

## ACROLEIN, CROTONALDEHYDE, AND ARECOLINE

**VOLUME 128** 

This publication represents the views and expert opinions of an IARC Working Group on the Identification of Carcinogenic Hazards to Humans, which met remotely, 29 October–13 November 2020

LYON, FRANCE - 2021

IARC MONOGRAPHS
ON THE IDENTIFICATION
OF CARCINOGENIC HAZARDS
TO HUMANS



## **CONTENTS**

NOTE TO	THE READER	1
LIST OF	PARTICIPANTS	3
	BLE	
A. GE	NERAL PRINCIPLES AND PROCEDURES	
1.	Background	
2.	Objective and scope	8
3.	Selection of agents for review	9
4.	The Working Group and other meeting participants	9
5.	Working procedures	11
6.	Overview of the scientific review and evaluation process	12
7.	Responsibilities of the Working Group	14
B. SC	IENTIFIC REVIEW AND EVALUATION	
1.	Exposure characterization	15
2.	Studies of cancer in humans	18
3.	Studies of cancer in experimental animals	23
4.	Mechanistic evidence	26
5.	Summary of data reported	
6.	Evaluation and rationale	30
Refere	nces.	35
GENERA	L REMARKS	39
A CDOLE	IN	45
	posure Characterization	
	Identification of the agent	
	Production and use	
	Methods of detection and quantification.	
	Occurrence and exposure.	
	Regulations and guidelines	
1.6	Quality of exposure assessment in key epidemiological studies	6

	2.	Cancer in Humans	
		2.1 Descriptions of individual studies	72
		2.2 Evidence synthesis for cancer in humans	83
	3.	Cancer in Experimental Animals	84
		3.1 Mouse	84
		3.2 Rat	99
		3.3 Hamster	. 102
		3.4 Evidence synthesis for cancer in experimental animals	. 103
	4.	Mechanistic Evidence.	. 104
		4.1 Absorption, distribution, metabolism, and excretion	. 104
		4.2 Evidence relevant to key characteristics of carcinogens	. 108
		4.3 Data relevant to comparisons across agents and end-points	. 154
	5.	Summary of Data Reported	. 154
		5.1 Exposure characterization	. 154
		5.2 Cancer in humans	. 154
		5.3 Cancer in experimental animals	. 155
		5.4 Mechanistic evidence	. 155
	6.	Evaluation and Rationale.	. 157
		6.1 Cancer in humans	. 157
		6.2 Cancer in experimental animals	. 157
		6.3 Mechanistic evidence	. 157
		6.4 Overall evaluation	. 157
		6.5 Rationale	. 157
	Re	ferences	158
CR		TONALDEHYDE	
	1.	Exposure Characterization	
		1.1 Identification of the agent	. 179
		1.2 Production and use	
		1.3 Methods of detection and quantification	
		1.4 Occurrence and exposure	. 185
		1.5 Regulations and guidelines	. 198
		1.6 Quality of exposure assessment in key epidemiological studies	.201
	2.	Cancer in Humans	.202
		2.1 Descriptions of individual studies	.202
		2.2 Evidence synthesis for cancer in humans	.208
	3.	Cancer in Experimental Animals	.209
		3.1 Mouse	.209
		3.2 Rat	.214
		3.3 Evidence synthesis for cancer in experimental animals	.215
	4.	Mechanistic Evidence.	
		4.1 Absorption, distribution, metabolism, and excretion	.216
		4.2 Evidence relevant to key characteristics of carcinogens	.220
		4.3 Other relevant evidence	. 241

5.	Summary of Data Reported	242
	5.1 Exposure characterization	242
	5.2 Cancer in humans	242
	5.3 Cancer in experimental animals	242
	5.4 Mechanistic evidence	243
6.	Evaluation and Rationale	244
	6.1 Cancer in humans	244
	6.2 Cancer in experimental animals.	244
	6.3 Mechanistic evidence	244
	6.4 Overall evaluation	244
	6.5 Rationale	244
R	eferences.	245
ARE	COLINE	259
1.	Exposure Characterization	259
	1.1 Identification of the agent	259
	1.2 Production and use	260
	1.3 Methods of detection and quantification	261
	1.4 Occurrence and exposure	263
	1.5 Regulations and guidelines	271
2.	Cancer in Humans	272
3.	Cancer in Experimental Animals	272
	3.1 Mouse	272
	3.2 Rat	286
	3.3 Hamster	287
	3.4 Carcinogenicity of metabolites	288
	3.5 Evidence synthesis for cancer in experimental animals	289
4.	Mechanistic Evidence.	
	4.1 Absorption, distribution, metabolism, and excretion	290
	4.2 Evidence relevant to key characteristics of carcinogens	295
	4.3 Data relevant to comparisons across agents and end-points	314
5.	Summary of Data Reported	315
	5.1 Exposure characterization	315
	5.2 Cancer in humans	
	5.3 Cancer in experimental animals.	315
	5.4 Mechanistic evidence	316
6.	Evaluation and Rationale.	317
	6.1 Cancer in humans	317
	6.2 Cancer in experimental animals.	317
	6.3 Mechanistic evidence	
	6.4 Overall evaluation	
	6.5 Rationale	
D	C	217

## IARC MONOGRAPHS - 128

LIST OF ABBREVIATIONS	327
ANNEX 1. Supplementary material for acrolein, Section 1, Exposure Characterization	331
ANNEX 2. Supplementary material for crotonaldehyde, Section 1, Exposure Characterization	333
SUMMARY OF FINAL EVALUATIONS.	335