

ASPARTAME, METHYLEUGENOL, AND ISOEUGENOL

VOLUME 134

This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met in Lyon, France, 6–13 June 2023

LYON, FRANCE - 2024

IARC MONOGRAPHS
ON THE IDENTIFICATION
OF CARCINOGENIC HAZARDS
TO HUMANS

CONTENTS

NOTE TO	THE READER	1	
LIST OF I	PARTICIPANTS	3	
PREAMB	LE	9	
A. GENERAL PRINCIPLES AND PROCEDURES			
1.	Background	9	
2.	Objective and scope		
3.	Selection of agents for review		
4.	The Working Group and other meeting participants	. 11	
5.	Working procedures		
6.	Overview of the scientific review and evaluation process	. 14	
7.	Responsibilities of the Working Group	. 16	
B. SCI	ENTIFIC REVIEW AND EVALUATION	. 17	
1.	Exposure characterization	. 17	
2.	Studies of cancer in humans	. 20	
3.	Studies of cancer in experimental animals	. 25	
4.	Mechanistic evidence	. 28	
5.	Summary of data reported		
6.	Evaluation and rationale	. 32	
Referei	nces	. 37	
GENERA	L REMARKS	. 41	
	ME		
	posure Characterization		
	Identification of the agent		
	Production and use		
	Detection and quantification		
	Occurrence and exposure.		
	Regulations and guidelines	. 96	
1.6	Quality of exposure assessment in key epidemiological studies of cancer and mechanistic		
	studies in humans	. 97	

2	Cancer in Humans	121
2.	Introduction.	
	2.1 Cancer of the liver, colon and rectum, pancreas, and other organs of the digestive tract	
	2.2 Cancers of the urinary tract	
	2.3 Cancers of the breast and prostate	
	2.4 Cancers of the brain, thyroid, and uterus, and other solid cancers	
	2.5 Cancers of lymphatic and haematopoietic tissues	
	2.6 Obesity-related cancers and other groupings	
	2.7 Cancer of all sites combined	
2	2.8 Evidence synthesis for cancer in humans	
3.	Cancer in Experimental Animals	
	3.1 Mouse	
	3.2 Rat	
	3.3 Hamster	
	3.4 Dog	
	3.5 Evidence synthesis for cancer in experimental animals	
4.	Mechanistic Evidence.	383
	4.1 Absorption, distribution, metabolism, and excretion	383
	4.2 Evidence relevant to key characteristics of carcinogens	394
	4.3 Other relevant evidence	458
5.	Summary of Data Reported	481
	5.1 Exposure characterization	481
	5.2 Cancer in humans	
	5.3 Cancer in experimental animals	
	5.4 Mechanistic evidence	
6	Evaluation and Rationale.	
0.	6.1. Cancer in humans	
	6.2 Cancer in experimental animals.	
	6.3. Mechanistic evidence	
	6.4 Overall evaluation	
	6.5 Rationale	
ъ		
Re	eferences	489
MET	HYLEUGENOL	517
	Exposure Characterization	
1.	1.1 Identification of the agent	
	1.2 Production and use	
	1.3 Detection and analysis	
	1.4 Occurrence and exposure.	
	1.5 Regulations and guidelines	
2	1.6 Quality of exposure assessment in key mechanistic studies in humans	
	Cancer in Humans	
3.	Cancer in Experimental Animals	
	3.1 Mouse	
	3.2 Rat	
	3.3 Evidence synthesis for cancer in experimental animals	550

4	Mechanistic Evidence.	551
	4.1 Absorption, distribution, metabolism, and excretion	
	4.2 Evidence relevant to key characteristics of carcinogens	
5	Summary of Data Reported	
٥.	5.1 Exposure characterization	
	5.2 Cancer in humans	
	5.3 Cancer in experimental animals.	
	5.4 Mechanistic evidence	
6	Evaluation and Rationale.	
0.	6.1 Cancer in humans	
	6.2 Cancer in experimental animals.	
	6.3 Mechanistic evidence	
	6.4 Overall evaluation	
	6.5 Rationale	
R	eferences.	
IX	Sicremees.	,
ISOF	UGENOL	603
	Exposure Characterization	
1.	1.1 Identification of the agent	
	1.2 Production and use	
	1.3 Detection and analysis	
	1.4 Occurrence and exposure.	
	1.5 Regulations and guidelines	
	1.6 Quality of exposure assessment in key mechanistic studies in humans	
2	Cancer in Humans	
	Cancer in Experimental Animals	
٦.	3.1 Mouse	
	3.2 Rat	
	3.3 Evidence synthesis.	
4	Mechanistic Evidence.	
٦.	4.1 Absorption, distribution, metabolism, and excretion	
	4.2 Evidence relevant to key characteristics of carcinogens	
5	Summary of Data Reported	
٥.	5.1 Exposure characterization	
	5.2 Cancer in humans	
	5.3 Cancer in experimental animals.	
	5.4 Mechanistic evidence	
6	Evaluation and Rationale.	
0.	6.1 Cancer in humans	
	6.2 Cancer in experimental animals.	
	6.3 Mechanistic evidence	
	6.4 Overall evaluation	
	6.5 Rationale	
D	eferences.	
K	JOICHOUS	
т іст	OE ADDDEVIATIONS	((1

ANNEX 1. Supplementary material for Section 1, Exposure characterization	667
ANNEX 2. Scientific and other publicly available data on aspartame use in artificially sweetened beverages	
ANNEX 3. Supplementary material for Section 2, Cancer in humans	679
ANNEX 4. Supplementary material for Section 4, Evaluation of high-throughput in vitro toxicity screening data	,
SUMMARY OF FINAL EVALUATIONS	685