

CONTENTS

NOTE TO THE READER	1
LIST OF PARTICIPANTS	3
PREAMBLE	11
A. GENERAL PRINCIPLES AND PROCEDURES	11
1. Background	11
2. Objective and scope	12
3. Selection of agents for review	13
4. Data for the <i>Monographs</i>	13
5. Meeting participants	14
6. Working procedures	15
B. SCIENTIFIC REVIEW AND EVALUATION	16
1. Exposure data	17
2. Studies of cancer in humans	18
3. Studies of cancer in experimental animals	22
4. Mechanistic and other relevant data	25
5. Summary	28
6. Evaluation and rationale	29
References	33
GENERAL REMARKS	35
EPSTEIN-BARR VIRUS	49
1. Exposure Data	49
1.1 Taxonomy, structure, and biology	49
1.2 Epidemiology of infection	56
2. Cancer in Humans	62
2.1 Virus-associated B-cell lymphoma	62
2.2 Virus-associated T-cell and NK-cell lymphomas	65
2.3 Cancers of the nasopharynx, stomach, and lymphoepithelium	66
2.4 Other cancers	67
3. Cancer in Experimental Animals	68
4. Other Relevant Data	68
4.1 Transforming capacity of EBV	68
4.2 Biochemical and biological properties of EBV gene products	70

4.3	In vivo and in vitro evidence for a role of EBV in human malignancies.....	75
4.4	Interaction between EBV and other agents; mechanisms involved in EBV reactivation	78
4.5	Transgenic models for EBV-associated cancers.....	79
4.6	Synthesis.....	80
5.	Evaluation	80
	References.....	80

HEPATITIS B VIRUS..... 93

1.	Exposure Data	93
1.1	Taxonomy, structure, and biology.....	93
1.2	Epidemiology of infection.....	98
2.	Cancer in Humans.....	105
2.1	Hepatocellular carcinoma	105
2.2	Cancers other than HCC	111
3.	Cancer in Experimental Animals	113
4.	Other Relevant Data	113
4.1	Introduction.....	113
4.2	Chronic necro-inflammatory hepatic disease in hepatocarcinogenesis	114
4.3	Direct mechanisms of hepatocarcinogenesis.....	115
4.4	Epigenetic mechanisms	120
4.5	Other major risk factors in hepatocarcinogenesis.....	121
4.6	Role of HBV in other cancers	122
4.7	Synthesis.....	123
5.	Evaluation	123
	References.....	123

HEPATITIS C VIRUS..... 135

1.	Exposure Data	135
1.1	Taxonomy, structure, and biology.....	135
1.2	Epidemiology of infection.....	138
2.	Cancer in Humans.....	141
2.1	Hepatocellular carcinoma	141
2.2	Cancers other than hepatocellular carcinoma.....	144
3.	Cancer in Experimental Animals	149
4.	Other Relevant Data	149
4.1	Biochemical properties of HCV proteins	150
4.2	Biological properties of HCV proteins	152
4.3	Experimental evidence for a role of HCV in malignant conversion	155
4.4	Interaction between HCV and environmental agents	157
4.5	Animal models for HCV-associated cancers.....	157
4.6	HCV, host immune system, and genetic susceptibility	158
4.7	Synthesis.....	158
5.	Evaluation	158
	References.....	158

KAPOSI SARCOMA HERPESVIRUS	169
1. Exposure Data	169
1.1 Taxonomy, structure, and biology	169
1.2 Epidemiology of infection	173
2. Cancer in Humans	175
2.1 Kaposi sarcoma	175
2.2 Primary effusion lymphoma	176
2.3 Multicentric Castleman disease	177
2.4 Multiple myeloma	177
2.5 Other cancers	179
2.6 Kaposi sarcoma and cofactors	179
3. Cancer in Experimental Animals	180
4. Other Relevant Data	180
4.1 Transforming capacity of KSHV	180
4.2 Biochemical and biological properties of KSHV proteins	181
4.3 Evidence for a role of KSHV in malignant conversion	192
4.4 Interaction between KSHV and environmental agents	193
4.5 Animal models	194
4.6 Transgenic mice models	194
4.7 Synthesis	195
5. Evaluation	195
References	196
HUMAN IMMUNODEFICIENCY VIRUS-1	215
1. Exposure Data	215
1.1 Taxonomy, structure, and biology	215
1.2 Epidemiology of infection	218
2. Cancer in Humans	221
2.1 Kaposi sarcoma	221
2.2 Non-Hodgkin lymphoma	222
2.3 Hodgkin lymphoma	225
2.4 Cervical and anogenital cancers	227
2.5 Cancer of the skin	229
2.6 Cancer of the conjunctiva	229
2.7 Cancer of the lung	230
2.8 Cancer of the liver	231
2.9 Other cancers	232
3. Cancer in Experimental Animals	232
4. Other Relevant Data	232
4.1 Biochemical and biological properties of relevant HIV-1 proteins	233
4.2 HIV-1, host immune system, and carcinogenesis	235
4.3 HIV-1 and other infectious agents associated with human cancers	237
4.4 Animal models for HIV-1-associated cancers	238
4.5 Synthesis	240
5. Evaluation	240
References	240

HUMAN PAPILLOMAVIRUSES	255
1. Exposure Data	255
1.1 Taxonomy, structure, and biology.....	255
1.2 Epidemiology of infection.....	257
2. Cancer in Humans.....	261
2.1 Cancer of the cervix	261
2.2 Cancer at other anogenital sites.....	268
2.3 Cancer of the upper aerodigestive tract.....	274
2.4 Cancer of the skin.....	277
2.5 Cancer at other sites.....	280
2.6 Cofactors of HPV in cervical cancer	282
3. Cancer in Experimental Animals	284
4. Other Relevant Data	285
4.1 Mechanisms of HPV-associated carcinogenesis.....	285
4.2 Biochemical properties of HPV proteins.....	286
4.3 Biological Properties of HPV.....	288
4.4 Role of HPVs in malignant conversion	290
4.5 Transgenic models for HPV-associated cancers	291
4.6 Synthesis.....	294
5. Evaluation	295
References	296
HUMAN T-CELL LYMPHOTROPIC VIRUS TYPE 1	315
1. Exposure Data	315
1.1 Taxonomy, structure, and biology.....	315
1.2 Epidemiology of infection.....	317
2. Cancer in Humans.....	321
2.1 T-cell malignancies	321
2.2 Other malignancies	323
2.3 Cofactors.....	325
3. Cancer in Experimental Animals	325
4. Other Relevant Data	325
4.1 Mechanism of HTLV-1-linked carcinogenesis.....	325
4.2 HTLV-1, host immune system, and genetic susceptibility.....	331
4.3 Synthesis.....	332
5. Evaluation	332
References	332
OPISTHORCHIS VIVERRINI AND CLONORCHIS SINENSIS	341
1. Exposure Data	341
1.1 Taxonomy, structure and biology	341
1.2 Epidemiology of infection.....	344
2. Cancer in Humans.....	347
2.1 Cholangiocarcinoma	347
2.2 Hepatocellular carcinoma	350
2.3 Cofactors.....	354
3. Cancer in Experimental Animals	354

4. Other Relevant Data	356
4.1 Pathological changes in vivo	356
4.2 Carcinogenicity of liver fluke infections	356
4.3 Gene mutation, methylation, and altered expression in cholangiocarcinoma	364
4.4 Host immune system and genetic susceptibility	364
4.5 Synthesis	365
5. Evaluation	365
References	365
SCHISTOSOMA HAEMATOBIMUM	371
1. Exposure Data	371
1.1 Taxonomy, structure, and biology	371
1.2 Epidemiology of infection	372
2. Cancer in Humans	375
2.1 Cancer of the urinary bladder	375
2.2 Others	376
2.3 Impact of <i>Schistosoma</i> eradication	377
3. Cancer in Experimental Animals	377
4. Other Relevant Data	378
4.1 Experimental data	378
4.2 Studies in exposed humans	379
4.3 Host susceptibility	381
4.4 Synthesis	382
5. Evaluation	382
References	382
HELICOBACTER PYLORI	385
1. Exposure Data	385
1.1 Taxonomy, structure, and biology	385
1.2 Epidemiology of infection	390
2. Cancer in Humans	393
2.1 Cancer of the stomach	393
2.2 Gastric mucosa-associated lymphoid tissue (MALT) lymphoma	399
2.3 Cancer of the oesophagus	400
2.4 Other cancers	401
2.5 Cofactors	404
3. Cancer in Experimental Animals	405
3.1 Mongolian gerbil	405
3.2 Mouse	406
4. Other Relevant Data	412
4.1 Data supporting the carcinogenicity of <i>H. pylori</i>	417
4.2 Host immune system and genetic susceptibility	418
4.3 Factors associated with gastric carcinogenesis	419
4.4 Mechanisms of lymphomagenesis	421
4.5 Synthesis	422
5. Evaluation	423
References	423

LIST OF ABBREVIATIONS437
CUMULATIVE CROSS INDEX TO *IARC MONOGRAPHS* 443

NOTE TO THE READER

The term ‘carcinogenic risk’ in the *IARC Monographs* series is taken to mean that an agent is capable of causing cancer. The *Monographs* evaluate cancer hazards, despite the historical presence of the word ‘risks’ in the title.

Inclusion of an agent in the *Monographs* does not imply that it is a carcinogen, only that the published data have been examined. Equally, the fact that an agent has not yet been evaluated in a *Monograph* does not mean that it is not carcinogenic. Similarly, identification of cancer sites with *sufficient evidence* or *limited evidence* in humans should not be viewed as precluding the possibility that an agent may cause cancer at other sites.

The evaluations of carcinogenic risk are made by international working groups of independent scientists and are qualitative in nature. No recommendation is given for regulation or legislation.

Anyone who is aware of published data that may alter the evaluation of the carcinogenic risk of an agent to humans is encouraged to make this information available to the Section of IARC Monographs, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France, in order that the agent may be considered for re-evaluation by a future Working Group.

Although every effort is made to prepare the *Monographs* as accurately as possible, mistakes may occur. Readers are requested to communicate any errors to the Section of IARC Monographs, so that corrections can be reported in future volumes.

