

CONTENTS

NOTE TO THE READER.....	1
LIST OF PARTICIPANTS.....	3
PREAMBLE	7
Background.....	7
Objective and Scope	7
Selection of Topics for Monographs	8
Data for Monographs	9
The Working Group	9
Working Procedures	9
Exposure Data.....	10
Studies of Cancer in Humans	12
Studies of Cancer in Experimental Animals.....	15
Other Data Relevant to an Evaluation of Carcinogenicity and its Mechanisms	18
Summary of Data Reported	20
Evaluation	21
References.....	25
GENERAL REMARKS.....	31
Internal irradiation	31
General aspects	31
Nomenclature	34
Radiation dose.....	34
Radiation dose and exposure to radon and its decay products: working-level month.....	35
Dose and dose limits of radiation from internalized radionuclides	37
Routes of internal exposure to ionizing radiation	37
Inhalation	39
Ingestion	42
Injection and entry through wounds or intact skin.....	42
Transport and deposition	43
Elimination	43
Doses from internal irradiation.....	44

Modes of decay of radionuclides	44
Decay by emission of α -particles	46
Decay by emission of β -particles	47
β^- -Particles (electron)	47
β^+ -Particles (positron)	48
Electron capture	48
Isomeric decay processes	49
Production of γ -rays	49
Internal conversion	49
Auger electrons and characteristic X-rays	50
Exposure to internal sources of radiation	51
Radionuclides considered in this monograph	51
Categorization of radionuclides	51
Types of radiation produced during decay of ‘mixed’ emitters	57
Physical aspects of exposure: Linear energy transfer	57
γ -Rays	62
α -Particles	62
β -Particles	62
Auger electrons	62
Biological aspects of exposure	63
Non-uniform distribution of radionuclides in organs and tissues	63
Non-uniform deposition of radionuclides at the cellular and subcellular level	66
Factors that may modify radionuclide metabolism and toxicity	67
Target tissues	68
Liver	68
Lung	68
Bone	69
Thyroid gland	70
Haematopoietic tissues	70
References	71
 SOME INTERNALLY DEPOSITED RADIONUCLIDES	79
Exposure data	81
Environmental exposure	81
Detonation of nuclear weapons	81
Sources	81
Global exposures	82
Local and regional exposures	82
Nevada test site, USA	84
Pacific test site, Marshall Islands	84
Semipalatinsk test site, Kazakhstan	86

CONTENTS

v

Novaya Zemlya, Russian Federation	87
Lop Nor, China.....	87
Mururoa and Fangataufa, French Polynesia	87
Emu, Maralinga and Montebello, Australia	87
Accidents at nuclear installations	88
Chernobyl	88
Emergency workers	88
Recovery operation workers.....	88
Evacuees	89
Unevacuated inhabitants of the former USSR	89
Inhabitants of countries outside the former USSR	92
Southern Ural Mountains	93
History	93
Dosimetry	93
Other accidents	95
Windscale	95
Three Mile Island	95
Routine releases from nuclear installations	95
Environmental exposure	95
Occupational exposure	97
Dosimetry of radon-222	99
Decay of radon and its progeny	100
Quantities and units	100
Dose	101
Occupational exposure	102
Monitoring	102
Internal exposure.....	102
Accuracy and reliability of measurements	103
Exposed populations	104
Uranium mining and milling	105
Uranium enrichment and conversion	106
Reactor fuel manufacture	107
Reactor operations	107
Fuel reprocessing	109
Waste management	110
Research in the nuclear fuel cycle	110
Mineral processing	111
Nuclear weapons production.....	113
Nuclear medicine	116
Luminizing	119
Radioisotope production and distribution.....	120
Research centres	121

Medical use of radionuclides	121
Diagnostic use	122
Procedures	122
Thyroid examinations.....	125
Bone examinations	125
Cardiovascular examinations	125
Pulmonary perfusion and ventilation tests.....	125
Doses.....	126
Therapeutic use	129
Other applications of radionuclides that could lead to exposure	132
Products in the home	132
Personal products	134
Products in the workplace.....	134
Exposure to radionuclides in cigarette smoke	135
Miscellaneous products and sources.....	135
Studies of cancer in humans	137
Radon	137
Occupational exposure in underground mining	138
Lung cancer.....	138
Mining	138
Inverse dose-rate effect	143
Effect in lifelong non-smokers.....	144
Exposure of women and children.....	145
Cancers other than lung cancer.....	145
Residential exposure	146
Lung cancer.....	146
New Jersey, USA	148
Shenyang, China.....	148
Stockholm, Sweden	149
Sweden	149
Winnipeg, Canada	150
Missouri, USA (study I)	150
South Finland	151
Finland	151
Israel	152
Port Hope, Canada	152
South-west England	153
Missouri, USA (study II)	153
Iowa, USA	154
Western Germany	154
Eastern Germany	155
Summary	155

CONTENTS

vii

Cancers other than lung cancer.....	157
Geographical correlation studies.....	159
Lung cancer.....	159
Cancers other than lung cancer.....	162
Estimation of risk	163
Risk models.....	164
Recent analysis of data on miners	165
Generalizability	166
Radium	167
Occupational exposure: Radium-dial painters	167
Iatrogenic exposure	170
Studies of patients treated with high doses of radium-224	171
Bone sarcomas	171
Mammary carcinomas	172
Leukaemia	172
Cancers at other sites	172
Studies of patients treated with lower doses of radium-224	173
Bone tumours	173
Leukaemia	173
Cancers at other sites	174
Thorium	174
Occupational exposure	174
Iatrogenic exposure	175
History.....	175
Distribution of Thorotrast after intravascular injection	177
Dosimetry	177
Epidemiological studies	179
Mortality from and incidence of cancer	182
Liver tumours	182
Haematological malignancies.....	186
Cancers at other sites	187
Plutonium	188
United Kingdom	188
USA.....	192
Russian Federation	194
Lung cancer.....	195
Cohort study by the epidemiology department	196
Cohort study by the internal dosimetry laboratory	201
Case-control study by the clinical department	202
Cancer location and histopathological analysis	203
Bone tumours	208
Liver tumours	212

Americium	218
Summary	218
Uranium	219
Polonium.....	222
Iodine	223
Iatrogenic exposure.....	224
Thyroid cancer.....	224
Leukaemia.....	228
Cancers at other sites	228
Gastrointestinal tract.....	228
Urinary tract	229
Breast	229
Accidents in or discharges from nuclear facilities	229
Windscale, United Kingdom.....	231
Hanford, Washington, USA	231
Three Mile Island, Pennsylvania, USA	231
Chernobyl, Ukraine.....	232
Thyroid cancer in young people.....	233
Thyroid cancer in adults.....	236
Other cancers	238
Phosphorus	239
Haematological malignancies	240
Other malignancies	242
Mixed exposures	242
Fall-out from atmospheric nuclear weapons testing.....	242
Nevada test site	243
Marshall islands	244
Other test sites.....	246
Techa River, Russian Federation	247
Caesium	249
Low-energy β -particle-emitting radionuclides	249
Studies of cancer in experimental animals	251
α -Particle-emitting radionuclides	251
Pure α -particle emitters	251
Radon-222.....	251
Polonium-210	251
Mixed α -particle emitters	253
Radium-224.....	253
Radium-226.....	256
Thorium-227, thorium-228, thorium-230 and thorium-232	261
Uranium (natural)	263

Plutonium-238 and plutonium-239	264
Inhalation	264
Injection	273
Neptunium-237	278
Americium-241	279
Curium-242	281
Californium-249 and californium-252	284
β-Particle-emitting radionuclides	285
Pure β-particle emitters.....	285
Hydrogen-3	285
Phosphorus-32.....	286
Strontium-90	287
Yttrium-90 and yttrium-91	295
Promethium-147	298
Mixed β-particle emitters	299
Iodine-131	299
Caesium-137	301
Cerium-144	303
Radium-228.....	310
Pre- and perinatal carcinogenesis	310
α-Particle emitters.....	311
Plutonium-238 and plutonium-239	311
Americium-241	314
β-Particle emitters	315
Hydrogen-3	315
³ H-Labelled water	315
[³ H]Thymidine	317
Carbon-14	320
Phosphorus-32.....	320
Strontium-90	321
Cerium-144	322
Iodine-131	323
Exposure of male parents	325
α-Particle emitter: Plutonium-239	325
β-Particle emitter: Hydrogen-3	326
Other data relevant to an evaluation of carcinogenicity and its mechanisms	329
Absorption, distribution, metabolism and excretion of radionuclides	329
Hydrogen-3	330
Inhalation	330
Dermal intake	330
Ingestion	330
Systemic distribution, retention and excretion	331

Placental transfer.....	332
Carbon-14	332
Inhalation	332
Ingestion	333
Systemic distribution, retention and excretion	333
Placental transfer.....	334
Phosphorus-32.....	334
Inhalation	334
Ingestion	334
Systemic distribution, retention and excretion	335
Placental transfer.....	335
Sulfur-35	335
Inhalation	335
Ingestion	336
Systemic distribution, retention and excretion	336
Placental transfer.....	336
Gallium-67	337
Inhalation and ingestion	337
Systemic distribution, retention and excretion	337
Strontium-89 and strontium-90.....	337
Inhalation	337
Ingestion	338
Systemic distribution, retention and excretion	338
Placental transfer.....	339
Technetium-99m	340
Inhalation	340
Ingestion	340
Systemic distribution, retention and excretion	340
Placental transfer.....	341
Iodine-123, iodine-125 and iodine-131	341
Inhalation	341
Ingestion	341
Systemic distribution, retention and excretion	341
Placental transfer.....	342
Caesium-137	342
Inhalation	342
Ingestion	342
Systemic distribution, retention and excretion	343
Placental transfer.....	343

CONTENTS

xi

Cerium-141 and cerium-144	344
Inhalation and ingestion	344
Systemic distribution, retention and excretion	344
Placental transfer.....	344
Rhenium-186 and rhenium-188	344
Bismuth-212	345
Inhalation and ingestion	345
Systemic distribution, retention and excretion	345
Polonium-210	345
Inhalation	345
Ingestion	345
Systemic distribution, retention and excretion	346
Placental transfer.....	346
Astatine-211	347
Radon-222.....	347
Radium-224, radium-226 and radium-228	348
Inhalation	348
Ingestion	348
Systemic distribution, retention and excretion	348
Placental transfer.....	349
Thorium-232	350
Inhalation	350
Ingestion	350
Systemic distribution, retention and excretion	351
Placental transfer.....	351
Uranium-234, uranium-235 and uranium-238	351
Inhalation	351
Ingestion	351
Systemic distribution, retention and excretion	351
Placental transfer.....	351
Neptunium-237	354
Inhalation	354
Ingestion	354
Systemic distribution, retention and excretion	354
Placental transfer.....	355
Plutonium-238 and plutonium-239.....	355
Inhalation	355
Ingestion	356
Systemic distribution, retention and excretion	357
Placental transfer.....	358

Americium-241	359
Inhalation	359
Ingestion	359
Systemic distribution, retention and excretion	360
Placental transfer.....	360
Curium-244	361
Inhalation	361
Ingestion	361
Systemic distribution, retention and excretion	361
Placental transfer.....	362
Biokinetics models and dose coefficients.....	362
Respiratory tract model.....	362
Gastrointestinal tract model	365
Bone models	366
Assumptions concerning elements	367
Hydrogen	367
Iodine	368
Caesium	368
Alkaline earth elements	369
Actinide elements	372
Dose coefficients.....	374
Models for the embryo and fetus	383
Dosimetry	383
Biokinetics	383
Studies of decorporation (chelation).....	385
Toxic effects	385
Deterministic effects	385
Effects on specific tissues and organs	389
Bone	390
Teeth	393
Eye	394
Skin	394
Liver	395
Haematopoietic bone marrow	397
Gonadal tissues	400
Lung	401
Thyroid	404
Gastrointestinal tract	406
Association between deterministic effects and cancer	407

Reproductive and developmental effects	409
Sensitivity at different stages of gestation	412
Preimplantation period	412
Embryonic stage	413
Fetal period	413
Malformations in human populations after the Chernobyl accident	414
Developmental responses to radionuclides.....	415
Radon and progeny	415
Radium	415
Uranium	417
Neptunium, plutonium and americium	417
Neptunium	418
Plutonium	418
Americium	422
Hydrogen.....	423
Carbon	431
Phosphorus	431
Strontium.....	433
Iodine	435
Cerium.....	437
Genetic and related effects	437
α -Particle emitters.....	438
In-vitro studies	438
DNA double-strand breaks	438
Chromosomal and chromatid aberrations	438
Mutation	439
Mutations in tumour-related genes.....	440
Cell transformation.....	441
Genomic instability	441
‘Bystander’ effects	442
In-vivo studies.....	443
Human studies.....	445
Workers exposed to radionuclides and residents of neighbouring areas	445
Patients exposed to Thorotrast	448
Residential exposure to radon	450
Mutations in tumour-related genes.....	451
β -Particle emitters	452
In-vitro studies	452
Low-energy electrons	452
DNA strand breaks	453
Chromosomal aberrations.....	453

Mutation	454
Cell transformation.....	454
In-vivo studies.....	454
Human studies.....	455
Radioiodine therapy	455
Technetium-99m.....	458
Other medical treatment	458
Hydrogen-3.....	459
Chernobyl accident.....	460
Techa River, southern Urals	461
Mutations in tumour-related genes.....	462
Summary of data reported and evaluation	465
Exposure data	465
Human carcinogenicity data	468
Radon	468
Radium	468
Thorium.....	469
Plutonium	469
Uranium	470
Polonium	470
Iodine	470
Phosphorus	471
Combined exposures (external and internal)	471
Other radionuclides	471
Animal carcinogenicity data	471
α -Particle-emitting radionuclides	472
β -Particle-emitting radionuclides	473
Perinatal carcinogenesis	474
Paternal exposure	475
Other relevant data	475
Absorption, distribution, metabolism and excretion.....	475
Toxic effects	475
Reproductive and developmental effects	476
Genetic and related effects	477
Evaluation	478
Summary of final evaluations.....	481
References.....	483
GLOSSARY	551

CONTENTS

xv

SUPPLEMENTARY CORRIGENDA TO VOLUMES 1–77	561
CUMULATIVE INDEX TO THE <i>MONOGRAPHS</i> SERIES.....	563

NOTE TO THE READER

The term ‘carcinogenic risk’ in the *IARC Monographs* series is taken to mean the probability that exposure to an agent will lead to cancer in humans.

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.

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 Unit of Carcinogen Identification and Evaluation, 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 Unit of Carcinogen Identification and Evaluation, so that corrections can be reported in future volumes.