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FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

WORLD HEALTH ORGANIZATION

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DISCUSSION PAPER ON BENZENE IN SOFT DRINKS

(Prepared by the electronic working group led by Nigeria)

BACKGROUND

1. The Codex Committee on Contaminants in Foods (CCCF) at its Second Session held in April 2008[1] considered issues related to the formation of benzene in soft drinks and agreed to establish an electronic working group (e-WG), led by Nigeria and open to all members, to prepare a discussion paper on benzene in soft drinks.

2. The purpose of the discussion paper was to clarify the state of knowledge and the extent of the issue. An invitation to participate in the e-WG was circulated to all Codex Contact Points and Belgium, Brazil, Canada, Costa Rica, Cuba, Denmark, France, Egypt, European Community, Ghana, Germany, Japan, Kenya, Malawi, Nigeria, United Kingdom, FAO, ICBA and IFT expressed their willingness to participate. The list of participants is provided in Annex I.

INTRODUCTION

3. Benzene is present in the environment through human activities and a variety of industrial processes, it is also released naturally. In particular, benzene is released from the burning of fossil fuels, cigarette smoke and also through gasoline vapour. It is produced commercially, is a chemical used in the manufacture of other chemicals, dyes, detergents and in some plastics. It may also be released to a lesser extent naturally from volcanoes and forest fires. Vehicle emissions are the major source of benzene release to the environment[2], with food and drinking water contributing only minor amounts to a populations' daily benzene exposure.

4. The presence of benzene in food can be attributed to several potential sources. It may occur (at trace levels) in food naturally, as a result of process-induced changes to the food from high-temperature transformations or cooking processes, from ionizing radiation, or through the migration or leaching of packaging materials.[3-11] Benzene may also be present in food as a result of the contamination of water supplies or carbon dioxide used for carbonation, through other storage environments, or due to the ubiquitous presence of benzene in the environment.[3-11]

Benzene has been detected in several foods, such as eggs, cheese, bananas, fruits, meats and various sauces, generally at low parts per billion (ppb or ng/g) levels.[3-5,10,12,13] Benzene concentrations in drinking water are generally less than 5 µg/L (ppb).[14,15]

5. In the early 1990's, it was found that benzene can be formed in certain beverages from the degradation and reaction of added or naturally occurring precursors, such as benzoate salts and ascorbic acid, under certain conditions.[3,4,17] This is of concern because benzene is considered to be a human carcinogen based on available inhalation data in occupationally exposed workers and as supported by oral evidence in animal studies [18-20]. People who have inhaled very high levels of benzene in the work place have been found to have an increased risk of cancer.[21,22] Benzene is a carcinogen that causes tumors in rodents at multiple sites and leukemia in humans[23], the International Agency for Research on Cancer[19] classifies benzene as a Group 1 human carcinogen. As a result, the US Food and Drug Administration (FDA) and the beverage industry initiated research and discovered that exposure to certain heat and light conditions can stimulate the formation of benzene in some beverages that contain both benzoic acid or benzoate salts and ascorbic acid (vitamin C)[17]. Benzoate salts are added to some beverages as preservatives to prevent the growth of bacteria, yeasts, and molds. Benzoic acid and its salts are also naturally present in some fruits and their juices such as cranberries, prunes, plums and most berries. Vitamin C may be used as an antioxidant or be present naturally in beverages.

6. After the discovery of the potential for benzene formation in some beverages, the beverage industry took steps to reformulate affected products. However, since the 1990s, many new beverage manufacturers have emerged into the market place and some manufacturers began fortifying beverages with ascorbic acid and other nutrients. In 2005, findings of benzene in some beverage products in the U.S. triggered surveys on the occurrence of benzene in beverages in many countries. Based on some national surveys, the levels of benzene found in soft drinks are generally less than the permitted levels for benzene in drinking water (<5-10 µg/L). The few findings of high levels were reported to producers and many of these products were reformulated to eliminate the formation of benzene. In 2006, the International Council of Beverages Associations (ICBA) published a guidance document on measures that beverage manufacturers can take to mitigate the potential for benzene formation.[24]

TOXICOLOGICAL EVALUATION

7. The following section presents a summary of the major conclusions and toxicological evaluation of benzene provided, for the most part, in the WHO background document on benzene in drinking water,[15].

Absorption and Distribution

8. Orally ingested benzene is readily absorbed from the gastrointestinal tract and widely distributed throughout the body. Levels of benzene in the body decline rapidly once exposure is stopped. Following uptake, adipose tissues contain the highest levels of benzene metabolites.

Metabolism and Excretion Elimination

9. The metabolism and elimination of absorbed benzene appear to follow similar pathways in laboratory animals and humans. Benzene is converted mainly to phenol by the mixed-function oxidase system, primarily in the liver, but also in bone marrow. A small amount of phenol is metabolized to hydroquinone and catechol, and an even smaller amount is transformed into phenylmercapturic or *trans*-muconic acid. Between 12% and 14% (up to 50% in laboratory animals) of the absorbed dose is excreted unchanged in expired air. In the urine, a small part is excreted unchanged, the remainder being excreted as phenol conjugates.

Health Effects of Benzene

Results from Laboratory Animal Experiments

10. In animal studies, benzene has been shown to have a low acute oral toxicity. However, repeated oral exposure of rodents to low levels of benzene produces toxic effects principally in the blood and blood-forming tissues (for example: lymphoid depletion of the splenic follicles (rats) and thymus (male rats), bone marrow haematopoietic hyperplasia (mice), lymphocytopenia, and associated leukocytopenia (rats and mice)).

11. Benzene is not teratogenic even at maternally toxic doses.

12. Benzene is not mutagenic but it can cause chromosomal damage in plants and in mammalian somatic cells both *in vitro* and *in vivo*. Its clastogenic potential is partly due to its hydroxylated metabolites.

13. The mode of action of benzene toxicity is not fully understood. Benzene and its metabolites may interfere with the formation of the mitotic spindle and perhaps do not interact directly with DNA. However, binding of benzene to nucleic acids has been reported. Benzene is carcinogenic in rats and mice after oral and inhalation exposure, producing malignant tumours of an epithelial origin at many sites (including: Zymbal gland, forestomach, and adrenal gland (rats and mice); oral cavity (rats); lung, liver, harderian gland, preputial gland, ovary, and mammary gland (mice)).

Effects on Humans

14. Benzene is reported to have a low degree of acute toxicity when administered to different animal species by various routes of exposure. The single acute oral lethal dose in humans has been estimated to be about 10 ml (about 125 mg kg^{-1} bw)[63]. Signs of toxicity are nausea, vomiting and abdominal pain[23]. Lethality (for both inhaled and ingested benzene) has been attributed to respiratory arrest, central nervous system depression, or suspected cardiac collapse. For inhalation exposure, another possible cause of death is asphyxiation resulting from pulmonary oedema or haemorrhaging[64]

15. There is some concordance between animals and humans with regard to effects in the blood and blood-forming tissue. For example, rodents exhibit lymphoid depletion of the splenic follicles and thymus, bone marrow haematopoietic hyperplasia, lymphocytopenia, and associated leukocytopenia after repeated low oral doses of benzene. Human subjects with benzene haemopathy exhibit cytogenetic effects in peripheral lymphocytes and there is considerable evidence that exposure to high benzene concentrations (325 mg/m^3) is associated with the development of pancytopenia or aplastic anaemia.

16. However, the epithelial origin tumours observed in the animal cancer model are not observed in either epidemiological studies or several case-studies. In contrast human exposure to benzene was correlated with the occurrence of leukaemia (particularly acute myeloid leukaemia), which is an effect not observed in the rodent bioassays.

Classification of Benzene

17. Because of the unequivocal evidence of the carcinogenicity of benzene in humans and laboratory animals and its documented chromosomal effects, the International Agency for Research on Cancer (IARC) considers benzene to be a human carcinogen and it is classified in Group 1.[19]

Key Toxicological Studies used in Risk Assessments and to Derive Drinking Water Guidelines

18. Guidelines for benzene in drinking water have been derived by various regulatory agencies.

19. The rodent carcinogenicity study[25] continues to be cited as the pivotal study for the WHO[14,15] and Health Canada[26, 27] drinking water risk assessments.

20. The U.S. Environmental Protection Agency (EPA) [20] established a chronic oral Reference Dose (RfD) based on benchmark dose modeling of a non-carcinogenic endpoint (decreased lymphocyte count) in the Rothman[28] study on human occupational inhalation exposure to benzene and applied route-to-route extrapolation (inhalation to oral) and safety factors.

21. The EPA[29] also established drinking water guidelines based on a human occupational inhalation study of benzene by Rinsky and colleagues[30] with leukemia as the endpoint and using a cancer oral slope factor and route-to-route extrapolation.

22. The Rinsky et al.[30] analysis was also selected as the basis for the Netherlands National Institute for Public Health and the Environment (RIVM) risk assessment for oral exposure to benzene.[31] Both the EPA-derived non-cancer RfD and cancer slope factors were employed in a quantitative risk assessment for general environmental exposures to benzene conducted by Toxicology Excellence for Risk Assessments (TERA).[32]

METHODS OF ANALYSIS AND SAMPLING

23. Techniques frequently cited as methods for determining benzene and other volatile organic compounds in foods are static and dynamic purge and trap (P&T), headspace (HS) sampling followed by gas chromatography/mass spectrometry (GC/MS), the preferred method, or GC/flame ionization detection (FID).[33,34] Several studies reported using static HS GC/MS to conduct surveys of various fruit juices and other beverages including water and soft drinks.[3,4,35,36]

24. Since levels of benzene in beverages are usually very low and interferences from other volatile chemicals that are constituents of beverages can generate false positive results, regulatory bodies such as Health Canada, the US FDA, and various European agencies use GC/MS because this instrument allows for confirmation of the identity of detected compounds.[35-37,21] The ICBA methods, based on the EPA methods and validated by the beverage industry, specify a GC/MS method using headspace sampling for the determination of benzene in carbonated and non-carbonated beverages, and a dynamic purge and trap headspace analysis for carbonated soft drinks and juice products.[24] Other published methods using static headspace sampling[36,38,39] include similar techniques but may include refinements such as cryofocusing of the sample to improve sensitivity and resolution[37]. Benzene in water and other beverages such as soft drinks is usually quantified by isotope dilution with a d_6-benzene internal standard. However, this method may not be adequate for other, more complex, food matrices.

25. Many published methods reported a limit of quantification of 1 µg/L.[4,21,35,40] A lower detection limit (0.016 µg/L) and a good repeatability were recently reported with an improved method by Health Canada.[37] In addition to static headspace as a means of sampling, some researchers have used purge and trap[4] or solid-phase microextraction (SPME) techniques.[7,21] In the 1990s, SPME and vacuum distillation (VD) were introduced as methods to extract VOCs from various matrices.[41,42] Although VD and SPME have not been widely reported for the quantitative determination of benzene in food, these techniques warrant future investigation.

26. Under certain conditions (low pH, high temperature, presence of benzoic acid) benzene formation can occur during head-space injection leading to false positive results[11]. Therefore, the analytical methods employed should be adopted appropriately in order to avoid artefactual

benzene formation. Many of the methods mentioned above provide means for addressing this issue.

FACTORS AFFECTING THE PRESENCE OF BENZENE IN SOFT DRINKS

27. The determination of the presence of benzene in soft drinks and other beverages prompted investigations into the pathways of benzene formation from benzoic acid and ascorbic acid.[4,17,24,43] Laboratory tests show that the primary driver for benzene formation in beverages under certain reaction conditions which may be prevalent in some beverages, is the presence of precursors such as benzoate salts (sodium, potassium or calcium benzoate) along with ascorbic acid.[17,24] The reaction of OH* radicals with benzoates is thought to lead to the formation of an unstable benzoic acid radical (C_6H_5—COO*) which readily loses CO_2 (decarboxylation) to form a benzene radical. Benzene then forms as a result of hydrogen abstraction from a suitable donor molecule. Benzoates are converted to free benzoic acid under acidic conditions, such as those present in many soft drinks and beverages. The source of hydrogen peroxide is an ascorbic acid assisted reaction, mediated by catalytic amounts of iron or copper salts, that produces the superoxide anion radical which spontaneously disproportionates to hydrogen peroxide.[8,17,43]

28. It is important to note however, that the presence of benzoic acid and ascorbic acid does not necessarily lead to the formation of benzene.[11,44]

29. A combination of benzoic acid and ascorbic acid, in the presence of certain minerals such as the salts of copper (II) and iron (III), which occur in low concentrations in drinking water, along with other factors such as beverage pH, the presence of oxygen, storage temperature and exposure to UV light have been implicated in the formation of benzene[4,17,43,8] where heat is the predominant factor for the latter two conditions.[24] The mechanism of formation is believed to be based on the Fenton reaction between metal ions [copper(I), iron(II)] found in the water and hydrogen peroxide, which produces hydroxyl radicals (OH*).Benzene formation may also occur when juices and other ingredients which naturally or otherwise, where permitted, contain benzoic acid sources and ascorbic acid are used in beverage formulations.[4]

30. Analysis conducted by the U.S. Food and Drug Administration (FDA), the United Kingdom and Health Canada showed wide variations in benzene concentrations for different lots of the same product, and in some cases between samples from the same lot, suggesting that storage conditions have an impact on the formation of benzene.[22,36,37,40] Benzene levels also appeared to be higher in diet soft drinks and beverages containing intense sweeteners.[24,36,38] Some studies suggest that erythorbic acid (an isomer of ascorbic acid, also known as d-ascorbic acid), where permitted, may lead to benzene formation in much the same way as ascorbic acid.[24,40]

31. Lachenmeier and colleagues[11] found that copper and iron concentrations were significantly higher in benzene positive samples than benzene negative samples, supporting earlier observations. However, some beverages containing higher concentrations of these ions, did not contain benzene. While studies suggest that the presence of benzoate salts, ascorbic acid and other precursors can lead to the formation of benzene, the reaction is complex and not completely understood.

32. Experiments by McNeil and colleagues[4] showed that substituting benzaldehyde (a flavouring compound used to simulate cherry flavor) for benzoate salts, could play a role in the formation of benzene. The mechanism for benzene formation in this instance is not known. However, trace amounts of metal ions may be sufficient to initiate hydroxyl radical formation.[4,43]

33. Van Poucke and colleagues[39], in a survey of beverages available on the Belgian retail market, found that the presence of benzoic acid and of an acidity regulator or combination of acidity regulators (e.g. citric acid, phosphoric acid), or ascorbic acid and an acidity regulator had an influence on benzene formation.

34. Some survey data[39] indicate that the type of packaging material, either alone or in combination with other factors (benzoates and ascorbic acid alone or in combination) may also play an important role in benzene formation that could be related to the material's degree of permeability to UV light. Benzene levels appeared greater in plastic bottles than those products sold in cans or glass bottles. Other factors such as storage conditions (heat, light) also may contribute.

35. To summarize, many factors can affect the oxidation of ascorbic acid and the subsequent generation of hydroxyl radicals including the concentrations of the benzoates and ascorbic acid, the type and presence of certain metal ions which act to catalyze the formation of benzene, the pH of the solution, exposure to heat and UV light, and the effects of different chelating agents. All of these factors interact in a complex manner. As such, whether and to what extent benzene is actually formed in the corresponding foods cannot be reliably assessed based on current knowledge.[8] Given the complexity of the reaction, a general relationship between the amount of benzoate and ascorbic acid (in beverages), and the amount of benzene that forms has not been successfully established. It has been suggested, based on current knowledge, that analytical testing of the soft drink formulations under accelerated test conditions is the best means of determining the potential for the formation of benzene.[24]

BENZENE OCCURRENCE

36. Heikes and colleagues[46] found benzene in 28 of 234 table-ready foods from the US FDA total diet study (TDS), ranging from 9.49 - 283 ppb, with the highest level being reported in sauerkraut. A five year study of TDS composited foods found benzene in almost all of the 70 foods analyzed, with the exception of American cheese and vanilla ice cream, at concentrations of 1 to 190 ppb.[13] However, the FDA has more recently recommended that the benzene TDS data be used with caution, due to an evaluation indicating that the analytical method used in that survey produced elevated and unreliable benzene results in some foods and in particular those containing benzoate preservatives, such as soft drinks. Levels of benzene in soft drinks from these surveys were inconsistent with levels reported in the literature and more recent beverage surveys.[47] Cao and colleagues[36,37] and Lachenmeir and colleagues[11] indicated that certain analytical conditions, as well as high temperatures and high benzoic acid concentrations can lead to formation of artifactual benzene.

37. In general, data from targeted sampling and total diet studies show that benzene concentrations in food seldom exceed low levels (generally at low ppb or ng/g).

38. Available data show that the majority of samples taken in national markets around the world are well below the WHO guideline level of 10 µg/L of benzene established for drinking water.

39. Shortly after the finding in the 1990's that benzoates and ascorbic acid can react to form benzene, Health Canada conducted a survey of benzene in fruits, fruit juices, fruit drinks, and soft drinks.[3] Benzene levels in these products were below the 5 ug/L maximum acceptable concentration (MAC) of benzene in Canadian drinking water. [3] Specifically, average levels of benzene in freshly expressed juice from fruits, juices with and without benzoates, noncarbonated drinks with and without benzoates, soft drinks with and without benzoates were 0.042, 0.672, 0.056, 0.395, 0.116, 0.793, and 0.062 ug/kg, respectively. Fruit juices and carbonated soft drinks labeled as containing benzoates contained approximately 10-fold higher benzene concentrations than those without benzoates. This same trend was not seen in fruit drinks, where the authors suggested that naturally occurring benzoic acid may be present in some juices. A similar survey conducted by the US to determine benzene levels in foods and beverages containing either naturally occurring or added benzoates and/or benzoates and ascorbic acid, found low levels of benzene, below 1 ppb, in the majority of the beverages analyzed.[4] The highest benzene concentration was found in a liquid smoke product.

40. A survey on the occurrence of benzene in 60 beverages available on the Italian market showed the presence of benzene at levels ranging from 1-3.8 ppb.[6]

41. In 2005, some beverage samples were found to contain elevated levels of benzene (US FDA 2006) which prompted many countries to conduct surveys on the occurrence of benzene in soft drinks and other beverages. Surveys were conducted in such countries as the USA (2005 - 2007), the UK (2006), Australia and New Zealand (2006), South Korea (2006), Japan (2006), Canada (2006 - 2007), Ireland (2006-2007), Belgium (2006 - 2007), and Germany (2006-2007).[11,22,35,36,38,39,47-55] In most surveys, sampling had been targeted to products that contained sodium benzoate and ascorbic acid. The results have been either published in scientific journals or websites of the regulatory agencies who conducted the studies. The results of the testing of hundreds of samples by national government agencies and the beverage industry were consistent; showing low µg/L levels of benzene in beverages containing specific ingredients that may lead to the formation of benzene. Additional details of these surveys can be found in Table 1.

42. The US FDA surveyed 199 samples of soft drinks and other beverages from 2005 through May 2007.[38,40] Only a small number of products (ten) contained more than 5 µg/L of benzene, a guideline established by the US Environmental Protection Agency in drinking water. Benzene levels greater than 5 µg/L were found in nine products that contained both added benzoate salts and ascorbic acid, and one cranberry juice beverage that contained added ascorbic acid but no added benzoate. Benzoates are found naturally in cranberries. The US manufacturers reformulated products that exceeded 5 µg/L of benzene. The US FDA tested samples of these reformulated products and found that benzene levels were less than 1.1 ng/g (roughly equivalent to 1.1 µg/L).

43. In 2006, the United Kingdom Food Standards Agency (FSA) collected 150 drinks from supermarkets and independent shops from four regions in the UK.[21,22,48] The samples consisted mainly of concentrates (squashes), carbonated drinks, and ready-to-drink still drinks (non-carbonated drinks with less than 25% juice content). The majority of drinks contained benzoates and ascorbic acid. A limited number of mango juices and cranberry drinks also were chosen as these fruits naturally contain benzene. Out of 150 soft drinks sampled, 107 (70%) did not contain detectable levels of benzene and four products contained average levels of benzene above 10 µg/L. These products which were produced prior to the industry guidance being implemented in the UK, were removed from sale. The FSA asked the soft drinks industry to ensure that levels of benzene are kept as low as practicable.

44. Food Standards Australia New Zealand (FSANZ) sampled 68 flavoured beverages in March/April 2006.[49] Sampling was targeted mainly at beverages that were more likely to contain benzene due to the presence of benzoate and ascorbate and included: cola and non cola soft drinks, flavoured mineral waters, cordial, fruit juice, fruit drinks, energy drinks, and flavoured/sports water. Of the 68 samples tested, 38 beverage products contained trace levels of benzene. The levels detected ranged from 1 to 40 µg/L. More than 90% of all beverages surveyed had levels of benzene below the WHO guidelines for drinking water (10 µg/L).

45. In March 2006 the Food Safety Authority of Ireland (FSAI) conducted a survey in conjunction with the Galway Public Analysts Laboratory in order to establish the levels of benzene present in 76 samples of soft drinks, squashes and flavoured waters available on the Irish market.[54] Only 7 beverages contained benzene above the detection limit and of those, 2 were above the WHO guideline for benzene in drinking water of 10 ug/L. In a follow-up survey, 63 samples of the same beverage types were analyzed for benzene. Of those, 9 were above the limit of detection and 2 were above the WHO guideline for benzene in drinking water.[55]

46. In 2006, Health Canada initiated a survey of benzene in soft drinks as well as some low alcohol drinks and cocktail mixers in order to assess benzene levels in products available in

Canada.[36,44,52] Samples of 118 products were analysed for benzene. Benzene was found in samples of four of the products at levels above the Canadian guideline of 5 µg/L benzene in drinking water. In these samples, average positive concentrations ranged from 6.0 to 23.0 µg/L. Benzene in most of the remaining products was either not detected or was detected at levels below 5 µg/L benzene in drinking water. For those few products in which benzene levels were initially found to be in excess of the Canadian guideline of 5 µg/L for drinking water, significant reductions of benzene levels were observed in reformulated products.

47. Health Canada conducted a follow up survey in 2007 to assess benzene levels in 139 samples of soft drink products and other beverages (110 were the same products as those analyzed in the 2006 survey) using a more sensitive method capable of a detection limit of 0.016 µg/L (11, 18).[37,53,56] Because of the lower method detection limit, benzene was detected in 67% of the 139 products tested, but the average benzene levels in most products remained low. With the exception of certain cocktail mixes and one carbonated soft drink sample, average levels found were below 5 µg/L. Cocktail mixes are intended to be diluted before drinking, resulting in a lower exposure to benzene.

48. The Belgian Federal Agency for the Safety of the Food Chain surveyed 134 low-calorie soft drinks samples that were collected from October 2006 until May 2007 on the Belgian market.[39] All samples, except one (10.98 µg/L), was below 10 µg/L and three were above 5 µg/L.

49. The Korean Food and Drug Administration conducted two surveys to determine the presence of benzene in beverages. In the first, benzene levels in 37 products ranged from 1.7 -263 ppb.[50] The follow-up survey was conducted to analyze benzene levels in 30 of the same products soon after their manufacture date, levels ranged from 5.7 to 87.7 ppb.[51] Manufacturers whose products contained benzene levels in excess of the WHO guideline for benzene in drinking water were advised to voluntarily recall their product.

50. A survey of benzene in German food products was conducted, concentrating on product groups that were previously described as likely to contain benzene (such as beverages containing ascorbic and benzoic acid), with a focus on products sold as baby or infant food.[11] Products were collected between 2006 and 2007 and consisted of 451 samples of different soft drinks, drinks intended for babies and infants (drinks with fruits, vegetables and/or tea), "alcopops", beer-mixed beverages, as well as carrot juices for the general consumer and infants. These samples were analyzed using an analytical method with a quantification limit of 0.13 µg/L. The average benzene level in soft drink samples was 0.24 µg/L. Out of 313 soft drink samples analyzed, only one sample exceeded 10 µg/L and 7 samples were above 1 µg/L. Interestingly, the concentrations in carrot juices, and especially in carrot juices intended for infants, were higher than those in all other groups of beverages. Approximately 88% of all carrot juices for infants had benzene levels above 1 µg/L. The authors suggested that the formation of benzene in carrot juice was predominantly caused by a heat-induced mechanism (infant juices are subject to heat for longer periods of time than carrot juices which are directed at the general population), as none of the carrot juices in the study contained benzoic acid. The authors indicated that further study would be required in order to determine responsible precursors, but suggested that a metal-catalyzed formation of benzene may also be possible since higher levels of these metals were found in carrot juices. The authors concluded that, with a few exceptions, benzene exposure of the consumer from soft drinks and alcoholic beverages on the German market appears to be very low and nearly negligible, considering exposure to benzene from other sources.

51. Wu and colleagues[10] found that 6 Chinese beers in a survey of 84 contained detectable levels of benzene (1.9-7.1 ug/L; mean 4.0ug/L). The authors, through subsequent investigation, theorized that the CO_2 utilized for carbonation could have caused benzene formation.

52. The Japanese National Institute of Health Sciences, from May to July 2006, carried out the surveillance for benzene on 31 commercial soft drink products to which both sodium benzoate and ascorbic acid (vitamin C) have been added as food additives. Thirty (30) items out of 31 contained benzene below 10 µg/L. The benzene at the level of 73.6 µg/L was detected from 1 item.

Table 1. Survey data on benzene in soft drinks and other beverages

Country/Organization	Year	N	LOD[1] and/ or LOQ[2] (ppb)	# of +ve's	range (ppb)	Types of products	Ref.
Benezene in soft drinks and other beverages (survey results after detection in the 1990's)							
Canada	1991/1992	97	LOD: 0.03	97	0.018 - 3.83	fruits as freshly expressed juice, and retail samples of fruit juices, fruit drinks and soft drinks	3
U.S.	1991/1992	59	LOQ: 1.0	19	<1 - 121	included foods previously reported as containing benzene (water, egg, jam, etc.)	4
U.S.	1991/1992	44	LOQ: 0.05	15	<0.05 - 9.0	soft drinks, juices, beers and waters from processed vegetables	45
Italy	2001	60	LOD: 0.05	60	1.00 - 3.93	cola beverages, light beverages made from cola, beverages made from orange juice and carbonated beverages	6
Benezene in soft drinks and other beverages (survey results after detection in 2005)							
FSANZ	2006	68	LOQ: 1.0	38	<1 - 40	cola and non-cola soft drinks, flavoured mineral water, cordial, fruit juice, fruit drinks, energy drinks, and flavoured/sports water	49
Belgum	2006/2007	134	LOD: 0.1; LOQ: 0.3	90	<0.1 - 10.98	low-calorie soft drinks	39
Health Canada	2006	124	LOD: 0.16 and 0.26; LOQ: 1.0	49	<1 - 23	soft drinks, juices, low-alcohol coolers, syrups (e.g. grenadine), and cocktail mixes	36,52
Health Canada	2007	139	LOD: 0.016	93	<1-18		37,53
China	2006	84	LOQ: 1.0	6	<1- 7.1	beer avaliable on retail market and breweries, 7 imported beers	10
Germany	2006/2007	451	LOD: 0.04 ; LOQ: 0.13	192	<0.04 - 41.8	soft drinks, alcopops, beer-mixed drinks and beverages for babies/infants, including carrot juice	11
FSAI	2006	76	LOQ: 1.0	7	<1 - 91	soft drinks, carbonated drinks, concentrates (squashes), still drinks and flavoured waters	54
FSAI	2007	63	LOQ: 1.0	9	<1 - 18.3		55
KFDA	2006	37	n/a	37	1.7 - 263 (+ve's)	Beverages containing benzoate and ascorbic acid, Vitamin C enriched drinks	50
KFDA (follow-up)	2006	30	n/a	27	5.7 - 87.8 (+ve's)	Vitamin C enriched drinks	51
UK (soft drink industry)	2006	230	n/a	n/a	8.0 (highest); most <	FSA asked industry to provide information on benzene levels in beverages - aggregate summary data	22,48
UK FSA	2006	150	LOQ: 1.0	43	<1-28	concentrates (squashes), carbonated drinks and ready-to-drink still drinks, also included mixers, sports/energy drinks and some fruit juices	22,48
Japan	2006	31	LOQ: 1	31	<1-73.6	Commercial soft drinks products containing both sodium benzoate and ascorbic acid	
U.S. FDA	2005/2006	113	LOD: 0.2 and 0.02; LOQ: 1.0	73	<1 - 87.9	soft drinks, and other beverages including other carbonated beverages, non-carbonated beverages and cranberry juice cocktails	40
U.S. FDA	2006/2007	86	LOD: 0.04	51	<1 - 88.9		40
U.S.	2008	199	LOD: 0.05; LOQ: 0.2	125	<0.05 - 88.9		38

n/a - not available, [1]LOD - Limit of Detection, [2]LOQ - Limit of Quantification

DIETARY EXPOSURE

Benzene in beverages

53. Some international food regulatory agencies have concluded that exposure to benzene from the consumption of soft drinks and other beverages is generally low and nearly negligible, representing a minor contribution compared to total benzene exposure from other sources (e.g. indoor/outdoor air, vehicular emissions and the consumption of drinking water and foods in which benzene may occur as an environmental contaminant).

54. Haws and colleagues[57], conducted a survey of benzene levels in the beverage product that was found to contain the most elevated levels of benzene (old formulation) in FDA's survey of benzene in beverages, as well as surveying the reformulated product. The authors utilized some very conservative exposure scenarios in which the 95% upper confidence limit of occurrence data from their survey was used to estimate consumers' daily exposure to benzene from this beverage type, for various age groups. The authors concluded that the exposure to benzene from beverages is insignificant relative to that of inhalation, and that there was no unacceptable health risk associated with the consumption of these products.

55. Health Canada conducted exposure assessments in 2006 and 2007[44,56] on the occurrence of benzene in soft drinks and other beverages. Probable Daily Intake (PDI) estimates for beverage products, excluding the most elevated products (which have since been reformulated) ranged from 6-9 ng/kg body weight/day for adults (60 kg body weight assumed), 8 ng/kg bw/day for 5-11 year old children (26.4 kg bw) and 6 ng/kg bw/day for 12-19 year olds (53.8 kg bw) for different beverage intake scenarios. Exposure estimates based on 2007 survey results, and updated consumption figures and body weights were 1.8 – 11 ng/kg bw/day for adults (70 kg body weight), 3.3 ng/kg bw/day for 5-11 year olds (30 kg bw), and 2.8 – 4.2 ng/kg bw/day for 12-19 year olds (60 kg bw) for the combination of all soft drink and other non-alcoholic beverage products combined, or all alcoholic beverages combined for age groups consuming these products.

Benzene exposure from other sources

56. The most significant exposure route for benzene in the general population is through the inhalation of ambient air.[2,18,23,58,59] The presence of benzene in gasoline (petrol), and its wide use as an industrial solvent, can result in significant and widespread emissions to the environment. Exposure inside homes can occur from cigarette smoke and from building materials.

57. Other possible sources of exposure to benzene include the consumption of drinking water and foods, in which benzene may occur as a result of environmental contamination, either industrial or production-related; naturally; through migration from packaging materials; because of heat-induced formation during cooking or production processes; or as a result of the irradiation of food.[3-6,8-11] In general, exposure from food and water is much less than that from air[15,59]. Water and food-borne benzene contribute only a small percentage of the total daily intake in non-smoking adults (between about 3 and 24 µg/kg body weight per day).[18] The intake by the general population through food products is estimated to be less than 2% of the total exposure to benzene from all sources.[2,58,59]

58. Various estimates of human exposure to benzene from air, food and water have been made and are presented in Table 2.

Table 2: General world population exposure to benzene categorised by activity and media. (Adapted from FSANZ (2006) and HC (2006))

Source of exposure	Estimated exposure	Reference
Air		
Inhalation exposure	220 µg (micrograms)/day	58
Ambient air	9-91 µg/day	2
Refilling car petrol tank	32 µg during refilling (3 mins)	58
Automobile-related activities	49 µg/day	2
Driving for one hour	40 µg/day	23

Diet		
Food and drink products	0.2-3.1 µg/day (eggs with no benzene or 2ppb benzene)	58
Food	0.42 - 1.65 µg/day	2
Drinking water	0.12 – 1.4 µg/day	2
Food	120-325 ng/kg bw/day	44
Water and food	1.4 µg/day	18
Food and drinking water	250 ug/day (4200ng/kg bw/day, 60-kg adult)	26
Food	180 ug/day (3000 ng/kg bw/day, 60-kg adult)	15
Cigarette smoking	7900 µg/day	58
	1815 - 1820 µg/day	2
	1800 µg/day	18
Passive smoking	6 - 63 µg/day	2
	50 µg/day	18

59. The exposure estimates presented in Table 2 do not include estimates using more recent survey data (2006/07) generated by various international regulatory bodies and food safety organizations on the occurrence of benzene in beverages. However, these more recent estimates either fall in the same range or are lower than occurrence levels that have been previously found in other foods. Further, they do not make a significant contribution to total benzene intake and for the general population would not represent a major source of exposure.

60. Differences between dietary intake estimates presented in Table 2 may be attributed to the survey data and/ or approaches used to derive these estimates. The presence of benzene in some foods may have occurred as a result of the analytical method used, as described previously.[11,36,47] The FDA recently stated that their TDS analytical method produced unreliable results for benzene. Some of the exposure estimates from food above may have been derived from this data.

PREVENTION OF BENZENE IN SOFT DRINKS

61. The International Council of Beverages Associations (ICBA) has developed and approved a *Guidance Document to Mitigate the Potential for Benzene Formation in Beverages* which has been adopted by the many National Beverages Councils and Associations, and been made available to beverage manufacturers around the world. The ICBA guidance document[24] summarizes factors which may mitigate the formation of benzene in beverages containing benzoic acid sources and ascorbic acid based on experience in the beverage industry and experiments that have been carried out on the formation of benzene.

62. In particular, evidence indicates that nutritive sweeteners (sugar, high fructose corn or starch syrup), where permitted, may delay or inhibit the reaction by reacting with and inactivating hydroxyl radicals, as the formation of benzene seems most noticeable in diet beverages containing intense sweeteners.[24,36,38] However, the longer a product is in the market (shelf-life), the greater the potential for benzene formation if its precursors are present. Evidence also suggests that chelating agents, such as calcium disodium ethylenediaminetetraacetic acid (EDTA) or diethylenetriamine pentaacetic acid (DTPA), where permitted, may mitigate the formation of benzene in products containing benzoates and ascorbic acid, possibly by complexing metal ions that may act as catalysts.[17,24,43] However, the effectiveness of EDTA as a chelating agent is not always obvious and the degree of mitigation may be lessened in products containing calcium or other minerals, such as mineral fortified products.[24,38] It is also suggested that sodium poly (or hexameta) phosphate, may mitigate benzene formation.

63. The ICBA Guidance Document[24] also provides advice and strategies to beverage manufacturers on ways to minimize the potential for benzene formation in beverages through formulation control. These strategies include: reviewing existing products and new formulations (including their ingredients, such as fruit juices, flavor emulsions, colours, clouding agents that may contain preservatives or antioxidants, either naturally or added intentionally for a technological effect, and storage and shelf-life considerations) for their potential to form benzene in consideration of the current knowledge on factors contributing to benzene formation; looking at alternative ingredients (the replacement/ reduction of benzoates with sorbates or other preservative systems, and/or ascorbic acid with attendant challenges addressed); or reviewing manufacturing processes that are available to prevent the formation of benzene. Advice is also provided on: performing accelerated

storage tests of products to determine the potential for benzene formation; reformulating affected products in which benzene may be present; confirming that new formulations and reformulations are effective in minimizing the potential for benzene formation through market sampling, etc.; and analytical procedures for the determination of benzene.

64. It is clear that several factors may be interacting to increase or decrease the formation of benzene in beverages including: the order of added ingredients, the specific formulation and precursors that may be present within the beverage, as well as storage conditions experienced throughout the life of the product. Reformulated products have been shown to contain reduced benzene levels, where levels are either not detected or detected at very low levels, generally below 1 ug/L.[36,40]

REGULATORY STATUS AND RISK MANAGEMENT

65. The WHO established a guideline value of 10 µg/L benzene in drinking water[1,15]; the US EPA, FDA and Health Canada have established a maximum contaminant level (MCL) and maximum acceptable concentration (MAC) of 5 ug/L[29,40,26], respectively; and Australia (1996) and the EU (1998) have established a guideline for benzene in drinking water of 1 ug/L.[60,61] Health Canada is intending to revise its current benzene guideline in drinking water of 5 ug/L to 1 ug/L.[27] In a number of cases, these limits have been used as a reference value for the presence of benzene in soft drinks and beverages other than water. [40,44,56] In fact, many government agencies have typically used these guidelines, as well as estimates of benzene exposure from dietary and other sources as a basis for risk management decisions and have asked manufacturers to reformulate or withdraw beverage products that exceed benzene in drinking water guidelines established in their own country or by the WHO. It is important to note however, that in many cases, regulatory bodies have conducted health risk assessments based on exposure to benzene from soft drinks and other beverages using both cancer (unit risk over a lifetime) and non cancer (TDI or RfD) toxicological endpoints to estimate exposure levels associated with a low level of risk.[44,56]

66. The guidelines for benzene in drinking water vary from country to country and are based on different consumption estimates than those of soft drinks. For example, the WHO[15] typically uses a consumption estimate of 2 liters per day and a source contribution factor for drinking water compared with other sources of benzene intake. Typically, the consumption of drinking water is more than six times that of the relevant flavoured beverages, but beverage consumption also varies considerably between countries and between age groups[49]. For example in Belgium, data obtained from the 2004 food consumption survey[65] indicate that the average usual intake for soft drinks is 213 ml a day, while for the subgroup of men aged 15-18 years, the average usual intake of soft drinks is 576 ml and the 97.5th percentile is 1412 ml[66] Because guidelines for safe levels of benzene in drinking water have been drawn upon as an appropriate comparator for risk management decisions, some countries have suggested action limits for benzene that are specific to soft drinks and other beverages. For example, at the European level, the Standing Committee on the Food Chain and Animal Health of DG Health and Consumer Protection suggested an action level for benzene in soft drinks of 10 µg/L.[62] The Scientific Committee of the Belgium Federal Agency for the Safety of the Food Chain has suggested 1ug/L as an acceptable reference point for benzene in soft drinks.[39]

67. In many cases, beverages containing benzene levels above drinking water guidelines for benzene (5-10 µg/L) have been voluntarily withdrawn from the markets and/or reformulated by beverage manufacturers. The follow-up studies by regulatory authorities and the beverage industry have shown that the reformulations lead to greatly reduced and acceptable levels in those products in which benzene was initially found above national action levels.[37,40,56]

68. The conclusions of some national governments such as those in Australia, the United Kingdom, the US, Germany and Canada are that survey results in relation to benzene levels in soft drinks do not raise public health concerns, as the trace amounts found make a very small impact on overall benzene exposure. For example, in 2007, Health Canada evaluated the health risk that could result from exposure to benzene in some soft drinks and concluded that “there is negligible health risk posed by consumption of soft drinks and other beverages which are available for sale in Canada”.[56] However, government agencies have worked with their local beverage industry groups to ensure that levels of benzene in beverages are kept as low as can be achieved, while still ensuring the microbiological safety of these products.

CONCLUSIONS

69. The potential for the formation of benzene in soft drinks has been recognized. Benzene formation may occur at part per billion levels in some beverage formulations containing sodium, potassium, or calcium benzoate along with ascorbic acid, under certain conditions. While the majority of beverages surveyed by

national authorities contain benzene at levels less than those permitted for drinking water, some products were initially found to contain 2-5 times the World Health Organization[14,15] (WHO) guideline level of 10 µg/L for drinking water. However, government agencies have worked with their local beverage industry groups and manufacturers to ensure that levels of benzene in beverages are kept as low as can be achieved, while still ensuring the microbiological safety of these products. The beverage industry has established guidance for beverage manufacturers on ways to mitigate benzene formation. This information has been made publicly available. Implementation of the industry guidance, including product reformulations where necessary, has been shown to reduce benzene levels well below current guidelines for benzene in drinking water.

70. Some National authorities have investigated the presence of benzene in soft drinks and other beverages available within their own countries, generally concluding that exposure to low levels of benzene from soft drinks do not raise any public health concerns and that beverages available for sale are safe. This is based on findings that the trace amounts of benzene found in soft drinks and other beverages make only a very small impact on overall benzene exposure, as well as on the successes of actions that have been taken by the industry to reformulate products where necessary. However, member countries in the tropical regions where some of the drinks are sold in the open tropical heat are yet to come to terms with the inherent risk, and the industry are obliged to use elevated level of benzoates salts (albeit within the max level of Codex) to preserve their products.

71. Some regulatory agencies have concluded that the levels of benzene found in beverages, as well as actions taken by the beverage industry including the reformulation of affected products and the availability of guidance provided by international and national beverage councils and associations do not warrant the formal setting of maximum limits and/or guidelines for benzene in soft drinks and beverages other than water. However, because benzene is a carcinogen, every effort should be made to ensure benzene levels in beverages are as low as is reasonably achievable.

72. Information provided in industry guidance documents[24] and by national food authorities will also help ensure that new beverage manufacturers are aware of the potential for benzene formation from precursor compounds.

RECOMMENDATIONS

73. Therefore the following recommendations are presented by the electronic working group for the consideration of the third CCCF:

a. Countries that have carried out national surveys are encouraged to update and target an all-year-round sampling to capture different climatic conditions

b. Codex Coordinating Committees for Africa, Asia, Latin America and the Caribbean, should appeal to their members, especially those in the tropics that are yet to carry out their national surveys to do so. The survey should incorporate exposure assessment and dietary intake studies.

c. Member governments are encouraged to work with their beverage manufacturers to ensure that the available information is communicated.

d. The CCCF is invited to consider producing a code of good practices for the prevention of benzene formation in soft drinks because of the inherent risks to public health.

e. In view of the challenges in methodology and instrumentation in the determination of benzene in soft drinks WHO and FAO should consider assistance to interested member countries for capacity building.

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