the actual components will have to be included in the work on the General Standard on Food Additives, after being evaluated by JECFA for all uses.
 - iv. *If* the active chlorine is to be regarded as a *contaminant*, then it should be included in the General Standard for Contaminants after evaluation by JECFA.
 - v. *If* the active chlorine is to be regarded as *pesticide or disinfectant (or decontaminant)*, the residues and the reaction products in the food would be regarded as contaminants, and they are to be identified, assessed and included in the General Standard for Contaminants after evaluation by JECFA.
 - vi. *If* the active chlorine is to be regarded as *processing aid*, the use of chlorine should be included under the agenda for processing aids. However, processing aids used in Codex Standards or Code of Practice should still be presented to CCFAC for adoption and it would be problematic for CCFAC to accept the use of substances that are not evaluated for safety (given the uncertain outcome of potential by-products).
34. The main point is consumer safety, no matter how the use of active chlorine is regarded under the Codex definitions; the use of active chlorine *should be evaluated for safety* in all cases. Codex provisions for the use of chemical substances are in many cases proposed by the Commodity Committees and other Committees like the CCFH. In general, these provisions should be sent to the CCFAC for adoption, before final adoption in CAC for Standards, Codes of Practice etc.
35. During the evaluation in CCFAC of chemicals used or found as contaminants, the normal procedure would be to consult with the risk assessors, JECFA, before decision is taken. The above-mentioned draft papers should also be sent to CCFAC for endorsement. The question whether active chlorine is used under one or the other definition could be discussed independently of and currently with the risk assessment.

REFERENCES

- Abdel-Rahman M.S., D. Couri & R.J. Bull (1984).** Effect of exogenous glutathione, glutathione reductase, chlorine dioxide, and chlorite on osmotic fragility of rat blood in vitro. *J. Am. Col. Toxicol.* 3, 269-275
- Aida Y., K. Yasuhara, K. Takada, Y. Kurokawa, M. Tobe (1992).** Chronic toxicity of microencapsulated bromodichloromethane administered in the diet to Wistar rats. *J. Toxicol. Sci.* 17, 51-68
- Anandh H., Westerhoff P. (1997)** Reactivity and by-products of bromine (HOBr/OBr⁻) reactions with organic carbon, *Annu. Conf. Proc. – Am. Water Works Assoc.*, 713-721.
- Balster R. L., J. F. Borzelleca (1982).** Behavioral toxicity of trihalomethane contaminants of drinking water in mice. *Environ. Health Perspect.* 46, 127-136
- Batterman S., Zhang L., Wang S. (2000)** Quenching of chlorination disinfection by-product formation in drinking water by hydrogen peroxide, *Wat. Res.*, 34(5), 1652-1658.
- Blazak W. F., J. R. Meier, B. E. Stewart, D. C. Blachman, J. T. Deahl (1988).** Activity of 1,1,1- and 1,1,3-trichloroacetones in a chromosomal aberration assay in CHO cells and the micronucleus and sperm-head abnormality assays in mice. *Mutation Res.* 206, 431-438
- Block, S.,S.. Disinfection, Sterilization and Preservation. Fourth edition, 1991. Lea & Fibiger.**
- Bourbigot, M.L., Hascoet, M.C., Levi, Y., Erb, F. and Pommerey, N. (1986)** Role of Ozone and Granular Activated Carbon in the Removal of Mutagenic Compounds. *Environmental Health Perspectives*, 69, 159-163
- Bousher A., Brimblecombe P., Midgley D. (1989)** Kinetics of reactions in solutions containing monochloramine and bromide, *Wat. Res. G.B.*, 23(8), 1049-1058.
- Bull R. J., J. R. Meier, M. Robinson, H. P. Ringhand, R. D. Laurie, J. A. Stober (1985).** Evaluation of mutagenic and carcinogenic properties of brominated and chlorinated haloacetonitriles: By-products of chlorination. *Fundam. Appl. Toxicol.* 5, 1065-1074
- Bull R. J., I. M. Sanchez, M. A. Nelson, J. L. Larson, A. L. Lansing (1990).** Liver tumor induction in B6C3F1 mice by dichloroacetate and trichloroacetate. *Toxicology* 63, 341-359
- Børgh-Sørensen, L., Jul, M., Jensen, J.H., Zeuthen, P. (1988)** Konserveringsteknik, vol. 2. DSR-forlag, København.
- Camel, V. and Bermond, A. (1998)** The use of ozone and associated oxidation processes in drinking water treatment. *Water Research*, 32, No. 11, 3208-3222.
- Christensen, A.S. and Wick, M.R. (1998)** Desinficering af rindvand med ultraviolet belysning-sansligt. *Vandteknik* 1, feb. 98, 12-15.
- Cicmanec J. L., L. W. Condie, G. R. Olson, S. R. Wang (1991).** 90-day toxicity study of dichloroacetate in dogs. *Fundam. Appl. Toxicol.* 17, 376-389
- Clarke, N.A. og Berman, M.S. (1983)** Disinfection of Drinking Water, Swimming-Pool Water, and Treated Sewage Effluents. I: Block, S.S. (ed) *Disinfection, Sterilization, and Preservation*. Lea & Febiger. Philadelphia.
- Colette T.W., Richardson S.D., Thruston Jr. A.D. (1994)** Identification of bromohydrins in ozonated waters, *Appl. Spectr.*, 48(10), 1181-1192.
- Crane A.M., Kovacic P., Kovacic E.D. (1980)** Volatile halocarbon production from the chlorination of marine alga by products, including D-Mannitol, *Environ. Sci. Technol.*, 14(11), 1371-1374.
- Craun G. F. (ed.) (1993).** Safety of water disinfection: Balancing chemical & microbial risks. ILSI Press, Washington D.C., USA
- Crochet R.A., Kovacic P. (1973)** Conversion of *o*-Hydroxyaldehydes and ketones into *o*-hydroxyanilids by monochloramine, *J. Chem. Soc. Chem. Comm.*, 716-717.
- Cunningham H.M., Lawrence G.A. (1977)** Effect of exposure of meat and poultry to chlorinated water on the retention of chlorinated compounds and water, *J. Food Sci.*, 42(6), 1504-1505, 1509.
- Daniel F. B., M. Robinson, J. A. Stober, N. P. Page, G. R. Olson (1992a).** Ninety-day toxicity study of chloral hydrate in the Sprague-Dawley rat. *Drug Chem. Tox.* 15, 217-232
- Daniel F. B., A. B. DeAngelo, J. A. Stober, G. R. Olson, N. P. Page (1992b).** Hepatocarcinogenicity of chloral hydrate, 2-chloroacetaldehyde, and dichloroacetic acid in male B6C3F1 mouse. *Fundam. Appl. Toxicol.* 19, 159-168
- Diehl A.C., Speitel jr. G.E., Symons J.M., Krasner S.W. (1995)** Factors affecting disinfection by-product formation during chloramination, *Annu. Conf. Proc. – Am. Water Works Assoc.*, 535-546.
- Dunnick J. K., R. L. Melnick (1993).** Assessment of the carcinogenic potential of chlorinated water: experimental studies of chlorine, chloramine, and trihalomethanes. *J. Natl. Cancer Inst.* 85, 817-822

- EHC 216:** Disinfectants and disinfectant by-products. IPCS. World Health Organization 2000.
- Entz R. C., Thomas K. W., Diachenko G. W. (1982)** Residues of volatile halocarbons in foods using Headspace Gas Chromatography, *J. Agric. Food Chem.*, 30, 846-849.
- Eustis S. L., J. K. Haseman, W. F. Mackenzie, K. M. Abdo (1995).** Toxicity and carcinogenicity of 2,3-dibromo-1-propanol in F344/N rats and B6C3F1 mice. *Fundam Appl Toxicol.* 26, 41-50
- Friedman M., Stevens K.L., Wilson R.E. (1995)** Inactivation of a tetrachloroimide mutagen from simulated processing water, *J. Agric. Food Chem.*, 43(9), 2424-2427.
- Furnus C. C., M. A. Ulrich, M. C. Terreros, F. N. Dulout (1990).** The induction of aneuploidy in cultured Chinese hamster cells by propionaldehyde and chloral hydrate. *Mutagenesis* 5, 323-326
- Ghanbari H.A., Wheeler W.B., Kirk J.R. (1982)** Reactions of aqueous chlorine and chlorine dioxide with lipids: Chlorine incorporation, *J. Food Sci.*, 47,482-485.
- Giller S., F. Le Curieux, L. Gauthier, F. Erb, D. Marzin (1995).** Genotoxicity assay of chloral hydrate and chloropicrine. *Mutat. Res.* 348,147-152
- Gordon G., Bubnis B. (1999)** Ozone and Chlorine Dioxide: Similar chemistry and measurement issues, *Ozone Sci. Eng.*, 21(5), 447-464.
- Gorman, B.M., Sofos, J.N., Morgan, J.B., Schmidt, G.R. og Smith, G.C. (1995)** Evaluation of Hand-Trimming, Various Sanitizing Agents, and Hot Water Spray as Decontamination Interventions for Beef Brisket Adipose Tissue. *Journal of Food Protection*, 58, 8, 899-907.
- Han, Y., Guentert, A.M., Smith, R.S., Linton, R.H. og Nelson, P.E. (1999)** Efficacy of chlorine dioxide gas as a sanitizer for tanks used for aseptic storage. *Food Mikrobiologi*, 16, 53-61.
- Harrington-Brock K., C. L. Doerr, M. Moore (1995).** Mutagenicity and clastogenicity of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX) in L5178y/TK^{+/}-3.7.2C mouse lymphoma cells. *Mutation Res.* 348, 105-110
- Hayashi M., M. Kishi, T. Sofuni, M. Ishidate (1988).** Micronucleus tests in mice on 39 food additives and eight miscellaneous chemicals. *Fd. Chem. Toxic.* 26, 487-500
- Hiddink J. (1995)** Water supply, sources, quality and water treatment in the dairy industry, *Bull. IDF.*, 308, 16-32.
- Hoign^a J. (1985)** Organic micropollutants and treatment processes: Kinetics and final effects of ozone and chlorine dioxide, *Sci. Tot. Environ.*, 47, 169-185.
- Holme J.A., Steffensen I.-L., Brunborg G., Becher G., Alexander J. (1999)** Klorering av drikkevann – mulig kreftisiko av et biprodukt, *Tidsskr. Nor. Lægeforen*, 119(17), 2528-2530.
- International Programme on Chemistry Safety (1998)**, Environmental health criteria monograph for disinfectants and disinfectant by-products, *Summary and conclusions of IPCS task group, Geneva.*
- Jansson K., V. Jansson (1992).** Genotoxicity of 2,4,6-trichlorophenol in V79 Chinese hamster cells. *Mutat. Res.* 280, 175-179
- Jansson K., J. Maki-Paakkanen, S. L. Vaitinen, T. Vartiainen, H. Komulainen, J. Tuomisto (1993).** Cytogenetic effects of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX) in rat peripheral lymphocytes in vitro and in vivo. *Mutation Res.* 229, 25-28
- Jolley R.L. (1989)** Trace substances present as chlorination by-products in drinking and process waters, *Trace Subst. Environ. Health*, 22, 205-214.
- Johnston J.J., Ghanbari H.A., Wheeler W.B., Kirk J.R. (1983)** Chlorine incorporation in shrimp, *J. Food Sci.*, 48, 668-670.
- Jorgenson T. A., E. F. Meierhenry, C. J. Rushbrook (1985).** Carcinogenicity of chloroform in drinking water to male Osborne-Mendel rats and female B6C3F₁ mice. *Fundam. Appl. Toxicol.* 5, 760-769
- Juven, J.B. og Pierson, M.D. (1996)** Antibacterial Effects of Hydrogen Peroxide and Methods for its Detection and Quantitation. *Journal of Food Protection*, 59, 11, 1233-1241.
- Kim, J.-G., Yousef, A.E. og Dave, S. (1999)** Application of Ozone for Enhancing the Microbiological Safety and Quality of Foods: A Review. *J. of Food Protection*, 62, No. 9, 1071-1087.
- Klein S. (1990)** Bildung von Organohalogenverbindungen bei der Wasserchlorung, *Z. Gesamte Hyg.*, 36(10), 532-535.
- Klinefelter G. R., J. D. Suarez, N. L. Roberts, A. B. DeAngelo (1995).** Preliminary screening for the potential of drinking water disinfection byproducts to alter male reproduction. *Reprod. Toxicol.* 9, 571-578
- Ko Y.-W., Chiang P.-C., Chang E.E. (1996)** The effect of bromide ion on the formation of organohalogen disinfection by-products during ozonation, *Ozone Sci. Eng.*, 18(4), 349-361.
- Kroll R. B., G. D. Robinson, J. H. Chung (1994).** Characterization of trihalomethane (THM)-induced renal dysfunction in the rat. I: Effects of THM on glomerular filtration and renal concentrating ability. *Arch. Environ. Contam. Toxicol.* 27, 1-4

- Kroneld R., Reunanen M. (1990)** Determination of volatile pollutants in human and animal milk by GC-MS, *Bull. Environ. Contam. Toxicol.*, 44, 917-923.
- Kurokawa Y., Y. Hayashi, A. Maekawa, M. Takahashi, T. Kokubo, S. Odashima (1983).** Carcinogenicity of potassium bromate administered orally to F344 rats. *JNCI* 71, 965-972
- Kurokawa Y., S. Takayama, Y. Konishi, Y. Hiasa, S. Asahina, M. Takahashi, A. Maekawa, Y. Hayashi (1986).** Long-term in vivo carcinogenicity tests of potassium bromate, sodium hypochlorite, and sodium chlorite conducted in Japan. *Environ. Health Persp.* 69, 221-235
- Kurokawa Y., A. Maekawa, M. Takahashi, Y. Hayashi (1990).** Toxicity and carcinogenicity of potassium bromate – A new renal carcinogen. *Environ. Health Persp.* 87, 309-335
- Lahl U., Cetinkaya M., Düszejn J.V., Gabel B., Stachel B., Thiemann W. (1982)** Health risks for infants caused by trihalomethane generation during chemical disinfection of feeding utensils, *Ecol. Food Nutr.*, 12, 7-17.
- LeBel G.L., Benoit F.M., Williams D.T. (1997)** A one-year survey of halogenated disinfection by-products in the distribution system of treatment plants using three different disinfection processes, *Chemosphere*, 34(11), 2301-2317.
- Le Curieux F., L. Gauthier, F. Erb, D. Marzin (1995).** The use of the SOS chromotest, the Ames-fluctuation test and the new micronucleus test to study the genotoxicity of four trihalomethanes. *Mutagenesis* 10, 333-341
- Lund E. (1991)** Desinfektion af vand i bryggeriet, *Brygmesteren*, 48(4), 9-11,13.
- Lykins jr. B.W., Koffskey W. (1986)** Products identified at an alternative disinfection pilot plant, *Environ. Health Perspect.*, 69, 119-128.
- Madaeni, S.S. (1999)** Review Paper: The Application of Membrane Technology for Water Disinfection. *Water Research*, 33, No. 2, 301-308.
- Magara Y., Sasaki T., Kozasa H., Asami M., Aizawa T. (1996)** Comparative study of disinfectants for water supply, *Wat. Supply*, 14(3/4), 381-386.
- Meier J. R., W. F. Blazek, R. B. Knohl (1987).** Mutagenic and clastogenic properties of 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone: A potent bacterial mutagen in drinking water. *Environ. Mol. Mutagenesis* 10, 411-424
- Meier J.R., Knohl R.B., Coleman W.E., Ringhand H.P., Munch J.W., Kaylor W.H., Streicher R.P., Kopfler F.C. (1987)** Studies on the potent bacterial mutagen, 3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone: Aqueous stability, XAD recovery and analytical determination in drinking water and in chlorinated humic acid solutions, *Mutation Res.*, 189(4), 363-373.
- Merlet N., Thibaud H., Dore M. (1985)** Chloropicrin formation during oxidative treatments in the preparation of drinking water, *Sci. Tot. Environ.*, 47, 223-228.
- Morin, P. (2000)** Identification of the bacteriological contamination of a water treatment line used for haemodialysis and its disinfection. *J. of Hospital Infection*, 45, 218-224.
- Neale R. (1964)** The chemistry of ion radicals. The free radical addition of N-chloroamines to olefinic and acetylenic hydrocarbons, *J. Am. Chem. Soc.*, 88, 5340-5342.
- Omura M., M. Hirata, M. Zhao, A. Tanaka, N. Inoue (1995).** Comparative testicular toxicities of two isomers of dichloropropanol, 2,3-dichloro-1-propanol, and 1,3-dichloro-2-propanol, and their metabolites alpha-chlorohydrin and epichlorohydrin, and the potent testicular toxicant 1,2-dibromo-3-chloropropane. *Bull Environ Contam Toxicol.* 55, 1-7
- Parker, I. and Hughes, D. (1998)** Activated Carbon. I: Water Treatment Primer. Civil Engineering Dept. Virginia Polytechnic Institute and State University.
- Pegram R. A., M. E. Andersen, S. H. Warren, T. M. Ross, L. D. Claxton (1997).** Glutathione S-transferase-mediated mutagenicity of trihalomethanes in *Salmonella Typhimurium*: contrasting results with bromodichloromethane and chloroform. *Toxicol. Appl. Pharmacol.* 144, 183-188
- Prieto R., E. Fernandez (1993).** Toxicity and mutagenesis by chlorate are independent of nitrate reductase in *Chlamydomonas reinhardtii*. *Mol. Gen. Genet.* 237, 429-438
- Porter K. E., A. R. Jones (1982).** The effect of the isomers of alpha-chlorohydrin and racemic beta-chlorolactate on the rat kidney. *Chem Biol Interact.* 41, 95-104
- Rathbun R.E. (1996)** Disinfection byproduct yields from the chlorination of natural waters, *Arch. Environ. Contam. Toxicol.* 31, 420-425.
- Reckhow D.A., Croue J.P. (1989)** Destruction of chlorinated byproducts with sulfite, *Environ. Sci. Technol.*, 23, 1412-1419.
- Rice R. G. (1999)** Ozone in the United States of America – State-Of-The-Art, *Ozone Sci. Eng.*, 21(2), 99-118.

- Rice R.G., Gomez-Taylor M. (1986)** Occurrence of by-products of strong oxidants reacting with drinking water contaminants – scope of the problem, *Environ. Health Perspect.*, 69, 31-44.
- Richardson S.D., Thruston jr. A.D., Caughran T.V., Chen P.H., Collette T.W., Floyd T.L., Schenck K.M., Lykins jr. B.W., Sun G., Majetich G. (1999)** Identification of new ozone disinfection byproducts in drinking water, *Environ. Sci. Technol.*, 33, 3368-3377.
- Richardson S.D., Thruston jr. A.D., Collette T.W., Patterson K.S., Lykins jr. B.W., Majetich G., Zhang Y. (1994)** Multispectral identification of chlorine dioxide disinfection byproducts in drinking water, *Environ. Sci. Technol.*, 28(4), 592-599.
- Richardson S.D., Thruston jr. A.D., Collette T.W., Patterson K.S., Lykins jr. B.W. Ireland J.C. (1996)** Identification of TiO₂/UV disinfection byproducts in drinking water, *Environ. Sci. Technol.*, 30, 3327-3334.
- Rijhsinghani K. S., C. Abrahams, M. A. Swerdlow, K. V. Rao & T. Ghose (1986).** Induction of neoplastic lesions in the livers of C57BLxC3HF1 mice by chloral hydrate. *Cancer Detect. Prev.* 9, 279-288
- Robinson D., Mead G.C., Barnes K.A. (1981)** Detection of chloroform in the tissues of freshly eviscerated poultry carcasses exposed to water containing added chlorine or chlorine dioxide, *Bull. Environ. Contam.*, 27(2), 145-150.
- Robinson M., R. J. Bull, G. R. Olson, J. Stober (1989).** Carcinogenic activity associated with halogenated acetones and acroleins in the mouse skin assay. *Cancer Lett.* 48, 197-203
- Sailienfait A. M., I. Langonne, J. P. Sabate (1995).** Developmental toxicity of trichloroethylene, tetrachloroethylene and four of their metabolites in rat whole embryo culture. *Arch. Toxicol.* 70, 71-82
- Smith M. K., E. L. George, H. Zenick, J. M. Manson, J. A. Stober (1987).** Developmental toxicity of halogenated acetonitriles: Drinking water by-products of chlorine disinfection. *Toxicology* 46, 83-93
- Smith M. K., J. L. Randall, E. J. Read, J. A. Stober (1992).** Developmental toxicity of dichloroacetate in the rat. *Teratology* 46, 217-223
- Soroushian F., Kwan A., Abramson C., Ferris M., Archer J., Mohammed A. (1996)** Pilot-scale studies of High-Intensity UV disinfection by-products, *Wat. Environ. Fed. Proc. (WEFTEC)*, 6, 55-60.
- Stauber A. J., R. J. Bull (1997).** Differences in phenotype and cell replicative behavior of hepatic tumors induced by dichloroacetate (DCA) and trichloroacetate (TCA). *Toxicol. Appl. Pharmacol.* 144, 235-246
- Stocker K. J., J. Statham, W. R. Howard & R. J. Proudlock (1997).** Assessment of the potential in vivo genotoxicity of three trihalomethanes: chlorodibromomethane, bromodichloromethane and bromoform. *Mutagenesis* 12, 169-173
- Suh D. H., M. S. Abdel-Rahman, R. J. Bull (1983).** Effect of chlorine dioxide and its metabolites in drinking water on fetal development in rats. *J. Appl. Toxicol.* 3, 75-79
- Tatken R. L., R. J. Lewis (1983).** Registry of toxic effects of chemical substances. Vol. 2. National Institute for Occupational Safety and Health, Cincinnati, OH
- Tsai L.S., Mapes C.J., Huxsoll C.C. (1987)** Aldehydes in poultry chiller water, *Poult. Sci.*, 66(6), 983-989.
- Uhler A.D., Diachenko G.W. (1987)** Volatile halocarbon compounds in process water and processed food, *Bull. Environ. Contam. Toxicol.*, 39, 601-607.
- Ventura F., Cancho B., Galceran M.T. (1999)** Behavior of halogenated disinfection by-products in the water treatment plant of Barcelona Spain, *Bull. Environ. Contam. Toxicol.*, 63, 610-617.
- Vetrano KM.** Molecular chlorine: Health and environmental effects. *Rev Environ Contam Toxicol* 2001; 170: 75-140
- von Bockelmann, B. og von Bockelmann, I. (1998)** Long-Life Products: A guide to quality. Förlth & Högssler, Sverige.
- von Gunten U. (1998)** Ozonanwendung in der Trinkwasseraufbereitung: Möglichkeiten und Grenzen, *Mitt. Gebiete Lebensmitt. Hyg.*, 89(6), 669-683.
- von Sonntag C., Dowideit P. (1998)** Reaction of ozone with ethene and its methyl- and chlorine-substituted derivatives in aqueous solution, *Environ. Sci. Technol.*, 32(8), 1112-1119.
- Waller K., S. H. Swan, G. DeLorenze, B. Hopkins (1998).** Trihalomethanes in drinking water and spontaneous abortion. *Epidemiology* 9, 134-40
- Wardle, M.D. og Renninger, G.M. (1975)** Bacterial Effect of Hydrogen Peroxide on Spacecraft Isolates. *Applied Microbiology*, 30, 4, 710-711.
- Weber, W.J. and LeBoeuf, E.J. (1999)** Processes for Advanced Treatment of Water. *Water Science and Technology*, 40, No. 5, 11-19.
- Wei C.-I, Fukayama M. Y., Hsioukun T., Wheeler W. B. (1986)** Reactions of aqueous chlorine and chlorine dioxide with model food compounds, *Environ. Health Perspect.*, 69, 267-274.
- Wei C.I., Ghanbari H.A., Wheeler W.B., Kirk J.R. (1984)** Fate of chlorine during flour chlorination, *J. Food Sci.*, 49, 1136-1138, 1153.

- Weinberg H. (1999)** Disinfection byproducts in drinking water, *Analytical Chem. News & Features*, 23(71), 801A-808A.
- World Health Organization (1996)**. Guidelines for drinking-water quality – 2. ed. Mastercom/Wiener Verlag, Austria
- Wright, J.R., Sumner,S.S.,Hackney,C.R.,Pierson,M.D. og Zoeklein,B.W. (2000)** Efficiency of Ultraviolet Light for Reducing *Eschericia coli* in Unpasteurized Apple Cider. *Journal of Food Protection*, 63, 5, 563-567.
- Yokose Y., K. Uchida, D. Nakae, K. Shiraiwa, K. Yamamoto & Y. Konishi (1987)**. Studies of carcinogenicity of sodium chlorite in B6C3F1 mice. *Environ. Health Persp.* 76, 205-210
- Yount E. A., S. Y. Felten, B. L. O'Connor, R. G. Peterson, R. S. Powell, M. N. Yum, R. A. Harris (1982)**. Comparison of the metabolic and toxic effects of 2-chloropropionate and dichloroacetate. *J. Pharmacol. Exp. Thera.* 222, 501-508.
- Zimmer G. (1996)** Kontinuierliche Überwachung der Anlagen-Desinfektion, *ZFL*, 47(10), 18-20.
- Zimmerli B., Schlatter J. (1993)** Vorkommen und gesundheitliche Bedeutung von Nebenprodukten der Trinkwasserchlorierung, speziell des Chlorhydroxyfuranons (MX), *Mitt. Geb. Lebensm. Hyg.*, 84, 662-676.