long-lived species, but also because the incidence of cancer is low in these species. Although transgenic mouse models have been developed for evaluating human cancer viruses, transgenic animal models are considered more informative in understanding cancer mechanisms than for human cancer risk assessment (see Lambert & Banks, this Volume).

The criteria for *sufficient evidence* of carcinogenicity in animals outlined in the *Preamble* to the *IARC Monographs* (IARC, 2015) generally require independent replication in two different animal species, or particularly strong results in a single species. *IARC Monographs* generally do not identify animal tumour sites for agents with only *limited evidence* of carcinogenicity in animals. The criteria developed by Grosse et al. (this Volume) further restrict the use of tumour data for agents with *sufficient evidence* in experimental animals (e.g., no tumour sites were identified in the absence of two (or more) animal studies of adequate design and quality pointing at the same tumour site with a similar histological origin in the same species). Although melphalan produced tumours of the forestomach, skin, and lung as well as lymphosarcomas in mice and mammary gland tumours and peritoneal sarcomas in rats (Vol 100F; IARC 2012f), none of these tumour sites were replicated in a second animal species, and hence are not included in the Grosse et al. data set.

Human evidence is also subject to limitations. As noted above, the opportunity to conduct further informative studies in humans of a substance like diethylstilbestrol may no longer be available. The absence of *sufficient evidence* in humans may be due to a lack of evidence in appropriate epidemiological or clinical studies, or to the inability of existing studies to detect an association between exposure to the agent of interest (including early or later-in-life exposures) and a tumour outcome. Study limitations may also include inadequate power caused by small sample size. If human exposures to the agent of interest are extremely low, a particularly large, well-conducted study would be required to achieve reasonable sensitivity.

The failure of human studies to identify tumour sites can occur when these studies do not consider all possible tumour sites: most case–control studies focus on only one or a limited number of tumour sites. Human studies that fail to identify a relevant tumour site may have low sensitivity, possibly because they do not focus on the most appropriate study population. As noted above for trichloroethylene, evidence on specific tumour sites may not yet have accrued at the time of an evaluation. Following the first evaluation of tobacco smoking in *IARC Monograph* Volume 38 (IARC, 1986), cigarette smoking was subsequently shown to cause cancer at a much larger number of tumour sites, including cancers of the nasal cavities and nasal sinuses, oesophagus, stomach, liver, kidney, uterine cervix, and myeloid leukemia (Vol 83; IARC 2004). Thus, the potential for underestimation of inter-species tumour-site concordance may result from missing tumour sites for agents for which *sufficient evidence* of carcinogenicity in humans already exists.

How human study data are reported in the *Monographs* may also affect the ability to conduct analyses to establish tumor-site concordance. Ionizing radiation is a specific example of this constraint. No specific human tumour sites were identified for ionizing radiation (all types); internalized radionuclides that emit alpha-particles; internalized radionuclides that emit beta-particles; and UV radiation (bandwidth 100-400 nm, encompassing UVC, UVB and UVA). Although the skin was not explicitly mentioned as a human tumour site for UV radiation in Volume 100D, the skin is implicitly suggested as being a human tumour site for this agent. In our analysis, the lack of explicit designation of the skin as a human tumour site for UV radiation precluded its use. A similar situation occurred for areca nut, for which the oral cavity might have been considered as a human tumour site, although this was site was not explicitly designated in the *Monograph*.

An agent can be categorized by IARC as Group-1 carcinogen in the absence of *sufficient evidence* for carcinogenicity in humans when it is clear that the mechanisms by which the agent causes cancer in animals also operate in humans. Such 'mechanistic upgrades' have occurred with various levels of human evidence, including for aristolochic acid (*limited evidence* of carcinogenicity in humans; Vol 100A, IARC 2012a); benzo(*a*)pyrene [B(*a*)P] (*inadequate evidence* in humans; Vol 100F, IARC 2012f); ethylene oxide (*limited evidence* in humans; Vol 100F, IARC 2012f); 4,4'-methylenebis(2-chlorobenzenamine)[MOCA] (*inadequate evidence* in humans; Vol 100F, IARC 2012f); and neutrons (*inadequate evidence* in humans; Vol 100D, IARC 2012d). For further discussion of mechanistic upgrades and key characteristics of Group-1 agents developed for this analysis see Birkett et al., Krewski et al., and Smith (this Volume) and Smith et al (2016). Ten key characteristics of human carcinogens described by Smith et al. (2016) focus on whether the agent is: is electrophilic or can be metabolically activated to electrophiles; is genotoxic; alters DNA repair or causes genomic instability; induces epigenetic alterations; induces oxidative stress; induces chronic inflammation; is immunosuppressive; modulates receptor-mediated effects; causes immortalization; or alters cell proliferation, cell death or nutrient supply. These considerations will be relevant in planned future analyses of coherence between animal and human tumours, taking into account key characteristics of carcinogens. However, mechanistic upgrades limit the ability to identify tumour-site concordance when human tumour sites are not identified. Of the ten agents placed in Group-1 as a consequence of mechanistic upgrades, specific human tumour sites were identified only for phenacetin.

Exposure assessment is one of the most difficult aspects of epidemiological investigations (Nieuwenhuijsen, 2003). In some cases, such as ecological studies comparing two population groups subject to notably different exposure circumstances, exposure may not be measured at all. In other cases, however, exposures may be very well determined, as with the use of personal dosimeters to measure exposures to agents such as ambient air pollution or ionizing radiation, or in the dose regimens of pharmaceutical drugs or medical radiation. In the future, enhanced exposure assessment methodologies may serve to strengthen the ability of epidemiological studies to identify Group-1 agents (Cohen-Hubal et al., 2010; NRC, 2012). Biomarkers of exposure are expected to play an important part in the future of exposure science (Gurusankar et al., 2016).

The data set assembled and evaluated by Grosse et al. (this Volume) was retrieved from the *IARC Monographs*. As such, these agents do not represent a 'random sample' of all potential human carcinogens and is populated by the available animal and human evidence that were the focus of the *Monographs* from which they were drawn. The ability to determine concordance may change as additional Group-1 agents are identified, or as additional animal or human evidence on current Group-1 agents becomes available. New mechanistic data could affect current IARC evaluations of agents in Groups 2a (*probably carcinogenic to humans*) and Group 2b (*possibly carcinogenic to humans*), hence impact the concordance estimates reported here. Birkett et al. (this Volume) noted that while the *IARC Monographs Programme* has done an excellent job of summarizing the key characteristics of agents evaluated to date, additional information on the ten key characteristics of human carcinogens described by Smith et al. (2016) beyond what is summarized in the *IARC Monographs* is available in the general scientific literature.

In addition to the restrictions used by Grosse et al. (this Volume) for inclusion of experimental animal data, other limitations of the database affect the ability to determine tumour-site concordance including: incomplete information on tumour histology; limited information on the effects of sex, strain, and route of exposure; and limited information on dose-dependent effects. These limitations are discussed briefly below.

a. *Lack of information on tumour histology.* Because of incomplete information on the histology of lesions in both animal and human studies, it was not possible to conduct concordance analyses for specific histological subtypes of cancers occurring at a given site (such as adenocarcinoma or squamous cell carcinoma of the lung). Concordance analyses reported here are necessarily restricted to tumours occurring in a given organ or tissue (such as lung cancer) or a more broadly defined organ or tissue system (such as the upper aero-digestive tract and respiratory system). Concordance analyses reported here are based either on 39 tumour sites or on the broader classification of 15 organ and tissue systems.

b. *Effects of sex, strain, and route of exposure.* Cancer risks can differ between males and females, among different strains of the same animal species, and by route of exposure. Because of incomplete information on these three factors in the database used in the present analysis, it was not possible to evaluate how concordance might vary by sex, strain, or exposure route.

c. *Effects of dose.* Because the primary objective of the *IARC Monographs Programme* is to identify agents with the potential to cause cancer in humans in qualitative terms, rather than to quantify the level of risk at a given dose, information on dose-dependency in cancer risk is not systematically collected in the *Monographs*, although this is currently under review by the Agency (Advisory Group to Recommend on Quantitative Risk Characterization for the *IARC Monographs*, 2013). As a consequence, analyses of concordance considering dose-response relationships seen in animals and humans were not attempted at this time.

d. *Multi-site/multi-organ Carcinogenicity.* A number of agents, notably radiation and tobacco smoke, induce malignant lesions at multiple sites or in multiple organ and tissue systems. *Monograph* Volume 100F (IARC 2012f) summarizes the evidence that 1,3-butadiene induces haemangiosarcomas of the heart, malignant lymphomas, alveolar-bronchiolar neoplasms, squamous cell neoplasms of the forestomach in male and female B6C3F1 mice, and acinar cell carcinomas of the mammary gland, granulosa cell neoplasms of the ovary, and hepatocellular neoplasms in females. Assessing species concordance with multi-site carcinogens is inherently more difficult than with carcinogens that affect a single organ or tissue. Understanding the mechanistic and other attributes of such multi-site carcinogens will be useful in translating results in experimental animals to humans.

e. *Measures of Concordance.* For simplicity of presentation, concordance was evaluated here in terms of the overlap between tumour sites seen in animals and humans. Although more formal statistical analyses of concordance as described in Supplemental Material II were considered during the course of this work, the consensus of the Working Group was to represent concordance in terms of the simpler, more directly interpretable, indicators of 'overlap' in Table 7 and Figure 10.

f. *Small Sample Size.* After filtering the 111 Group-1 agents tabulated by Grosse et al. (this Volume) through Volume 109 of the IARC Monographs to include only agents that provided *sufficient evidence* of carcinogenicity in at least one tumour site in humans and at least one tumour site in animals, 60 agents remained for concordance analysis. As the sample size for some tumour sites is small (only two agents – asbestos and erionite – caused tumours in the mesothelium), caution is warranted in interpreting the concordance results presented in this chapter when the sample size is small.

g. *Predictive Value of Animal Tests for Carcinogenicity.* Using a database comprised of 150 agents tested for toxicity in animals and humans, Olson et al. (2000) estimated the positive predictive value (PPV) and negative predictive value (NPV) for human toxicity (excluding cancer). In this context, the PPV is defined as the probability of observing human toxicity in clinical testing, given that toxicity has been observed in animal tests. The PPV for human toxicity was estimated to be 71% for rodent and non-rodent species combined; 63% for non-rodents alone; and 43% for rodents alone. While a statement of the PPV and NPV of animal cancer tests for human carcinogenicity may be desirable, this cannot be done on the basis of the IARC concordance database considered in this chapter. This is because both the PPV and NPV depend on the prevalence of true positives in the database (Altman & Bland, 1994). Since the IARC concordance database is comprised of Group-1 agents that are known causes of cancer in humans, the PPV of animal cancer tests will artificially be calculated as 100%, whereas a lower PPV would be obtained with a more representative database that includes other agents that do not cause cancer in humans. However, identifying agents that do not cause cancer in humans is not the focus of the *IARC Monographs Programme*: at present, there is only one agent – caprolactam – in Group 4, *probably not carcinogenic to humans*.

In considering the relevance of animal data in the context of the *IARC Monographs*, it is important to keep in mind how animal data are used in the identification of Group-1 agents, according to the criteria outlined in the *Preamble* to the *IARC Monographs* (IARC, 2006). Most Group-1 agents are identified on the basis of *sufficient evidence* in humans, and for the purpose of the overall evaluation, there is no immediate recourse to animal data. Of the 111 Group-1 agents considered in this chapter, 102 demonstrated *sufficient evidence* of carcinogenicity in humans; the remaining nine agents were placed in Group-1 because the mechanisms by which tumours occurred in animals were considered to be directly relevant to humans, or on the basis of other relevant mechanistic considerations. Neutron radiation, for example, was placed in Group-1 in the presence of *inadequate evidence* in humans, as the biophysics of radiation damage is similar for different types of ionizing radiation. Bearing in mind the contribution of animal data to the identification of Group-1 agents in the *IARC Monographs*, it is possible with the present IARC concordance database to make a statement about the likelihood of positive results in animals among the Group-1 agents that have been shown to cause cancer in humans. Excluding mechanistic upgrades (ten agents) and Group-1 agents lacking appropriate animal data (20 agents) , *all* Group-1 agents with *sufficient evidence* of carcinogenicity in humans have also provided *sufficient* or *limited evidence* of carcinogenicity in one or more animal species, representing a PPV of 100%. Because the concordance database is comprised entirely of Group-1 agents, estimation of the predictive value (positive, negative, or overall) is not possible.

Conclusion

The *Monographs Programme* of the International Agency for Research on Cancer is widely recognized as one of the most authoritative sources of information on the identification of agents that may be carcinogenic to humans. The *Monographs* are prepared with the involvement of leading scientific experts worldwide, who apply the guidance provided in the *Preamble* to the *IARC Monographs* to evaluate the weight of evidence that an agent may present a cancer risk to humans. Through *Monograph* Volume 109, over 2,000 scientists have contributed to the development of the *IARC Monographs*, with nearly 200 scientists involved in Volume 100 alone. Since its beginning in 1971-72 (Saracci & Wild, 2015), the *Programme* has evaluated 990 agents for their potential to cause cancer in humans, with 118 of these

agents assigned to Group 1, indicating that the weight of evidence supports the conclusion that the agent is *carcinogenic to humans*.

A noteworthy aspect of the process used by the IARC to identify the cause of human cancer is the reliance on leading experts in the Working Groups that conduct the evaluations documented in the *IARC Monographs* to interpret the data according to the weight-of-evidence guidelines provided in the *Preamble* to the *IARC Monographs* (IARC, 2006). With the trend towards greater reliance on systematic review (NRC, 2014) and structured weight-of-evidence approaches to the evaluation of toxic substances (Rhomberg et al., 2013), the continued involvement of international experts in the *IARC Monographs* to interpret the often extensive human, animal and mechanistic data represents a major strength of the *Programme*.

Collectively, the *IARC Monographs* provide a rich source of information on the causes of human cancer. In particular, Volume 100 presents a review and update of 107 Group-1 agents identified in the previous 99 volumes, providing a veritable 'encyclopaedia of carcinogens.' This information, supplemented with that on six *Group-1* agents identified in Volumes 101 through 109, formed the basis for the analyses included in the present chapter. Subsuming both PCB-126 and dioxin-like PCBs within the broader category of PCBs, 113 – 2 = 111 district *Group-1* agents were included in the concordance analyses presented in this chapter. All but nine of these 111 *Group-1* agents demonstrated *sufficient evidence* of carcinogenicity in humans.

Analysis of concordance between animal and human tumour sites was restricted to 60 Group-1 agents demonstrating *sufficient evidence* of at least one tumour site in animals and in humans. Substantial overlap between animal and human tumours was seen in some organ and tissue systems, but not in others. This analysis focused on tumours seen in the 15 organ and tissue systems in our anatomically based tumour classification system rather than 39 individual tissue sites, because of the sparseness of data at the individual tumour site level. The importance of human data in the IARC carcinogen evaluation process is highlighted by the observation that 102 of the 111 distinct Group-1 agents identified at the time this analysis was done demonstrated *sufficient evidence* of carcinogenicity in humans.

The principle that agents that are carcinogenic in experimental animals should be regarded as presenting a carcinogenic risk to humans, is further confirmed in the course of this investigation. Excluding agents for which animal data are lacking or otherwise uninformative, all agents that cause cancer in humans also cause cancer in one more animal species. It is important to note, however, that the present database cannot be used to estimate the predictive value of animal cancer tests for humans, as it comprised by design only Group-1 agents: the positive and negative predictive values of the animal data for humans would be 100% and 0%, respectively (an artifact of a database comprising human carcinogens only).

Despite the challenges in evaluating concordance between animal and human tumour sites, the IARC concordance database represents a useful source of information for comparing animal and human data with respect to the tumours caused in different species by the 111 distinct Group 1 agents identified by the IARC through Volume 109 of the *IARC Monographs*. Future *Monographs* may benefit from a more systematic summary of the animal and human data on agents evaluated within the *IARC Monographs Programme*, including data on the types of tumours seen in animal and human studies, possibly using the anatomically based tumour nomenclature system introduced in this chapter to facilitate comparisons between animals and humans. Data on route of exposure, sex, and animal strain would also

support comparisons of animal and human tumours at a finer level of biological resolution. Data on the exposure or dose levels at which tumours are seen in animals and humans would further support evaluation of the relative carcinogenic potency of agents evaluated in animals and humans. Information on tumour sites affected by agents evaluated within the *IARC Monographs Programme* should be recorded in as much detail as possible to facilitate future evaluations of the concordance between tumours seen in animals and humans on a site-specific basis.

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Figure 10. Overlap between Group-1 Agents with Sufficient Evidence of Carcinogenicity in Humans and Animals Expressing Tumours in Specific Organ and Tissue Systems. (A. Overlap between animals and humans; B. Overlap between humans and animals. Number of Group-1 agents expressing tumours in specific organ/tissue systems shown in Panel A; number of animal Group-1 agents expressing tumours in specific organ/tissue systems shown in Panel B.)

Table 1: Group-1 Agents included in Volumes 100A-F, 105, 106, 107 and 109[1]

Volume	Type of Agent	Number of Agents	Agents
100A	Pharmaceuticals	23	Aristolochic acid; Aristolochic acid, plants containing; Azathioprine; Busulfan; Chlorambucil; Chlornaphazine; Cyclophosphamide; Ciclosporine; Diethylstilbestrol; Estrogen-only menopausal therapy; Estrogen-progestogen menopausal therapy (combined); estrogen-progestogen oral contraceptives (combined); Etoposide; Etoposide in combination with cisplatin and bleomycin; Melphalan; Methoxsalen in combination with UVA; MOPP and other combined chemotherapy including alkylating agents; Phenacetin; Phenacetin, analgesic mixtures containing; 1-(2-Chloroethyl)-3-(4-methylcyclohexyl)- 1-nitrosourea (Methyl-CCNU); Tamoxifen; Thiotepa; Treosulfan
100B	Biological agents	11	*Clonorchis sinensis* (infection with); Epstein-Barr virus; *Helicobacter pylori* (infection with); Hepatitis B virus; Hepatitis C virus; Human immunodeficiency virus type 1; Human papillomavirus type 16; Human T-cell lymphotropic virus type 1; Kaposi sarcoma herpesvirus; *Opisthorchis viverrini* (infection with); *Schistosoma haematobium* (infection with)
100C	Arsenic, metals, fibres, and dusts	10	Arsenic and inorganic arsenic compounds; Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite); Beryllium and beryllium compounds; Cadmium and cadmium compounds; Chromium (VI) compounds; Erionite; Leather dust; Nickel compounds; Silica dust, crystalline, in the form of quartz or cristobalite; Wood dust
100D	Radiation	18	Fission products including Sr-90; Haematite mining with exposure to radon (underground); Ionizing radiation (all types); Neutron radiation; Phosphorus-32, as phosphate; Pu-239; Radio-iodines, including I-131; Internalized radionuclides that emit alpha particles; Internalized radionuclides that emit beta particles; Ra-224 and its decay products; Ra-226 and its decay products; Ra-228 and its decay products; Rn-222 and its decay products; Solar radiation; Th-232 (as Thorotrast); UV radiation (bandwidth 100-400 nm, encompassing UVC, UVB and UVA); UV-emitting tanning devices; X- and Gamma radiation
100E	Personal habits and indoor combustions	12	Acetaldehyde associated with consumption of alcoholic beverages; Alcoholic beverages; Areca nut; Betel quid with tobacco; Betel quid without tobacco; Coal, indoor emissions from household combustion of; Ethanol in alcoholic beverages; N'-Nitrosonornicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanon (NNK); Salted fish, Chinese style; Second-hand tobacco smoke; Tobacco smoking; Tobacco, smokeless

Table 1. Group-1 Agents included in Volumes 100A-F, 105, 106, 107 and 109 (continued)

Volume	Type of Agent	Number of Agents	Agents
100F	Chemical agents and related occupations	32	Acid mists, strong inorganic; Aflatoxins; Aluminum production; 4-Aminobiphenyl; Auramine production; Benzene; Benzidine; Benzidine, dyes metabolized to; Benzo[*a*]pyrene; Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade); 1,3-Butadiene; Coal gasification; Coal-tar distillation; Coal-tar pitch; Coke production; Ethylene oxide; Formaldehyde; Iron and steel founding, occupational exposure during; Isopropyl alcohol manufacture using strong acids; Magenta production; 4,4'-Methylenebis(2-chloroaniline) (MOCA); Mineral oils, untreated or mildly treated; 2-Naphthylamine; *ortho*-Toluidine; Painter, occupational exposure as a; 3,4,5,3D,4D-Pentachloro-biphenyl (PCB-126)[1]; 2,3,4,7,8-Pentachlorodibenzofuran; Rubber manufacturing industry; Shale oils; Soot (as found in occupational exposure of chimney sweeps); Sulfur mustard; 2,3,7,8-Tetrachlorodibenzo-para-dioxin; Vinyl chloride
105[2]	Diesel and gasoline engine exhausts and some nitroarenes	1	Engine exhaust, diesel
106[2]	Trichloroethylene and some chlorinated agents	1	Trichloroethylene
107[2]	Polychlorinated biphenyls and polybrominated biphenyls	1	Polychlorinated biphenyls (PCBs) and dioxin-like PCBs[1]
109[2]	Outdoor air pollution	2	Outdoor air pollution; Particulate matter in outdoor air pollution

[1]Although 113 Group-1 agents have been identified through Volume 109, the present analysis is based on 111 distinct agents remaining after considering PCBs and dioxin-like PCBs within the broader category of PCBs, and including PCB-126 within the broader category of PCBs.

[2] During the concordance analyses, the Group-1 agents in these Volumes were included with 'chemicals and related occupations' in Vol 100F*.

Table 2. Coding of Tumours Occurring in Animals and Humans

Organ System	Sites Coded from Volume 100 (A,B,C,D,E, and F*)
Upper aero-digestive tract	Nasal cavity and paranasal sinuses Nasopharynx Oral cavity Pharynx Tongue Tonsil Salivary gland
Respiratory system	Larynx Lung Lower respiratory tract
Mesothelium	Mesothelium
Digestive Tract	Oesophagus Stomach Intestine (including colon and rectum)
Digestive Organs	Liver parenchyma and bile ducts Pancreas NOS Gall bladder
Nervous System and Eye	Brain and spinal cord (CNS) Eye
Endocrine System	Thyroid, follicular epithelium Adrenal gland (medulla, cortex, NOS) Pituitary
Kidney	Kidney (renal cortex, renal medulla, kidney NOS)
Urothelium	Urothelium (renal pelvis or ureter or urinary bladder)
Lymphoid and Haematopoietic Tissues	Haematopoietic tissue Lymphoid tissue
Skin	Skin and adnexae Cutaneous melanocytes
Connective Tissues	Soft connective tissue Blood vasculature (endothelium) Hard connective tissue (bone, cartilage)
Female Breast, Female Reproductive Organs and Reproductive Tract	Breast Ovary Uterine Cervix Uterus Vulva/vagina
Other Groupings	All cancers combined All solid cancers Exocrine glands NOS

* These sites are derived from all site descriptors used in *IARC Monographs* to describe human and experimental animal data (see Supplemental Table 1. Animal and Human Tumour Sites for 111 Group-1 Agents Identified through Volume 109 of the *IARC Monographs*). NOS, not otherwise specified

Table 3: Information on Animal and Human Tumours and Tumour Sites for Group-1 Agents in the *IARC Monographs* (adapted from Grosse et al., this Volume)

Volume	Agent No	Agent	Sites with sufficient evidence in humans	Sites with limited evidence in humans	Agent tested in experimental animals	Species	Site	Histology	Study/Gender/Strain/Exposure route
100A	3	Azathioprine	Non Hodgkin lymphoma, skin (squamous cell carcinoma)		Azathioprine	Mouse	thymus	lymphoma	Imamura et al. (1973) (Vol 26 p. 51), MF, C57BL, s.c.; Casey et al. (1968b) (Vol 26 p. 52), M, New Zealand Black, i.m.; Casey et al. (1968a), (Vol 26 p.52),M, New Zealand Black, i.m.
100B	25	Epstein-Barr virus	Burkitt lymphoma, immune-suppression-related non Hodgkin lymphoma, estranodal NK/T-cell lymphoma (nasal type), Hodgkin lymphoma, nasopharyngeal carcinoma	lympho-epithelioma-like carcinoma, gastric carcinoma					
100C	35	Arsenic and inorganic arsenic compounds	lung, urinary bladder, skin	kidney, liver, prostate	Dimethylarsinic acid (DMAv), Monomethylarsonous acid (MMAIII), Sodium arsenite	Mouse	lung	bronchiolo-alveolar carcinoma	DMAv: Tokar et al. (2012a), M, CD1, d.w.; Sodium arsenite: Waalkes et al. (2003), F, C3H/HeNCr, in utero; Waalkes et al. (2006a), M, CD1, in utero; Tokar et al. (2011), MF, CD1, in utero + p.o.; Tokar et al. (2012), M, CD1, in utero; MMAIII: Tokar et al. (2012b), M, CD1, in utero
100D	45	Fission products including Sr-90	Solid cancers, leukaemia						
100E	68	coal, indoor emissions from household combusion of	lung		coal soot extract	Mouse	lung	bronchiolo-alveolar carcinoma	Yin et al. (1984), NR, Kunming, i.t.; Liang et al. (1983), M, Kunming, s.c.; Liang et al. (1984), M, Kunming, s.c.
100F	80	Benzene	Acute myeloid leukaemia/ acute non-lymphocytic leukemia	acute lymphocytic leukaemia, chronic lymphocytic leukaemia, multiple myeoloma, non Hodgkin lymphoma	Benzene	Mouse	thymus	lymphoma	Snyder et al. (1980), M, C57Bl/6J, inh.; Cronkite et al. (1984), F, C57Bl/6 BNL, inh.
V105	108	Engine Exhaust, diesel	Lung	Urinary bladder	Whole diesel engine exhaust	Rat	Lung	bronchiolo-alveolar carcinoma	Ishinishi et al. (1986), MF, F344, inh.; Mauderly et al. (1986, 1987), MF, F344, inh.; Iwai et al. (1986), F, F344, inh.; Heinrich et al. (1995), F, Wistar, inh.; Nikula et al. (1995), F, F344, inh.; Iwai et al. (2000), F, F344, inh.
V106	109	Trichloroethylene	Kidney	non-Hodgkin's lymphoma, liver	Trichloroethylene	Rat	Kidney	renal-cell carcinoma	NTP (1990), M, F344/N, g.; NTP (1988), M, Osborne-Mendel, g.; NTP (1988), F, ACI, g.

Table 4. Agents placed in Group 1 based on Mechanistic Upgrades[1]

Agent	Human/Animal Evidence	**Human Tumour Site**	**Basis for Mechanistic Upgrade**
Aristolochic acid	Limited/Sufficient	Not specified	Herbal remedies containing aristolochic acid provide *sufficient evidence* for upper urinary tract cancer in humans; genotoxic mechanistic data
Benzo(*a*)pyrene (B*a*P)	[No epidemiological data]/Sufficient	Not specified	PAH mixtures containing B*a*P provide *sufficient evidence* for lung or skin cancer in humans; extensive mechanistic data on B*a*P linking animal and human biology
Dyes metabolized to benzidine	Inadequate/Sufficient	Not specified	Benzidine provides *sufficient evidence* of being a human bladder carcinogen
Ethylene oxide	Limited/Sufficient	Not specified	*Limited evidence* for non-Hodgkin lymphoma, breast cancer in humans; genotoxic mechanistic data
Etoposide	Limited/Inadequate	Not specified	*Limited evidence* of acute myeloid leukaemia in humans, with distinctive chromosomal translocations
4,4'-methylenebis(2-chlorobenzenamine) (MOCA)	Inadequate/Sufficient	Not specified	Bladder cancer expected in humans, based on mechanistic data and human case report.
Neutron radiation	Inadequate/Sufficient	Not specified	Biophysics of radiation damage induction similar across different types of radiation
NNN and NNK	Inadequate/Sufficient	Not specified	Target sites correspond to those of smokeless tobacco; mechanistic data on tobacco smoke

Penta(2,3,4,7,8)chlorodibenzofuran (PeCDF)	[No epidemiological data]/Sufficient	Not specified	*Sufficient evidence* in experimental animals combined with strong mechanistic support for receptor-mediated mechanism, with biological activity identical to that of TCDD for every mechanistic step
Phenacetin[2]	Sufficient/Sufficient	Renal pelvis, ureter	Phenacetin was determined to cause tumours of the renal pelvis and ureter, based on evaluation of phenacetin as the active ingredient in analgesic mixtures

[1] Although dioxin-like PCBs evaluated in Volume 107, were also upgraded to Group-1 on the basis of support for receptor-mediated mechanisms and analogies with TCDD (IARC, 2015), dioxin-like PCBs have been subsumed within the broader category of PCBs for purposes of the present analysis of 111 distinct Group-1 agents, and are therefore not included in Table 4.

[2] Phenacetin (Vol 100A) was placed in Group 1 in the absence of *sufficient evidence* of carcinogenicity from epidemiological studies in humans. It was concluded that phenacetin caused tumours of the renal pelvis and ureter in humans as part of the evaluation of the overall evidence for analgesic mixtures containing phenacetin, including human, animal, and mechanistic evidence.

Nature of Human Evidence (number of agents)	Volume: Agent(s)
Mechanistic Upgrades	
Mechanistic upgrade with no human tumour site specified (9 agents)	**Volume 100A:** Aristolochic acid; etoposide. **Volume 100D:** Neutron radiation. **Volume 100E:** Nitrosonornicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3- pyridyl)-1-butanon (NNK). **Volume 100F:** Benzo(*a*)pyrene (B*a*P); dyes metabolized to benzidine; ethylene oxide; 4,4'-methylenebis(2-chlorobenzenamine) (MOCA); (2,3,4,7,8)penta-chloro-dibenzofuran (PeCDF).
Generic Evaluations	
Generic evaluation, of all types of ionizing radiation; internalized radionuclides that emit alpha-particles; internalized radionuclides that emit beta-particles; and the UV region (100-400 nm) of the electromagnetic spectrum (4 agents)	**Volume 100D:** Ionizing radiation (all types); internalized radionuclides that emit alpha-particles; internalized radionuclides that emit beta-particles; UV radiation (bandwidth 100-400 nm, encompassing UVC, UVB and UVA)
Absence of Epidemiologic Data on the Agent Alone	
No epidemiological data available for agent alone (2 agents)	**Volume 100E:** Areca nut; ethanol in alcoholic beverages.

Table 5. Group-1 Agents with No Human Tumour Sites Specified (15 agents)

Table 6. Group-1 Agents with No Animal Tumour Sites Specified (38 agents)

Nature of Animal Evidence (number of agents)	Volume: Agent(s)
Agents with Inadequate Evidence in Animals	
Occupational exposures are complex and likely could not be reliably replicated in the laboratory (7 agents)	**Volume 100F:** Auramine production; magenta production; mists from strong inorganic acids; occupational exposures during iron and steel founding; isopropyl alcohol manufacture by the strong-acid process; occupational exposure as a painter; occupational exposures in the rubber-manufacturing industry.
Used in combination; no animal data available on mixture (2 agents)	**Volume 100A:** Etoposide in combination with cisplatin and bleomycin; MOPP.
Use of animal models problematic due to species-specificity and other limitations (7 agents)	**Volume 100B:** Infection with Epstein-Barr virus; hepatitis B virus; hepatitis C virus; human immunodeficiency virus type 1; human papillomaviruses; human T-cell lymphotropic virus type 1; Kaposi sarcoma herpes virus.
Animal tests conducted but considered inadequate (2 agents)	**Volume 100 A:** Etoposide. **Volume 100C:** Wood dust.
No animal data available (2 agents)	**Volume 100A:** Treosulfan. **Volume 100C:** Leather dust.
Agents with Limited Evidence in Animals	
Evidence of carcinogenicity in animals judged as limited for	**Volume 100A:** Busulfan; chlornaphazine; ciclosporin; estrogen-progestogen menopausal therapy (combined); methyl-CCNU;

various reasons (10 agents)	phenacetin, analgesic mixtures containing. **Volume 100B:** *Clonorchis sinensis* (infection with); *Opisthorchis viverrini* (infection with); *Schistosoma haematobium* (infection with). **Volume 100F**: Sulfur mustard.
Agents with Sufficient Evidence in Animals	
Sufficient evidence in animals, but no tumour sites specified[1] (8 agents)	**Volume 100A:** Melphalan. **Volume 100D:** P-32, as phosphate. **Volume 100E:** Acetaldehyde associated with the consumption of alcoholic beverages; betel quid with tobacco. **Volume 100F:** Aluminium production; PeCDF; **Volume 109:** Outdoor air pollution; particulate matter in outdoor air pollution.

[1] *Sufficient evidence* in experimental animals but no organ sites identified due to the absence of at least two studies of adequate design and quality showing tumours at the same organ site with a similar histological origin in the same species.

Table 7. Concordance between Tumours seen in Humans and Animals for 60 Group-1 Agents by Organ and Tissue System/Tumour Site

Organ and Tissue System[1] *Tissue Site*[1]	Number of Agents			Overlap[2] (%)
	Humans	Animals	Both	
Upper Aero-digestive Tract	9	9	4	28.6
Nasal cavity and paranasal sinuses	*3*	*3*	*0*	*0.0*
Nasopharynx	*3*	*1*	*1*	*33.3*
Oral cavity	*4*	*6*	*2*	*25.0*
Pharynx	*2*	*0*	*0*	*N/A*
Tongue	*0*	*1*	*0*	*N/A*
Salivary gland	*1*	*0*	*0*	*N/A*
Respiratory System	21	22	16	59.3
Larynx	*3*	*1*	*1*	*33.3*
Lung	*20*	*22*	*16*	*61.5*
Mesothelium	2	2	2	100.0
Mesothelium	*2*	*2*	*2*	*100.0*
Digestive Tract	6	6	2	20.0
Oesophagus	*5*	*0*	*0*	*N/A*
Stomach	*3*	*5*	*1*	*14.3*
Intestine (including colon and rectum)	*3*	*1*	*0*	*0.0*
Digestive Organs	8	14	4	22.2
Liver parenchyma and bile ducts	*7*	*14*	*4*	*23.5*
Pancreas NOS	*2*	*0*	*0*	*N/A*
Gall bladder	*1*	*0*	*0*	*N/A*
Nervous System and Eye	2	0	0	N/A
Brain and spinal cord (CNS)	*1*	*0*	*0*	*N/A*
Eye	*1*	*0*	*0*	*N/A*

Endocrine System	2	3	2	66.7
Thyroid, follicular epithelium	*2*	*2*	*2*	*100.0*
Adrenal gland (medulla, cortex, NOS)	*0*	*1*	*0*	*N/A*
Pituitary	*0*	*1*	*0*	*N/A*
Kidney	3	5	2	33.3
Kidney (renal cortex, renal medulla, kidney NOS) (26)	*3*	*5*	*2*	*33.3*
Urothelium	10	7	7	70.0
Urothelium (renal pelvis or ureter or urinary bladder)	*10*	*7*	*7*	*70.0*
Lymphoid and Haematopoietic Tissues	12	10	7	46.7
Haematopoietic tissus	*10*	*2*	*2*	*20.0*
Lymphoid tissue	*2*	*10*	*1*	*9.1*
Skin	11	16	7	35.0
Skin and adnexae	*9*	*16*	*6*	*31.6*
Cutaneous melanocytes	*3*	*0*	*0*	*N/A*
Connective Tissues	6	14	6	42.9
Soft connective tissue	*0*	*9*	*0*	*N/A*
Blood vasculature (endothelium)	*1*	*0*	*0*	*N/A*
Hard connective tissue (bone, cartilage)	*5*	*5*	*4*	*66.7*
Female Breast, Female Reproductive Organs and Reproductive Tract	8	9	4	30.8
Breast (35)	*4*	*7*	*1*	*10.0*
Ovary (36)	*3*	*1*	*0*	*0.0*
Uterine cervix (37)	*3*	*3*	*2*	*50.0*
Uterus (38)	*2*	*3*	*1*	*25.0*
Vulva/vagina (39)	*1*	*0*	*0*	*N/A*
Other Groupings	2	4	0	0.0
All cancers combined	*1*	*0*	*0*	*N/A*
All solid cancers	*1*	*0*	*0*	*N/A*
Exocrine glands NOS	*0*	*4*	*0*	*N/A*

[1] Systems/sites in the anatomically based tumour nomenclature system (see Table 2) lacking *sufficient evidence* in both humans and animals not shown. (For example, there was insufficient evidence of tumours of the male reproductive tract in both humans and animals.)

[2] Percentage overlap calculated as $(N_b/(N_h+N_a-N_b))x100\%$, where N_h, N_a, and N_b denote the number of agents with *sufficient evidence* in humans, animals, or both humans and animals, respectively.

N/A: entry assigned to sites/systems when overlap is not possible (positive data available in either humans or animals, but not in both).

Table 8. Comparison of 60 Group-1 Agents with *Sufficient* or *Limited Evidence* of Carcinogenicity in Humans and *Sufficient Evidence* in Animals Expressing Tumours in Specific Organ and Tissue Systems[1]

Humans[2] Agent (*Monograph* Volume)[4]	Humans and Animals[2] Agent (*Monograph* Volume)	Animals[2] Agent (*Monograph* Volume)
Upper Aero-digestive Tract (28.6% overlap[3])		
Chromium (VI) compounds (C) Nickel Compounds (C) Ra-226 and decay products(D) X-and Gamma radiation (D) *Radioiodines including I-131(D)* Betel Quid W/O tobacco (E) Alcoholic Beverages (E) Salted Fish (E) *Second-hand tobacco smoke (E)* Smokeless Tobacco (E) Tobacco Smoking (E) Formaldehyde (F)	Alcoholic Beverages (E) Salted Fish (E) Smokeless Tobacco (E) Formaldehyde (F) *Chromium (VI) compounds (C)*	Chromium VI (C) Alcoholic Beverages (E) Salted Fish (E) Smokeless Tobacco (E) Formaldehyde (F) Benzene (F) TCDD (F) Polychlorinated biphenyls (F) Bis(Chloromethyl)ether/Chloromethylmethyl ether (F)
Respiratory System (59.3% overlap)		
Arsenic and inorganic arsenic compounds (C) Asbestos (all forms), including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite) (C) Beryllium and beryllium compounds (C) Cadmium and cadmium compounds (C) Chromium (VI) compounds (C) Nickel compounds (C) Silica dust, crystalline, in the form of quartz or cristobalite (C) Haematite mining with exposure to radon (underground) (D)	Arsenic and inorganic arsenic compounds (C) Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite) (C) Beryllium and beryllium compounds (C) Cadmium and cadmium compounds (C) Chromium (VI) compounds (C) Nickel compounds (C) Silica dust, crystalline, in the form of quartz or cristobalite (C) Haematite mining with exposure to radon (underground) (D)	Cyclophosphamide (A) Arsenic and inorganic arsenic compounds (C) Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite(C) Beryllium and beryllium compounds (C) Cadmium and cadmium compounds (C) Chromium (VI) compounds (C) Nickel compounds (C) Silica dust, crystalline, in the form of quartz or cristobalite (C)

Pu-239 (D) **Rn-222 and its decay products (D)** **X- and Gamma radiation (D)** **Alcoholic beverages (E)** **Coal, indoor emissions from household combustion of (E)** **Second-hand tobacco smoke (E)** **Tobacco smoking (E)** **Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade) (F)** **Coal gasification (F)** **Coal-tar pitch (F)** **Coke production (F)** **Soot (as found in occupational exposure of chimney sweeps) (F)** **Engine Exhaust, diesel (F)**	**Pu-239 (D)** **Rn-222 and its decay products (D)** **X- and Gamma radiation (D)** **Coal, indoor emissions from household combustion of (E)** **Second-hand tobacco smoke (E)** **Tobacco smoking (E)** **Coke production (F)** **Engine Exhaust, diesel (F)**	**Haematite mining with exposure to radon (underground)(D)** **Pu-239 (D)** **Rn-222 and its decay products (D)** **X- and Gamma radiation (D)** **Coal, indoor emissions from household combustion of (E)** **Second-hand tobacco smoke (E)** **Tobacco smoking (E)** **Benzene (F)** **1,3-Butadiene (F)** **Coke production (F)** **Vinyl Chloride (F)** **Engine Exhaust, diesel (F*)** **2,3,7,8-Tetrachlorodibenzo-para-dioxin (F*)** **Trichloroethylene (F*)**
Mesothelium (100.0% overlap)		
Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite) (C) **Erionite (C)**	**Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite) (C)** **Erionite (C)**	**Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite) (C)** **Erionite (C)**
Digestive Tract (20.0% overlap)		
***Helicobacter pylori* (infection with) (B)** **X- and Gamma radiation (D)** *Radioiodines including I-131(D)* **Alcoholic beverages (E)** **Betel quid without tobacco (E)** *Salted fish, chinese style (E)* **Tobacco smoking (E)**	***Helicobacter pylori* (infection with) (B)** **Betel quid without tobacco (E)**	**Aristolochic acid, plants containing (A)** ***Helicobacter pylori* (infection with) (B)** **Chromium (VI) compounds (C)** **Betel quid without tobacco (E)** **Benzene (F)** **1,3-Butadiene (F)**

Tobacco, smokeless (E)		
Digestive Organs (22.2% overlap)		
Estrogen-progestogen oral contraceptives (combined) (A) *Arsenic and inorganic arsenic compounds (C)* **Th-232 (as Thorotrast) (D)** **Pu-239 (D)** *X-and Gamma radiation (D)* **Alcoholic beverages (E)** *Betel quid without tobacco (E)* **Tobacco smoking (E)** **Tobacco, smokeless (E)** **Aflatoxins (F)** **Vinyl chloride (F)** *Trichloroethylene (F*)*	Arsenic and inorganic arsenic compounds (C) **Pu-239 (D)** **Th-232 (as Thorotrast) (D)** X-and Gamma radiation (D) **Aflatoxins (F)** **Vinyl chloride (F)** Trichloroethylene (F*)	**Tamoxifen (A)** **Arsenic and inorganic arsenic compounds (C)** **Th-232 (as Thorotrast) (D)** **Pu-239 (D)** **X- and Gamma radiation (D)** **Aflatoxins (F)** **4-Aminobiphenyl (F)** **Benzidine (F)** **1,3-Butadiene (F)** **2-Naphthylamine (F)** **2,3,7,8-Tetrachlorodibenzo-para-dioxin (F)** **Vinyl chloride (F)** **Trichloroethylene (F*)** **Polychlorinated biphenyls (F)**
Nervous System and Eye (N/A)		
UV-emitting tanning devices (D) **X- and Gamma radiation (D)** *Solar radiation (D)*		
Endocrine System (66.7% overlap)		
Radioiodines, including I-131 (D) **X- and Gamma radiation (D)**	**Radioiodines, including I-131 (D)** **X- and Gamma radiation (D)**	**Nickel compounds (C)** **Radioiodines, including I-131 (D)** **X- and Gamma radiation (D)**
Kidney (33.3% overlap)		
Arsenic and inorganic arsenic (C) *Cadmium and cadmium compounds (C)* **X- and Gamma radiation (D)** **Tobacco smoking (E)**	**X- and Gamma radiation (D)** **Trichloroethylene (F*)**	**Diethylstilbestrol (A)** **Estrogen-only menopausal therapy (A)** **Phenacetin (A)** **X- and Gamma radiation (D)**

Trichloroethylene (F*)		Trichloroethylene (F*)
Urothelium (70.0% overlap)		
Aristolochic acid, plants containing (A) **Cyclophosphamide (A)** **Phenacetin (A)** **Arsenic and inorganic arsenic compounds (C)** **X- and Gamma radiation (D)** **Tobacco smoking (E)** *Coal-tar pitch (F)* *Soot (as found in occupational exposure of chimney sweeps) (F)* **4-Aminobiphenyl (F)** **Benzidine (F)** **2-Naphthylamine (F)** ***ortho*-Toluidine (F)** Engine Exhaust, diesel (F*)	**Aristolochic acid, plants containing (A)** **Cyclophosphamide (A)** **Phenacetin (A)** **Arsenic and inorganic arsenic compounds (C)** **4-Aminobiphenyl (F)** **2-Naphthylamine (F)** ***ortho*-Toluidine (F)**	**Aristolochic acid, plants containing (A)** **Cyclophosphamide (A)** **Phenacetin (A)** **Arsenic and inorganic arsenic compounds (C)** **2-Naphthylamine (F)** **4-Aminobiphenyl (F)** ***ortho*-Toluidine (F)**
Lymphoid and Haematopoietic Tissues (46.7% overlap)		
Azathioprine (A) **Chlorambucil (A)** **Cyclophosphamide (A)** **Thiotepa (A)** ***Helicobacter pylori* (infection with) (B)** **Fission products including Sr-90 (D)** **Th-232 (as Thorotrast) (D)** **X- and Gamma radiation (D)** *Radioiodines including I-131(D)* *Rn-222 and its decay products (D)* **Tobacco smoking (E)** *Ethylene oxide (F)* **Benzene (F)**	**Azathioprine (A)** **Chlorambucil (A)** **Cyclophosphamide (A)** **Thiotepa (A)** **X- and Gamma radiation (D)** **Benzene (F)** **1,3-Butadiene (F)**	**Azathioprine (A)** **Chlorambucil (A)** **Cyclophosphamide (A)** **Estrogen-only menopausal therapy (A)** **Thiotepa (A)** **Silica dust, crystalline, in the form of quartz or cristobalite (C)** **X- and Gamma radiation (D)** **Ethylene oxide (F)** **Benzene (F)** **1,3-Butadiene (F)**

1,3-Butadiene (F) **Formaldehyde (F)** *Trichloroethylene (F*)* *Polychlorinated biphenyls (F*)*		
Skin (35.0% overlap)		
Azathioprine (A) **Methoxsalen in combination with UVA (A)** **Arsenic and inorganic arsenic compounds (C)** **Solar radiation (D)** **UV-emitting tanning devices (D)** **X- and Gamma radiation (D)** **Coal-tar distillation (F)** **Mineral oils, untreated or mildly treated (F)** **Shale oils (F)** **Soot (as found in occupational exposure of chimney sweeps) (F)** **Polychlorinated biphenyls (F*)**	**Methoxsalen in combination with UVA (A)** **Solar radiation (D)** **UV-emitting tanning devices (D)** **Coal-tar distillation (F)** **Mineral oils, untreated or mildly treated (F)** **Shale oils (F)** **Soot (as found in occupational exposure of chimney sweeps) (F)**	**Methoxsalen in combination with UVA (A)** **Solar radiation (D)** **UV-emitting tanning devices (D)** **Coal, indoor emissions from household combustion of (E)** **Tobacco smoking (E)** **Benzene (F)** **Bis(chloromethyl)ether;chloromethyl methyl ether (technical-grade) (F)** **Coal gasification (F)** **Coal-tar distillation (F)** **Coal-tar pitch (F)** **Coke production (F)** **Mineral oils, untreated or mildly treated (F)** **Shale oils (F)** **Soot (as found in occupational exposure of chimney sweeps) (F)** **2,3,7,8-Tetrachlorodibenzo-para-dioxin (F)** ***ortho*-Toluidine (F)**
Connective Tissues (42.9% overlap)		
Pu-239 (D) **Ra-224 and its decay products (D)** **Ra-226 and its decay products (D)** **Ra-228 and its decay products (D)** **X- and Gamma radiation (D)**	**Pu-239 (D)** **Ra-224 and its decay products (D)** **Ra-226 and its decay products (D)** **Ra-228 and its decay products (D)** **X- and Gamma radiation (D)**	**Cadmium and cadmium compounds (C)** **Chromium (VI) compounds (C)** **Nickel compounds (C)** **Fission products including Sr-90 (D)** **Pu-239 (D)**

Radioiodines including I-131(D) **Vinyl chloride (F)**	**Vinyl chloride (F)**	**Ra-224 and its decay products (D)** **Ra-226 and its decay products (D)** **Ra-228 and its decay products (D)** **X- and Gamma radiation (D)** **4-Aminobiphenyl (F)** **Bis(chloromethyl)ether;chloromethyl methyl ether (technical-grade) (F)** **1,3-Butadiene (F)** ***ortho*-Toluidine (F)** **Vinyl chloride (F)**
Female Breast, Female Reproductive Organs and Reproductive Tract (30.8% overlap)		
Diethylstilbestrol (A) **Estrogen-only menopausal therapy (A)** **Estrogen-progestogen oral contraceptives (combined) (A)** **Tamoxifen (A)** **Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite) (C)** **X- and Gamma radiation (D)** **Alcoholic beverages (E)** **Tobacco smoking (E)** *Ethylene oxide (F)* *Polychlorinated biphenyls (F*)*	**Diethylstilbestrol (A)** **Estrogen-only menopausal therapy (A)** **Estrogen-progestogen oral contraceptives (combined) (A)** **X- and Gamma radiation (D)**	**Cyclophosphamide(A)** **Diethylstilbestrol (A)** **Estrogen-only menopausal therapy (A)** **Estrogen-progestogen oral contraceptives (combined) (A)** **X- and Gamma radiation (D)** **Benzene (F)** **Benzidine (F)** **1,3-Butadiene (F)** **Vinyl chloride (F)**
Male Reproductive Organs Including Prostate and Testicular Tumours (NA overlap)		
Diethylstilbestrol (A) *Arsenic and inorganic arsenic compounds (C)* *Cadmium and cadmium compounds (C)* *Th-232 (as Thorotrast) D* *X-and Gamma radiation (D)*		
All Cancers Combined		

2,3,7,8-Tetrachlorodibenzo-para-dioxin (F)		

[1]Organ and tissue systems in the anatomically based tumour nomenclature system (see Supplemental Table 1. 'Animal and Human Tumour site for 111 Group 1 identified through Volume 108 of the *IARC Monographs'*). Data inputs for human and animal data with *sufficient evidence* of carcinogenicity are from Supplemental Table 2 'Database of Animal and Human Tumour Sites for 111 Distinct Group-1 Agents Through Volume 109 of the *IARC Monographs*.' Agents lacking sufficient evidence in both humans and animals are not shown with the exception of limited additional data inputs for limited evidence of human sites are from Monographs 100A-F, Monograph 107, and Monograph109 (in italics) and included data for ethylene oxide estrogens and progestogen oral contraceptives, diethylstilbestrol. Data for male reproductive organs are also included in although not part of the concordance analyses. 2,3,7,8-Tetrachlorodibenzo-para-dioxin is included to but its designation of all cancers combined for human data precludes specific site analyses between species.

[2]Agents with *sufficient evidence* in humans, animals, and both humans and animals.

[3]Number of agents with *sufficient evidence* in both humans and animals, as a percentage of the total number agents expressing tumours in either humans or animals (or both) in the specified organ and tissue system (see Table X).

[4]Volume A, B, C, D, E or F in Volume 100 of the Monographs in which the agent is included. F* denotes chemical and related occupations identified as Group-1 agents after Volume 100.

N/A denotes organ/tissue systems when overlap is not possible (positive data is available in either humans or animals, but not both).

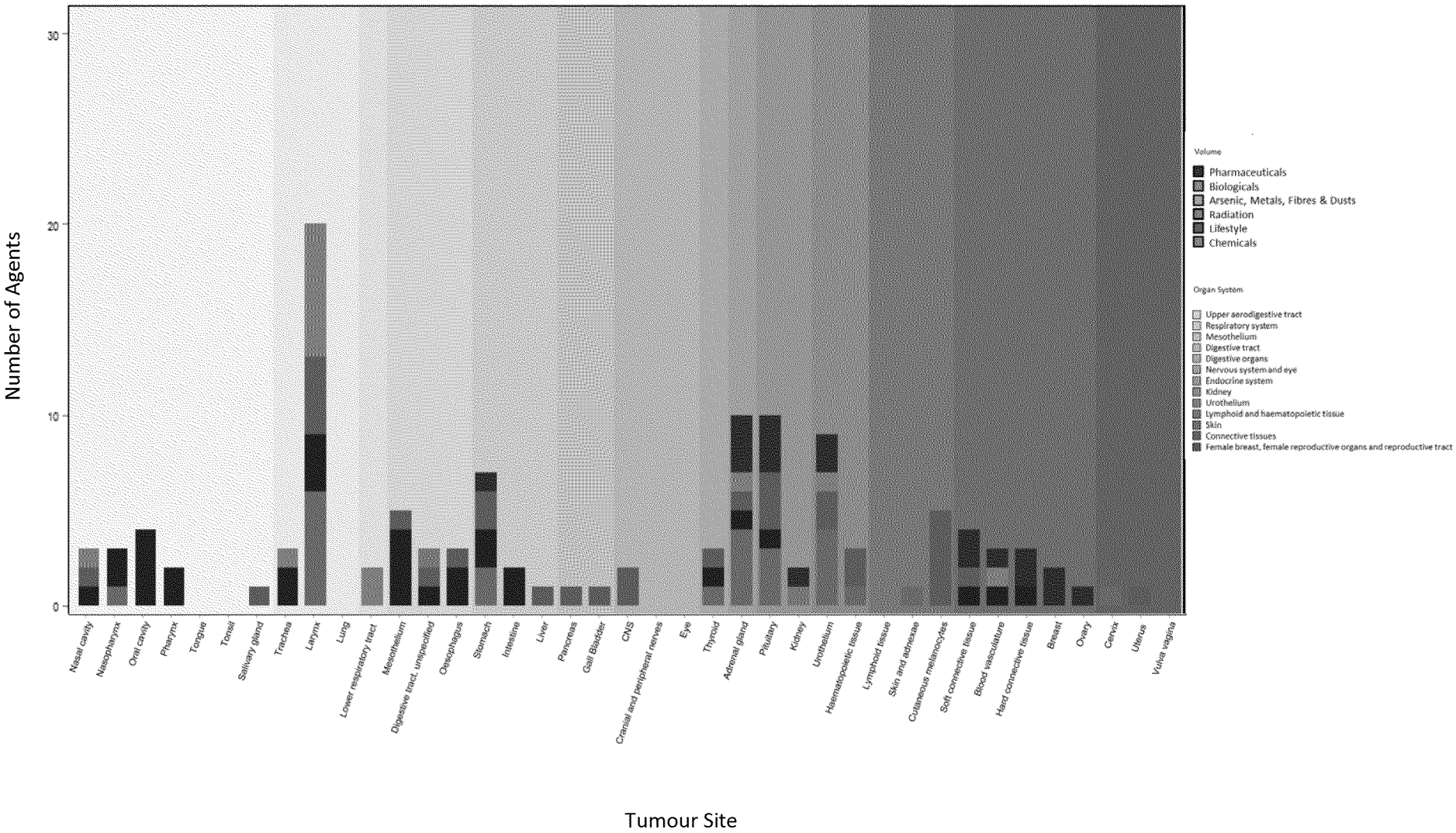


Figure 1. Number of Agents Inducing Tumours in Humans in Each of 39 Tumour sites by Type of Agent

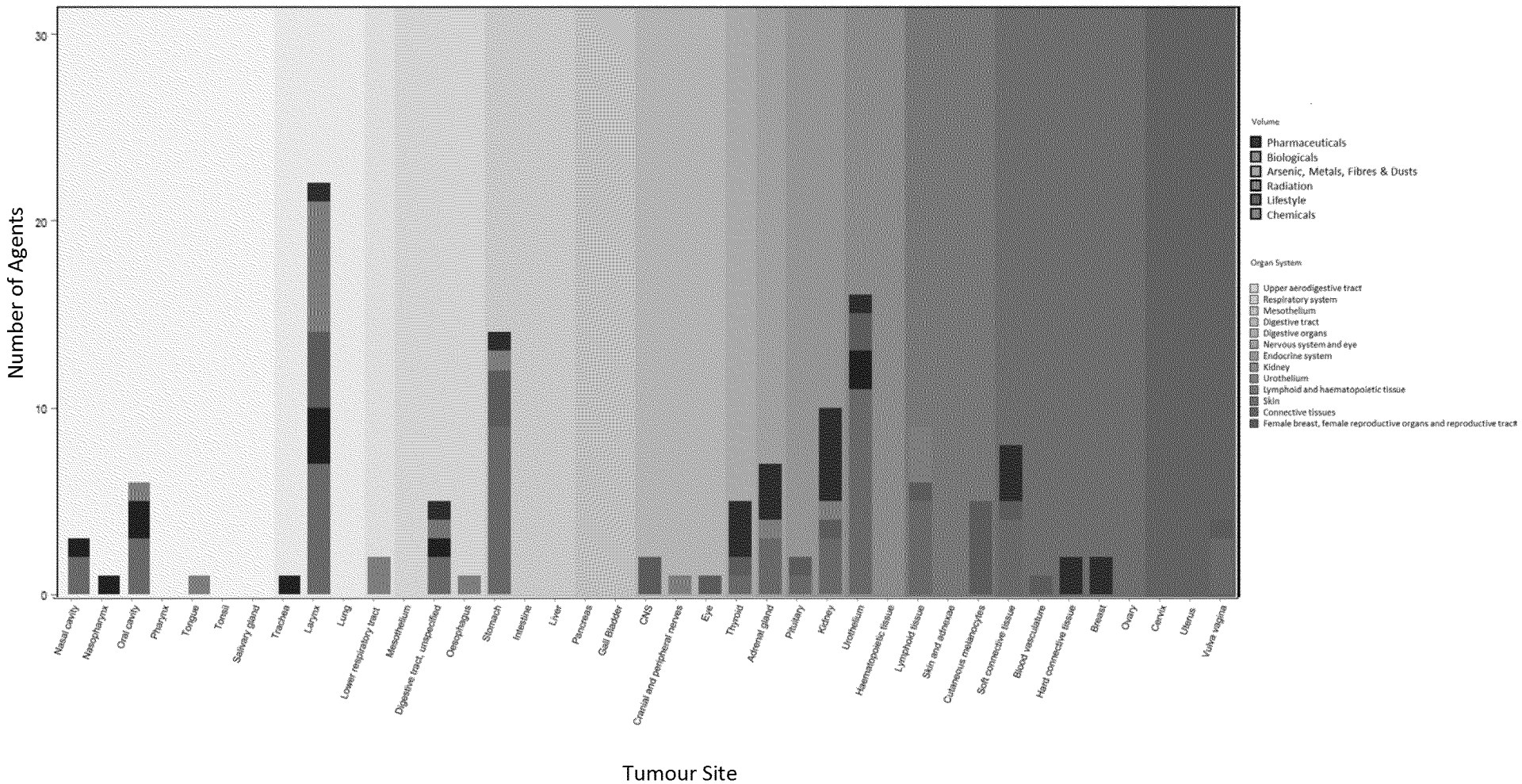


Figure 2. Number of Agents Inducing Tumours in Animals in Each of 39 Tumour sites by Type of Agent

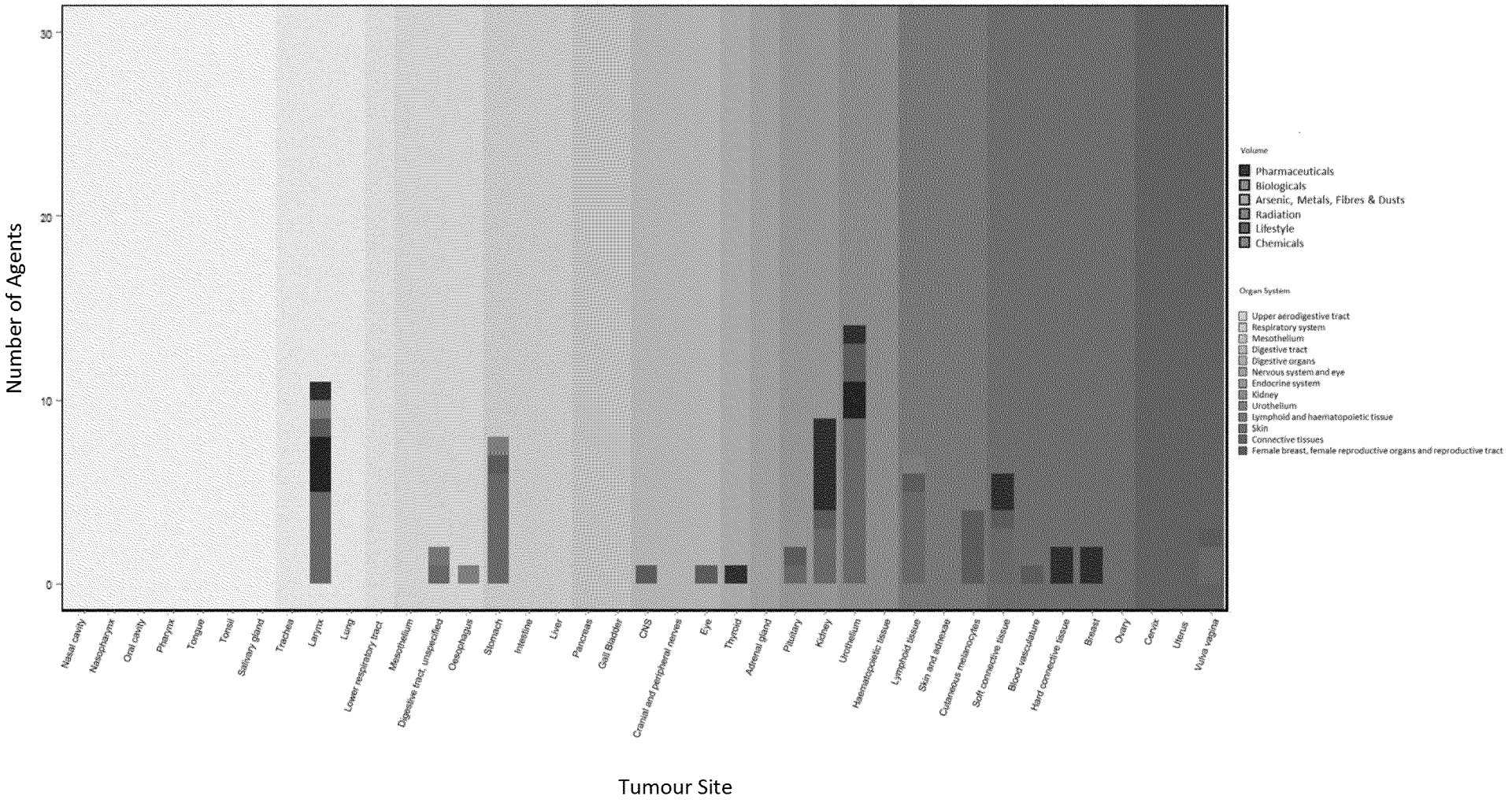
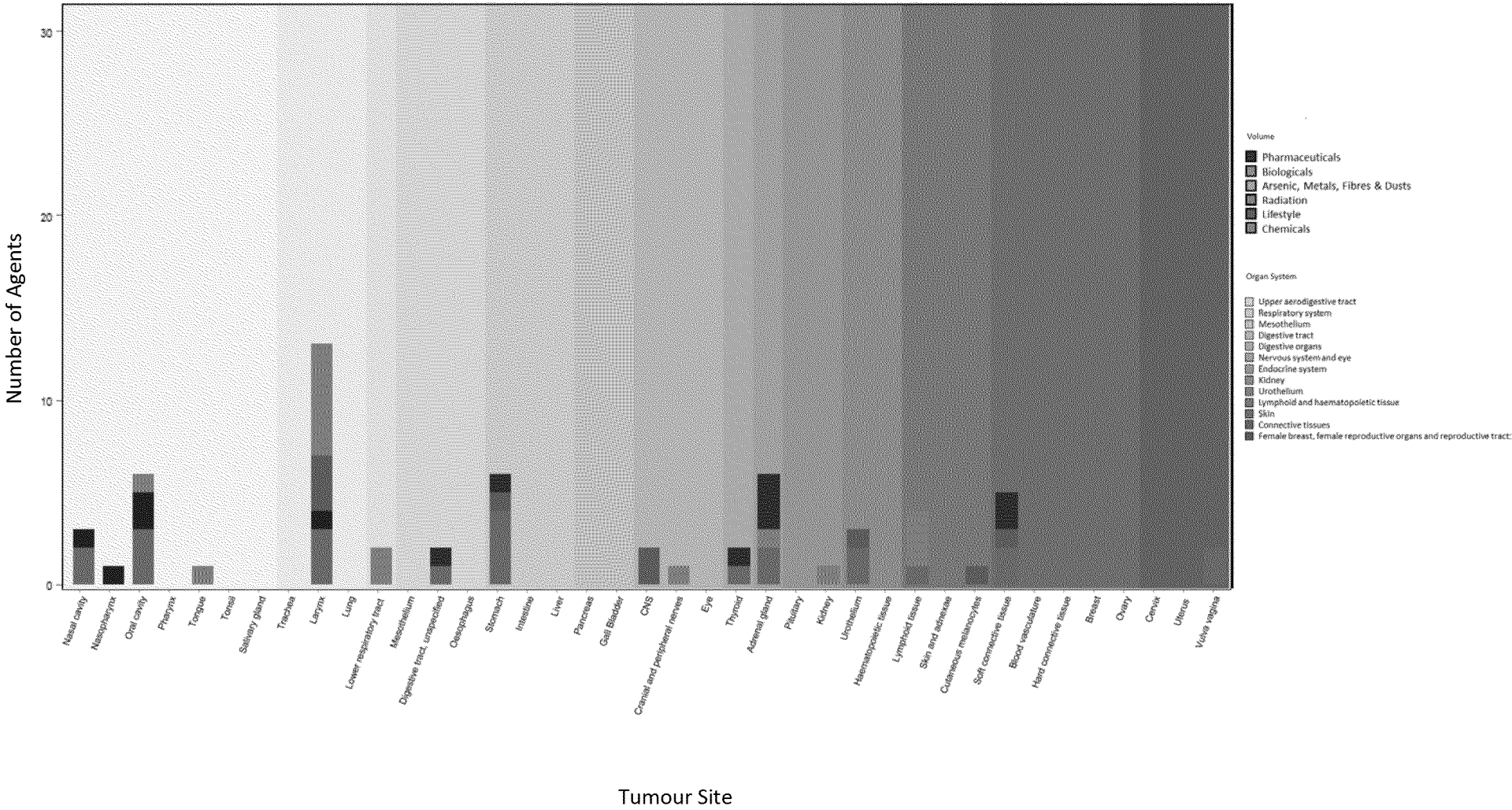


Figure 3. Number of Agents Inducing Tumours in Mice in Each of 39 Tumour sites by Type of Agent



Tumour Site

Figure 4. Number of Agents Inducing Tumours in Rats in Each of 39 Tumour sites by Type of Agent

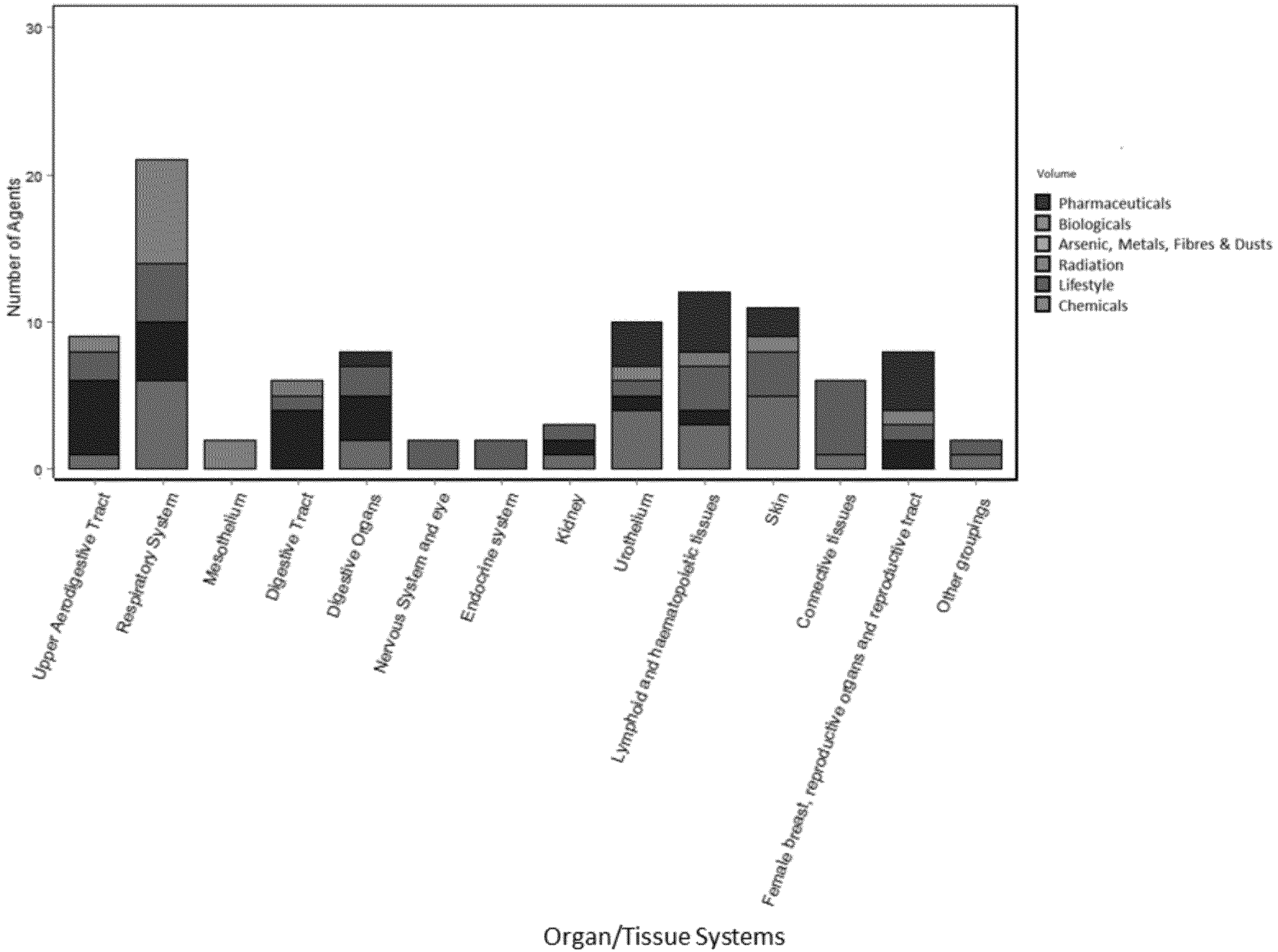


Figure 5. Number of Agents Inducing Tumours in Humans in Each of 15 Organ/Tissue Systems by Type of Agent

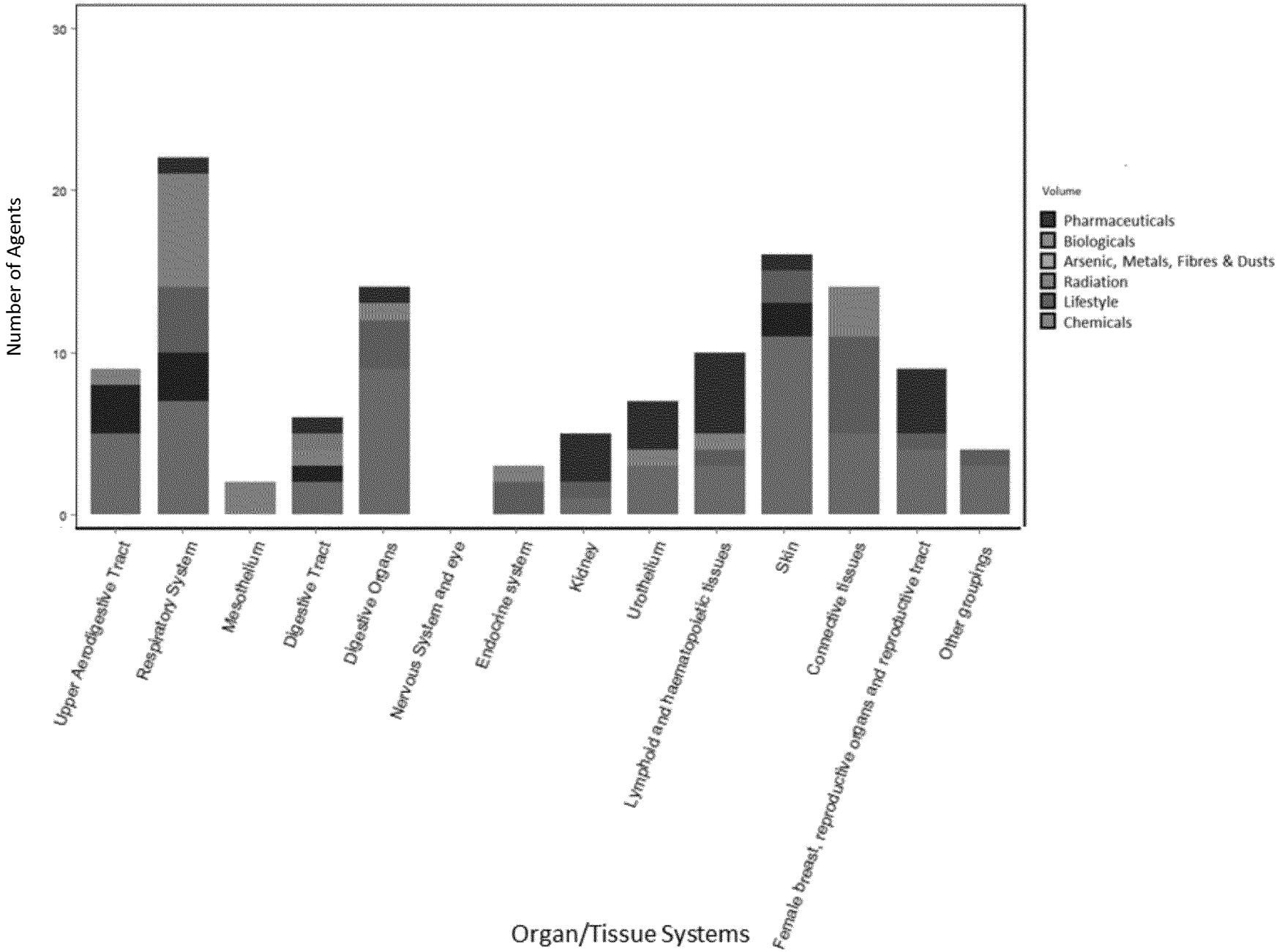


Figure 6. Number of Agents Inducing Tumours in Animals in Each of 15 Organ/Tissue Systems by Type of Agent

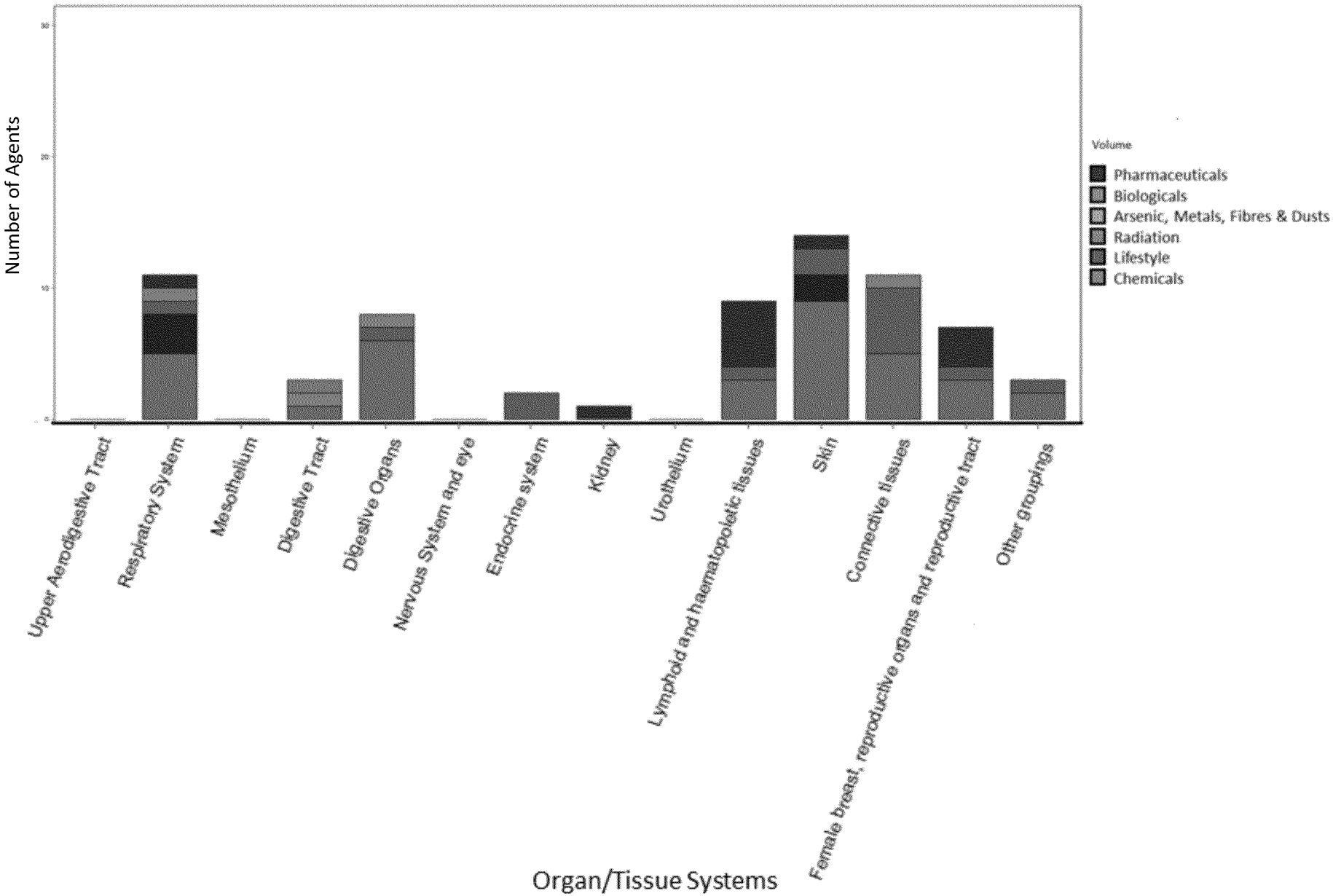


Figure 7. Number of Agents Inducing Tumours in Mice in Each of 15 Organ/Tissue Systems by Type of Agent

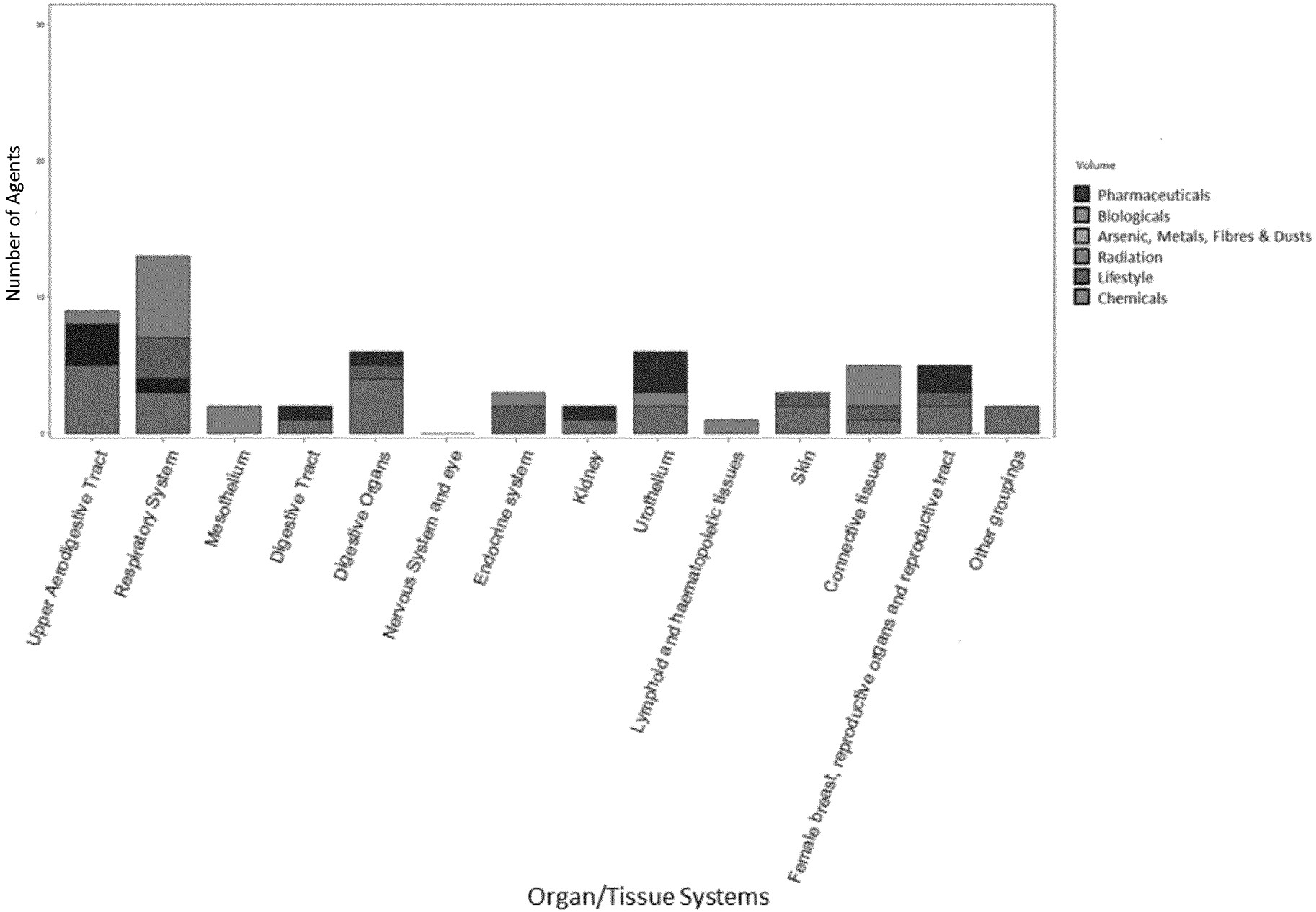


Figure 8. Number of Agents Inducing Tumours in Rats in Each of 15 Organ/Tissue Systems by Type of Agent

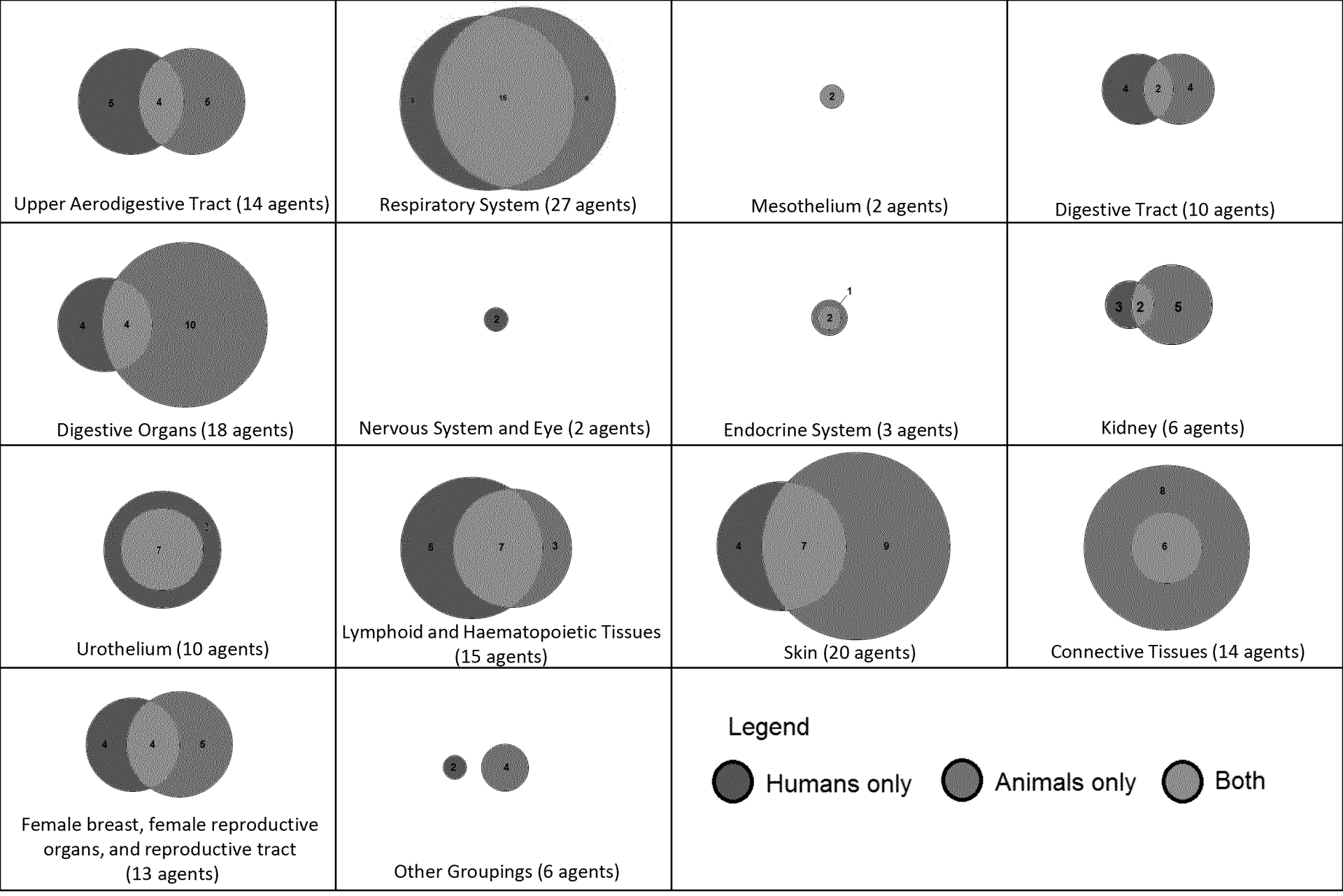


Figure 9. Concordance between Tumour sites seen in Humans and Animals for 60 Group-1 Agents by Organ and Tissue System

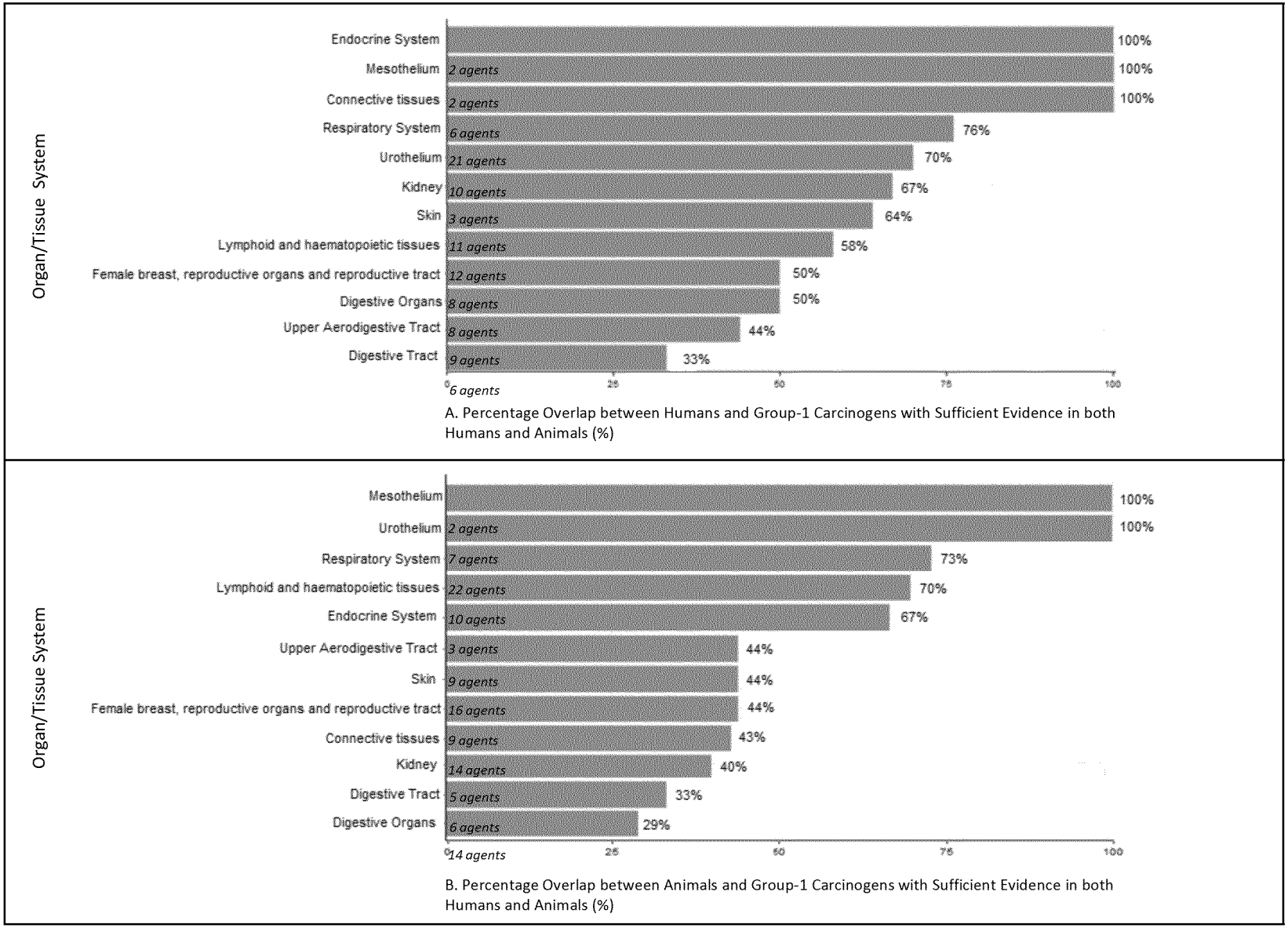


Figure 10. Overlap between Group- 1 Agents with Sufficient Evidence of Carcinogenicity in Humans and Animals Expressing Tumours in Specific Organ and Tissue Systems. (A. Overlap between animals and humans; B. Overlap between humans and animals. Number of Group-1 agents expressing tumours in specific organ/tissue systems shown in Panel A; number of animal Group-1 agents expressing tumours in specific organ/tissue systems shown in Panel B.)

Concordance between Animal and Human Tumours: An Analysis of 111 Agents Known to Cause Cancer in Humans

Supplemental Material I: Database of Anatomically-based Tumour Sites in Animals and Humans

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on behalf of the IARC Working Group on 'Tumour-site Concordance and Mechanisms of Carcinogenesis' which convened in Lyon April/November 2012

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Krewski et al. (2016) conducted a comprehensive analysis of the concordance between tumours seen in animals and humans for 111 distinct Group-1 agents identified in the IARC Monographs programme through Volume 109, based on information abstracted from the IARC Monographs by Grosse et al. (2016). The format of data abstracted from the Monographs by Grosse et al. (2016) is illustrated in Table 3 of Krewski et al. (2016), which includes histological information on animal and human tumours associated with these 111 agents, as well as information on the route of exposure and the gender and species of experimental animal models used.

Because there currently exists no common tumour nomenclature for animal and human tumours, Krewski et al. (2016, Table 2) developed an anatomically-based tumour nomenclature system that permits comparison of tumours seen in animals and humans on a site-specific basis, as well as on the basis of organ and tissue systems comprised of anatomically-related tumour sites. This system was developed by first identifying the anatomical tumour sites seen in both animals and humans for the 111 Group-1 agents based on the data abstracted from the Monographs by Grosse et al. (2016), as summarized in Supplemental Table 1. This was done by recording the individual tumour sites seen in humans and animals in columns 3 and 4 in Supplemental Table 1, respectively, organized by the organ and tissue systems in column 1; column 2 provides the common anatomically-based tumour site used for both animal and human tumours occurring at this site. It should be noted that although *sufficient evidence* for sites in italics in Supplementary Table 1 was not available in either animals or humans for any of the 111 Group-1 agents, these sites are included to record that they were considered, but not observed for various reasons noted in the footnotes to Supplementary Table 1, including the possibility that only *limited*

evidence of carcinogenicity was available. This analysis formed the basis for the harmonized, anatomically-based tumour nomenclature system used by Krewski et al. (2016) as the basis for evaluating concordance between animal and human tumours.

The IARC tumour site concordance database based on this anatomically-based tumour nomenclature system (Supplemental Table 2). A data dictionary describing the elements of Supplemental Table 2 is provided in Supplemental Table 3. Supplemental Table 4 provides the numerical codes assigned to the 47 individual tumour sites and 13 organ and tissue systems included in the database.

Distributions of tumours expressed by across the tumour sites listed in Supplemental Table 4 for humans, (all) animals, mice, and rats are shown in Supplemental Figures 1-4, respectively, by type of agent. [Although there are 47 tumour sites listed in Supplemental Table 4, the 111 Group-1 agents considered here demonstrated animal and/or human tumours at only 39 of these 47 sites.] Similar results for the 15 organ and tissue systems are shown in Supplemental Figures 5-8.

The 60 Group-1 agents included in the analysis of concordance between animal and human tumours reported by Krewski et al. (2016) are summarized in Supplemental Table 5. Concordance analysis was necessarily restricted to these 60 agents because of the requirement of sufficient evidence of at least one tumour site in animals and sufficient evidence of at least one tumour site in humans.

References

Gross et al. (2016). Database of Animal and Human Tumours Based on 111 Group-1 Distinct Agents Known to Cause Cancer in Humans. [This volume.]

Krewski et al. (2016). Concordance between Animal and Human Tumours: An Analysis of 111 Agents Known to Cause Cancer in Humans. [This volume.]

List of Tables

List of Figures

Supplemental Table 1. Animal and Human Tumour Sites for 111 Group-1 Agents Identified through Volume 109 of the IARC Monographs[i]

Organ and Tissue System	Tumour Site	Sites with *Sufficient Evidence* for Cancer in Humans	Sites with *Sufficient Evidence* for Cancer in Experimental Animals
Upper aerodigestive tract	Nasal cavity and paranasal sinuses Nasopharynx Oral cavity Pharynx Tongue Tonsil Salivary gland	Nasal cavity and paranasal sinuses Nasopharynx Oral cavity Pharynx (incl. oropharynx & hypopharynx) Tonsil Salivary gland	Nasal cavity Oral cavity Lip (inner) [ii] Tongue
Respiratory system	*Trachea* [iii] Larynx Lung Lower respiratory tract	*Trachea* Larynx Lung	*Trachea* Larynx Lung Lower respiratory tract (larynx, trachea, and lung)
Mesothelium	Mesothelium	Mesothelium	Pleural mesothelium Peritoneal mesothelium *Peritesticular mesothelium*
Digestive tract	Digestive tract (unspecified) Oesophagus Stomach Intestine, including colon and rectum	Digestive tract (unspecified) Oesophagus Stomach Colon and rectum	 Oesophagus Forestomach Glandular stomach Small and/or large intestine
Digestive organs	Liver parenchyma and bile ducts Pancreas NOS Gall bladder	Liver (parenchyma) and bile ducts Gall bladder Pancreas NOS	Liver parenchyma *Bile ducts* *Gall bladder* [iv] *Pancreas, exocrine*
Nervous system and eye	Brain and spinal cord (CNS) *Cranial and peripheral nerves* [v] Eye	Brain and spinal cord (CNS) *Cranial and peripheral nerves* Eye (melanoma)	Brain and spinal cord (CNS) *Cranial and spinal nerves*
Endocrine system	Thyroid, follicular epithelium	Thyroid	Thyroid, follicular epithelium

	Adrenal gland (medulla, cortex, NOS) Pituitary		Adrenal gland (medulla, cortex, NOS) Pituitary
Kidney	Kidney (renal cell carcinoma)	Kidney, unspecified	Kidney, unspecified
Urothelium	Urothelium (renal pelvis, ureter, urinary bladder)	Renal pelvis Ureter Urinary bladder	Renal pelvis Ureter Urinary bladder
Lymphoid and haematopoietic tissues	Haematopoietic tissue Lymphoid tissue	Haematopoietic tissue (AML, ANLL) [vi] Leukaemia, unspecified Lymphoid tissue (lymphoid leukaemia/lymphoma)	Haematopoietic tissue (granulocytic leukaemia) Lymphoid tissue including thymus (leukaemia/ lymphoma)
Skin	Skin and adnexae Cutaneous melanocytes	Skin and adnexae (general body surface including scrotum, penis, anus and conjunctivae) *Lip (outer)*[vii] Cutaneous melanocytes (malignant melanoma)	Skin and cutaneous sebaceous glands
Connective tissues	Soft connective tissue Blood vasculature (endothelium) Hard connective tissue (bone, cartilage)	Soft connective tissue Blood vasculature (endothelium) Angiosarcoma of the liver Hard connective tissue (bone, cartilage)	Soft connective tissue (incl. haemangiosarcoma) Hard connective tissue (bone, cartilage)
Female breast, female reproductive organs and reproductive tract	Breast Ovary Uterus Uterine cervix Vulva/vagina	Breast Ovary Uterus NOS Endometrium Uterine cervix Vulva/vagina	Mammary gland Ovary Uterus NOS
Male reproductive system [viii]	*Testis, germ cells* *Testis, specialized gonadal stroma*	*Testis, germ cells* *Testis, specialized gonadal stroma*	*Testis, specialized gonadal stroma (Leydig cells)*

	Prostate	*Prostate*	*Prostate*
Other groupings (not included in the concordance analysis)	All cancers combined All solid cancers *Solid cancers, aside from lung* *Multiple or unspecified sites* Exocrine glands NOS	All cancers combined All solid cancers *Solid cancers aside from lung* *Multiple or unspecified sites* *Exocrine glands NOS*	Non-digestive exocrine glands (including Harderian gland, Zymbal gland [ear duct], preputial gland)

[i] Although sites in italics were not in the concordance developed by Grosse et al. (2015) , they are included in the anatomically-based tumour taxonomy system for completeness.

[ii] The monographs do not distinguish between inner and outer lip; this was inferred to be lip inner because of the Group-1 agent it relates to 'smokeless tobacco'

[iii] Trachea was not found as a distinct site in the concordance database.

[iv] The rat has no gall bladder

[v] Cranial and peripheral nerves were not found as a distinct site in the current database.

[vi] AML: Acute myeloid leukemia; ANLL: Acute non-lymphocytic leukemia.

[vii] Lip (outer) provided only *limited evidence* in humans for solar radiation.

[viii] The male reproductive system provided on *limited evidence* in humans (in all three listed tumour sites).

Suplemental Table 2. Database of Animal and Human Tumour Sites for 111 Distinct Group-1 Agents through Volume 109 of the IARC Monographs													
Volume	Agent Number	Agent Name	Species	Site	Anatomical Site	Anatomical Site Label	Anatomical Site Number	Organ System	Organ System Number	Animal Tumour Site Specified	Reason for Lack of Animal Data*	Mechanistic Upgrade	Human Tumour Site Specified
A	1	Aristolochic acid	Rat	Forestomach	Stomach	Stomach	15	Digestive tract	4	1		1	0
A	1	Aristolochic acid	Rat	Renal pelvis	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		1	0
A	1	Aristolochic acid	Human	Not specified						1		1	0
A	2	Aristolochic acid, plants containing	Rat	Forestomach	Stomach	Stomach	15	Digestive tract	4	1		0	1
A	2	Aristolochic acid, plants containing	Human	Renal pelvis	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
A	2	Aristolochic acid, plants containing	Rat	Renal pelvis	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
A	2	Aristolochic acid, plants containing	Human	Ureter	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
A	3	Azathioprine	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
A	3	Azathioprine	Human	Non-Hodgkin lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
A	3	Azathioprine	Mouse	Thymus	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
A	3	Azathioprine	Human	Skin (squamous cell carcinoma)	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
A	4	Busulfan	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	6	0	1
A	5	Chlorambucil	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
A	5	Chlorambucil	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
A	6	Chlomaphazine	Human	Bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	6	0	1
A	7	Cyclophosphamide	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
A	7	Cyclophosphamide	Human	Bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
A	7	Cyclophosphamide	Rat	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
A	7	Cyclophosphamide	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
A	7	Cyclophosphamide	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
A	7	Cyclophosphamide	Mouse	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	8	Ciclosporine	Human	Non-Hodgkin lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	6	0	1
A	8	Ciclosporine	Human	Squamous cell carcinoma	Skin and adnexae	Skin and adnexae	30	Skin	11	0	6	0	1
A	9	Diethylstilbestrol	Hamster	Kidney	Kidney	Kidney	26	Kidney	8	1		0	1
A	9	Diethylstilbestrol	Human	Breast (exposure while pregnant)	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	9	Diethylstilbestrol	Human	Cervix (clear cell adenocarcinoma, exposure in utero)	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	9	Diethylstilbestrol	Mouse	Uterine cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	9	Diethylstilbestrol	Mouse	Uterus	Uterus	Uterus	38	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	9	Diethylstilbestrol	Human	Vagina (clear cell adenocarcinoma, exposure in utero)	Vulva/vagina	Vulva/vagina	39	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	10	Estrogen-only menopausal therapy	Hamster	Kidney	Kidney	Kidney	26	Kidney	8	1		0	1
A	10	Estrogen-only menopausal therapy	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
A	10	Estrogen-only menopausal therapy	Mouse	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	10	Estrogen-only menopausal therapy	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	10	Estrogen-only menopausal therapy	Human	Ovary	Ovary	Ovary	36	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	10	Estrogen-only menopausal therapy	Mouse	Uterine cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	10	Estrogen-only menopausal therapy	Human	Endometrium	Uterus	Uterus	38	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	10	Estrogen-only menopausal therapy	Mouse	Uterus	Uterus	Uterus	38	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	11	Estrogen-progestogen menopausal therapy (combined)	Human	Breast	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	0	6	0	1
A	11	Estrogen-progestogen menopausal therapy (combined)	Human	Endometrium (increased risk for estrogen-induced endometrial cancer decreases with the number of days per month that progestogens are used)	Uterus	Uterus	38	Female breast, female reproductive organs and reproductive tract	13	0	6	0	1
A	12	Estrogen-progestogen oral contraceptives (combined)	Human	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
A	12	Estrogen-progestogen oral contraceptives (combined)	Human	Breast	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	12	Estrogen-progestogen oral contraceptives (combined)	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	12	Estrogen-progestogen oral contraceptives (combined)	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	13	Etoposide	Human	Not specified						0	4	1	0
A	14	Etoposide in combination with cisplatin and bleomycin	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	2	0	1
A	15	Melphalan	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	7	0	1
A	16	Methoxsalen in combination with UVA	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
A	16	Methoxsalen in combination with UVA	Human	Skin (squamous cell carcinoma)	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1

Suplemental Table 2. Database of Animal and Human Tumour Sites for 111 Distinct Group-1 Agents through Volume 109 of the IARC Monographs													
Volume	Agent Number	Agent Name	Species	Site	Anatomical Site	Anatomical Site Label	Anatomical Site Number	Organ System	Organ System Number	Animal Tumour Site Specified	Reason for Lack of Animal Data*	Mechanistic Upgrade	Human Tumour Site Specified
A	17	MOPP and other combined chemotherapy including alkylating agents	Human	Lung	Lung	Lung	10	Respiratory system	2	0	2	0	1
A	17	MOPP and other combined chemotherapy including alkylating agents	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	2	0	1
A	18	Phenacetin	Mouse	Kidney	Kidney	Kidney	26	Kidney	8	1		1	1
A	18	Phenacetin	Rat	Kidney	Kidney	Kidney	26	Kidney	8	1		1	1
A	18	Phenacetin	Human	Renal pelvis	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		1	1
A	18	Phenacetin	Rat	Renal pelvis	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		1	1
A	18	Phenacetin	Human	Ureter	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		1	1
A	19	Phenacetin, analgesic mixtures containing	Human	Renal pelvis	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	6	0	1
A	19	Phenacetin, analgesic mixtures containing	Human	Ureter	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	6	0	1
A	20	1-(2-Chloroethyl)-3-(4-methylcyclohexyl)- 1-nitrosourea (Methyl-CCNU)	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	6	0	1
A	21	Tamoxifen	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
A	21	Tamoxifen	Human	Endometrium	Uterus	Uterus	38	Female breast, female reproductive organs and reproductive tract	13	1		0	1
A	22	Thiotepa	Human	Leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
A	22	Thiotepa	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
A	23	Treosulfan	Human	Acute myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	5	0	1
B	24	Clonorchis sinensis (infection with)	Human	Cholangiocarcinoma	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	0	6	0	1
B	25	Epstein-Barr virus	Human	Nasopharyngeal carcinoma	Nasopharynx	Nasopharynx	2	Upper aerodigestive tract	1	0	3	0	1
B	25	Epstein-Barr virus	Human	Hodgkin lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	25	Epstein-Barr virus	Human	Immune-suppression-related non-Hodgkin lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	25	Epstein-Barr virus	Human	Burkitt lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	25	Epstein-Barr virus	Human	Extranodal NK/T-cell lymphoma (nasal type)	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	26	Helicobacter pylori (infection with)	Mouse	Glandular stomach	Stomach	Stomach	15	Digestive tract	4	1		0	1
B	26	Helicobacter pylori (infection with)	Human	Non-cardiac gastric carcinoma	Stomach	Stomach	15	Digestive tract	4	1		0	1
B	26	Helicobacter pylori (infection with)	Human	Low-grade B-cell MALT gastric lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
B	27	Hepatitis B virus	Human	Hepatocellular carcinoma	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	0	3	0	1
B	28	Hepatitis C virus	Human	Hepatocellular carcinoma	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	0	3	0	1
B	28	Hepatitis C virus	Human	Non-Hodgkin lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	29	Human immunodeficiency virus type 1	Human	Hodgkin lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	29	Human immunodeficiency virus type 1	Human	Non-Hodgkin lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	29	Human immunodeficiency virus type 1	Human	Anus	Skin and adnexae	Skin and adnexae	30	Skin	11	0	3	0	1
B	29	Human immunodeficiency virus type 1	Human	Conjuctiva	Skin and adnexae	Skin and adnexae	30	Skin	11	0	3	0	1
B	29	Human immunodeficiency virus type 1	Human	Kaposi sarcoma	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	0	3	0	1
B	29	Human immunodeficiency virus type 1	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 16	Human	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	0	3	0	1
B	30	Human papillomavirus type 16	Human	Oropharynx	Pharynx	Pharynx	4	Upper aerodigestive tract	1	0	3	0	1
B	30	Human papillomavirus type 16	Human	Tonsil	Tonsil	Tonsil	6	Upper aerodigestive tract	1	0	3	0	1
B	30	Human papillomavirus type 16	Human	Anus	Skin and adnexae	Skin and adnexae	30	Skin	11	0	3	0	1
B	30	Human papillomavirus type 16	Human	Penis	Skin and adnexae	Skin and adnexae	30	Skin	11	0	3	0	1
B	30	Human papillomavirus type 16	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 18	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 31	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 33	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 35	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 39	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 45	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 51	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 52	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 56	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 58	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 59	Human	Cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	30	Human papillomavirus type 16	Human	Vagina	Vulva/vagina	Vulva/vagina	39	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1

Suplemental Table 2. Database of Animal and Human Tumour Sites for 111 Distinct Group-1 Agents through Volume 109 of the IARC Monographs													
Volume	Agent Number	Agent Name	Species	Site	Anatomical Site	Anatomical Site Label	Anatomical Site Number	Organ System	Organ System Number	Animal Tumour Site Specified	Reason for Lack of Animal Data*	Mechanistic Upgrade	Human Tumour Site Specified
B	30	Human papillomavirus type 16	Human	Vulva	Vulva/vagina	Vulva/vagina	39	Female breast, female reproductive organs and reproductive tract	13	0	3	0	1
B	31	Human T-cell lymphotropic virus type 1	Human	Adult T-cell leukaemia/lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	32	Kaposi sarcoma herpesvirus	Human	Primary effusion lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	3	0	1
B	32	Kaposi sarcoma herpesvirus	Human	Kaposi sarcoma	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	0	3	0	1
B	33	Opisthorchis viverrini (infection with)	Human	Cholangiocarcinoma	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	0	6	0	1
B	34	Schistosoma haematobium (infection with)	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	6	0	1
C	35	Arsenic and inorganic arsenic compounds	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	35	Arsenic and inorganic arsenic compounds	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	35	Arsenic and inorganic arsenic compounds	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
C	35	Arsenic and inorganic arsenic compounds	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
C	35	Arsenic and inorganic arsenic compounds	Rat	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
C	35	Arsenic and inorganic arsenic compounds	Human	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Human	Larynx	Larynx	Larynx	9	Respiratory system	2	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Human	Mesothelioma	Mesothelium	Mesothelium	12	Mesothelium	3	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Baboon	Mesothelium	Mesothelium	Mesothelium	12	Mesothelium	3	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Hamster	Mesothelium	Mesothelium	Mesothelium	12	Mesothelium	3	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Rat	Mesothelium	Mesothelium	Mesothelium	12	Mesothelium	3	1		0	1
C	36	Asbestos (all forms, including actinolite, amosite, anthophyllite, chrysotile, crocidolite, tremolite)	Human	Ovary	Ovary	Ovary	36	Female breast, female reproductive organs and reproductive tract	13	1		0	1
C	37	Beryllium and beryllium compounds	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	37	Beryllium and beryllium compounds	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	38	Cadmium and cadmium compounds	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	38	Cadmium and cadmium compounds	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	38	Cadmium and cadmium compounds	Rat	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
C	39	Chromium (VI) compounds	Rat	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
C	39	Chromium (VI) compounds	Rat	Tongue	Tongue	Tongue	5	Upper aerodigestive tract	1	1		0	1
C	39	Chromium (VI) compounds	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	39	Chromium (VI) compounds	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	39	Chromium (VI) compounds	Mouse	Ileum	Intestine, including colon and rectum	Intestine	16	Digestive tract	4	1		0	1
C	39	Chromium (VI) compounds	Mouse	Jejunum	Intestine, including colon and rectum	Intestine	16	Digestive tract	4	1		0	1
C	39	Chromium (VI) compounds	Mouse	Small intestine	Intestine, including colon and rectum	Intestine	16	Digestive tract	4	1		0	1
C	39	Chromium (VI) compounds	Mouse	Duodenum	Intestine, including colon and rectum	Intestine	16	Digestive tract	4	1		0	1
C	39	Chromium (VI) compounds	Rat	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
C	40	Erionite	Human	Mesothelioma	Mesothelium	Mesothelium	12	Mesothelium	3	1		0	1
C	40	Erionite	Rat	Mesothelium	Mesothelium	Mesothelium	12	Mesothelium	3	1		0	1
C	41	Leather dust	Human	Nasal sinus	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	0	5	0	1
C	42	Nickel compounds	Human	Nasal cavity and paranasal sinuses	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
C	42	Nickel compounds	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	42	Nickel compounds	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	42	Nickel compounds	Rat	Adrenal medulla	Adrenal gland	Adrenal gland	24	Endocrine system	7	1		0	1
C	42	Nickel compounds	Hamster	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
C	42	Nickel compounds	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
C	42	Nickel compounds	Rat	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
C	43	Silica dust, crystalline, in the form of quartz or cristobalite	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	43	Silica dust, crystalline, in the form of quartz or cristobalite	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
C	43	Silica dust, crystalline, in the form of quartz or cristobalite	Rat	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
C	44	Wood dust	Human	Nasal sinus	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	0	4	0	1
C	44	Wood dust	Human	Nasopharynx	Nasopharynx	Nasopharynx	2	Upper aerodigestive tract	1	0	4	0	1
D	45	Fission products including Sr-90	Human	Leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
D	45	Fission products including Sr-90	Dog	Bone	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	45	Fission products including Sr-90	Mouse	Bone	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	45	Fission products including Sr-90	Human	Solid cancers	All solid cancers	All solid cancers	44	Other groupings	15	1		0	1
D	46	Haematite mining with exposure to radon (underground)	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	46	Haematite mining with exposure to radon (underground)	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	47	Ionizing radiation (all types)	Human	Not specified						1		0	0

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D	48	Neutron radiation	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		1	1
D	48	Neutron radiation	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		1	1
D	48	Neutron radiation	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		1	1
D	48	Neutron radiation	Mouse	Adrenal gland	Adrenal gland	Adrenal gland	24	Endocrine system	7	1		1	1
D	48	Neutron radiation	Mouse	Pituitary gland	Pituitary	Pituitary	25	Endocrine system	7	1		1	1
D	48	Neutron radiation	Monkey (Rhesus)	Kidney	Kidney	Kidney	26	Kidney	8	1		1	1
D	48	Neutron radiation	Mouse	Haematopoietic tissue	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		1	1
D	48	Neutron radiation	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		1	1
D	48	Neutron radiation	Mouse	Thymus	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		1	1
D	48	Neutron radiation	Mouse	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		1	1
D	48	Neutron radiation	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		1	1
D	48	Neutron radiation	Mouse	Ovary	Ovary	Ovary	36	Female breast, female reproductive organs and reproductive tract	13	1		1	1
D	48	Neutron radiation	Mouse	Harderian gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		1	0
D	48	Neutron radiation	Human	Not specified						1		1	0
D	49	P-32, as phosphate	Human	Leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	7	0	1
D	50	Pu-239	Dog	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	50	Pu-239	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	50	Pu-239	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	50	Pu-239	Dog	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
D	50	Pu-239	Human	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
D	50	Pu-239	Human	Bone	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	50	Pu-239	Dog	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	50	Pu-239	Mouse	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	50	Pu-239	Rat	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	51	Radioiodines, including I-131	Human	Thyroid	Thyroid	Thyroid	23	Endocrine system	7	1		0	1
D	51	Radioiodines, including I-131	Mouse	Thyroid	Thyroid	Thyroid	23	Endocrine system	7	1		0	1
D	51	Radioiodines, including I-131	Rat	Thyroid	Thyroid	Thyroid	23	Endocrine system	7	1		0	1
D	52	Internalized radionuclides that emit alpha particles	Human	Not specified						1		0	0
D	52	Internalized radionuclides that emit alpha particles	Dog	Lung	Lung	Lung	10	Respiratory system	2	1		0	0
D	52	Internalized radionuclides that emit alpha particles	Hamster	Lung	Lung	Lung	10	Respiratory system	2	1		0	0
D	52	Internalized radionuclides that emit alpha particles	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	0
D	52	Internalized radionuclides that emit alpha particles	Dog	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	0
D	52	Internalized radionuclides that emit alpha particles	Mouse	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	0
D	52	Internalized radionuclides that emit alpha particles	Rat	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	0
D	53	Internalized radionuclides that emit beta particles	Human	Not specified						1		0	0
D	53	Internalized radionuclides that emit beta particles	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	0
D	53	Internalized radionuclides that emit beta particles	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	0
D	53	Internalized radionuclides that emit beta particles	Mouse	Thymus	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	0
D	53	Internalized radionuclides that emit beta particles	Dog	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	0
D	53	Internalized radionuclides that emit beta particles	Rat	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	0
D	53	Internalized radionuclides that emit beta particles	Dog	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	0
D	53	Internalized radionuclides that emit beta particles	Mouse	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	0
D	53	Internalized radionuclides that emit beta particles	Rat	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	0
D	53	Internalized radionuclides that emit beta particles	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	0
D	54	Ra-224 and its decay products	Human	Bone	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	54	Ra-224 and its decay products	Dog	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	54	Ra-224 and its decay products	Mouse	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	55	Ra-226 and its decay products	Human	Paranasal sinus	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
D	55	Ra-226 and its decay products	Human	Bone	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	55	Ra-226 and its decay products	Human	Mastoid process	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	55	Ra-226 and its decay products	Dog	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	55	Ra-226 and its decay products	Mouse	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	56	Ra-228 and its decay products	Human	Bone	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	56	Ra-228 and its decay products	Dog	Skeletal system	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	57	Rn-222 and its decay products	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	57	Rn-222 and its decay products	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	58	Solar radiation	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
D	58	Solar radiation	Rat	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
D	58	Solar radiation	Human	Skin (basal cell carcinoma, squamous cell carcinoma)	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
D	58	Solar radiation	Human	Skin (malignant melanoma)	Cutaneous melanocytes	Cutaneous melanocytes	31	Skin	11	1		0	1
D	59	Th-232 (as Thorotrast)	Human	Extrahepatic bile ducts	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
D	59	Th-232 (as Thorotrast)	Hamster	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
D	59	Th-232 (as Thorotrast)	Human	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
D	59	Th-232 (as Thorotrast)	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
D	59	Th-232 (as Thorotrast)	Human	Gall bladder	Gall bladder	Gall bladder	19	Digestive organs	5	1		0	1

Suplemental Table 2. Database of Animal and Human Tumour Sites for 111 Distinct Group-1 Agents through Volume 109 of the IARC Monographs													
Volume	Agent Number	Agent Name	Species	Site	Anatomical Site	Anatomical Site Label	Anatomical Site Number	Organ System	Organ System Number	Animal Tumour Site Specified	Reason for Lack of Animal Data*	Mechanistic Upgrade	Human Tumour Site Specified
D	59	Th-232 (as Thorotrast)	Human	Leukaemia (excluding chronic lymphocytic leukaemia)	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
D	60	UV radiation (bandwidth 100-400 nm, encompassing UVC, UVB and UVA)	Human	Not specified						1		0	0
D	60	UV radiation (bandwidth 100-400 nm, encompassing UVC, UVB and UVA)	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	0
D	60	UV radiation (bandwidth 100-400 nm, encompassing UVC, UVB and UVA)	Rat	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	0
D	61	UV-emitting tanning devices	Human	Eye (melanoma)	Eye	Eye	22	Nervous system and eye	6	1		0	1
D	61	UV-emitting tanning devices	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
D	61	UV-emitting tanning devices	Human	Skin (melanoma)	Cutaneous melanocytes	Cutaneous melanocytes	31	Skin	11	1		0	1
D	62	X- and Gamma radiation	Human	Salivary gland	Salivary gland	Salivary gland	7	Upper aerodigestive tract	1	1		0	1
D	62	X- and Gamma radiation	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	62	X- and Gamma radiation	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
D	62	X- and Gamma radiation	Human	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	1		0	1
D	62	X- and Gamma radiation	Human	Stomach	Stomach	Stomach	15	Digestive tract	4	1		0	1
D	62	X- and Gamma radiation	Human	Colon	Intestine, including colon and rectum	Intestine	16	Digestive tract	4	1		0	1
D	62	X- and Gamma radiation	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
D	62	X- and Gamma radiation	Human	Brain and CNS	Brain and spinal cord (CNS)	CNS	20	Nervous system and eye	6	1		0	1
D	62	X- and Gamma radiation	Human	Thyroid	Thyroid	Thyroid	23	Endocrine system	7	1		0	1
D	62	X- and Gamma radiation	Rat	Thyroid	Thyroid	Thyroid	23	Endocrine system	7	1		0	1
D	62	X- and Gamma radiation	Mouse	Pituitary gland	Pituitary	Pituitary	25	Endocrine system	7	1		0	1
D	62	X- and Gamma radiation	Human	Kidney	Kidney	Kidney	26	Kidney	8	1		0	1
D	62	X- and Gamma radiation	Monkey (Rhesus)	Kidney	Kidney	Kidney	26	Kidney	8	1		0	1
D	62	X- and Gamma radiation	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
D	62	X- and Gamma radiation	Mouse	Haematopoietic tissue	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
D	62	X- and Gamma radiation	Human	Leukaemia (excl. chronic lymphocytic leukaemia)	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
D	62	X- and Gamma radiation	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
D	62	X- and Gamma radiation	Mouse	Thymus	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
D	62	X- and Gamma radiation	Human	Basal cell of the skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
D	62	X- and Gamma radiation	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
D	62	X- and Gamma radiation	Human	Bbone	Hard connective tissue (bone, cartilage)	Hard connective tissue	34	Connective tissues	12	1		0	1
D	62	X- and Gamma radiation	Human	Female breast	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
D	62	X- and Gamma radiation	Mouse	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
D	62	X- and Gamma radiation	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
D	62	X- and Gamma radiation	Mouse	Ovary	Ovary	Ovary	36	Female breast, female reproductive organs and reproductive tract	13	1		0	1
D	62	X- and Gamma radiation	Mouse	Harderian gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		0	1
E	63	Acetaldehyde associated with consumption of alcoholic beverages	Human	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	0	7	0	1
E	63	Acetaldehyde associated with consumption of alcoholic beverages	Human	Pharynx	Pharynx	Pharynx	4	Upper aerodigestive tract	1	0	7	0	1
E	63	Acetaldehyde associated with consumption of alcoholic beverages	Human	Larynx	Larynx	Larynx	9	Respiratory system	2	0	7	0	1
E	63	Acetaldehyde associated with consumption of alcoholic beverages	Human	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	0	7	0	1
E	64	Alcoholic beverages	Human	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	64	Alcoholic beverages	Rat	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	64	Alcoholic beverages	Human	Pharynx	Pharynx	Pharynx	4	Upper aerodigestive tract	1	1		0	1
E	64	Alcoholic beverages	Human	Larynx	Larynx	Larynx	9	Respiratory system	2	1		0	1
E	64	Alcoholic beverages	Human	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	1		0	1
E	64	Alcoholic beverages	Human	Colorectum	Intestine, including colon and rectum	Intestine	16	Digestive tract	4	1		0	1
E	64	Alcoholic beverages	Human	Hepatocellular carcinoma	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
E	64	Alcoholic beverages	Human	breast	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
E	65	Areca nut	Human	Not specified						1		0	0
E	65	Areca nut	Hamster	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	65	Areca nut	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
E	66	Betel quid with tobacco	Human	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	0	7	0	1
E	66	Betel quid with tobacco	Human	Pharynx	Pharynx	Pharynx	4	Upper aerodigestive tract	1	0	7	0	1
E	66	Betel quid with tobacco	Human	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	0	7	0	1
E	67	Betel quid without tobacco	Human	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	67	Betel quid without tobacco	Human	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	1		0	1
E	67	Betel quid without tobacco	Hamster	Forestomach	Stomach	Stomach	15	Digestive tract	4	1		0	1
E	68	Coal, indoor emissions from household combusion of	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
E	68	Coal, indoor emissions from household combusion of	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
E	68	Coal, indoor emissions from household combusion of	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
E	69	Ethanol in alcoholic beverages	Human	Not specified						1		0	0
E	69	Ethanol in alcoholic beverages	Rat	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	0
E	70	N'-Nitrosonomicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanon (NNK)	Hamster	Nasal cavity	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		1	0
E	70	N'-Nitrosonomicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanon (NNK)	Hamster	Lung	Lung	Lung	10	Respiratory system	2	1		1	0
E	70	N'-Nitrosonomicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanon (NNK)	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		1	0
E	70	N'-Nitrosonomicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanon (NNK)	Rat	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	1		1	0
E	70	N'-Nitrosonomicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanon (NNK)	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		1	0

Suplemental Table 2. Database of Animal and Human Tumour Sites for 111 Distinct Group-1 Agents through Volume 109 of the IARC Monographs													
Volume	Agent Number	Agent Name	Species	Site	Anatomical Site	Anatomical Site Label	Anatomical Site Number	Organ System	Organ System Number	Animal Tumour Site Specified	Reason for Lack of Animal Data*	Mechanistic Upgrade	Human Tumour Site Specified
E	70	N'-Nitrosonomicotine (NNN) and 4-(N-Nitrosomethylamino)-1-(3-pyridyl)-1-butanon (NNK)	Human	Not specified						1		1	0
E	71	Salted fish, chinese style	Rat	Nasal cavity	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
E	71	Salted fish, chinese style	Rat	Paranasal sinus	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
E	71	Salted fish, chinese style	Rat	Nasopharynx	Nasopharynx	Nasopharynx	2	Upper aerodigestive tract	1	1		0	1
E	71	Salted fish, chinese style	Human	Nasopharynx	Nasopharynx	Nasopharynx	2	Upper aerodigestive tract	1	1		0	1
E	72	Second-hand tobacco smoke	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
E	72	Second-hand tobacco smoke	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
E	73	Tobacco smoking	Human	Nasal cavity	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
E	73	Tobacco smoking	Human	Paranasal sinus	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
E	73	Tobacco smoking	Human	Nasopharynx	Nasopharynx	Nasopharynx	2	Upper aerodigestive tract	1	1		0	1
E	73	Tobacco smoking	Human	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	73	Tobacco smoking	Human	pharynx (incl. oropharynx & hypopharynx)	Pharynx	Pharynx	4	Upper aerodigestive tract	1	1		0	1
E	73	Tobacco smoking	Human	Larynx	Larynx	Larynx	9	Respiratory system	2	1		0	1
E	73	Tobacco smoking	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
E	73	Tobacco smoking	Hamster	Larynx	Larynx	Larynx	9	Respiratory system	2	1		0	1
E	73	Tobacco smoking	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
E	73	Tobacco smoking	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
E	73	Tobacco smoking	Human	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	1		0	1
E	73	Tobacco smoking	Human	Stomach	Stomach	Stomach	15	Digestive tract	4	1		0	1
E	73	Tobacco smoking	Human	Colorectum	Intestine, including colon and rectum	Intestine	16	Digestive tract	4	1		0	1
E	73	Tobacco smoking	Human	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
E	73	Tobacco smoking	Human	Hepatoblastoma in children (parental smoking)	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
E	73	Tobacco smoking	Human	Pancreas	Pancreas NOS	Pancreas	18	Digestive organs	5	1		0	1
E	73	Tobacco smoking	Human	Kidney	Kidney	Kidney	26	Kidney	8	1		0	1
E	73	Tobacco smoking	Human	Ureter	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
E	73	Tobacco smoking	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
E	73	Tobacco smoking	Human	Myeloid leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
E	73	Tobacco smoking	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
E	73	Tobacco smoking	Human	ovary	Ovary	Ovary	36	Female breast, female reproductive organs and reproductive tract	13	1		0	1
E	73	Tobacco smoking	Human	Uterine cervix	Uterine cervix	Cervix	37	Female breast, female reproductive organs and reproductive tract	13	1		0	1
E	74	Tobacco, smokeless	Rat	Lip	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	74	Tobacco, smokeless	Human	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	74	Tobacco, smokeless	Rat	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
E	74	Tobacco, smokeless	Human	Oesophagus	Oesophagus	Oesophagus	14	Digestive tract	4	1		0	1
E	74	Tobacco, smokeless	Human	Pancreas	Pancreas NOS	Pancreas	18	Digestive organs	5	1		0	1
F	75	Acid mists, strong inorganic	Human	Larynx	Larynx	Larynx	9	Respiratory system	2	0	1	0	1
F	76	Aflatoxins	Human	Hepatocellular carcinoma	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	76	Aflatoxins	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	77	Aluminum production	Human	Lung	Lung	Lung	10	Respiratory system	2	0	7	0	1
F	77	Aluminum production	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	7	0	1
F	78	4-Aminobiphenyl	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	78	4-Aminobiphenyl	Dog	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	78	4-Aminobiphenyl	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	78	4-Aminobiphenyl	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
F	79	Auramine production	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	1	0	1
F	80	Benzene	Rat	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
F	80	Benzene	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	80	Benzene	Rat	Forestomach	Stomach	Stomach	15	Digestive tract	4	1		0	1
F	80	Benzene	Human	Acute myeloid leukaemia/acute non-lymphocytic leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
F	80	Benzene	Mouse	Haematopoietic tissue	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
F	80	Benzene	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
F	80	Benzene	Mouse	Thymus	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
F	80	Benzene	Rat	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	80	Benzene	Mouse	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
F	80	Benzene	Mouse	Preputial gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		0	1
F	80	Benzene	Mouse	Zymbal gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		0	1
F	80	Benzene	Rat	Zymbal gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		0	1
F	81	Benzidine	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	81	Benzidine	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	81	Benzidine	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
F	82	Benzidine, dyes metabolized to	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		1	0
F	82	Benzidine, dyes metabolized to	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		1	0
F	82	Benzidine, dyes metabolized to	Human	Not specified						1		1	0
F	83	Benzo[a]pyrene	Hamster	Lung	Lung	Lung	10	Respiratory system	2	1		1	0
F	83	Benzo[a]pyrene	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		1	0
F	83	Benzo[a]pyrene	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		1	0
F	83	Benzo[a]pyrene	Hamster	Lower respiratory tract (larynx, trachea, lung)	Lower respiratory tract	Lower respiratory tract	11	Respiratory system	2	1		1	0
F	83	Benzo[a]pyrene	Hamster	Forestomach	Stomach	Stomach	15	Digestive tract	4	1		1	0
F	83	Benzo[a]pyrene	Mouse	Forestomach	Stomach	Stomach	15	Digestive tract	4	1		1	0
F	83	Benzo[a]pyrene	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		1	0
F	83	Benzo[a]pyrene	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		1	0

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Volume	Agent Number	Agent Name	Species	Site	Anatomical Site	Anatomical Site Label	Anatomical Site Number	Organ System	Organ System Number	Animal Tumour Site Specified	Reason for Lack of Animal Data*	Mechanistic Upgrade	Human Tumour Site Specified
F	83	Benzo[*a*]pyrene	Hamster	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		1	0
F	83	Benzo[*a*]pyrene	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		1	0
F	83	Benzo[*a*]pyrene	Rat	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		1	0
F	83	Benzo[*a*]pyrene	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		1	0
F	83	Benzo[*a*]pyrene	Human	Not specified						1		1	0
F	84	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Rat	Nasal cavity	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
F	84	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	84	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	84	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
F	85	1,3-Butadiene	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	85	1,3-Butadiene	Mouse	Forestomach	Stomach	Stomach	15	Digestive tract	4	1		0	1
F	85	1,3-Butadiene	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	85	1,3-Butadiene	Human	Haematolymphatic organs	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
F	85	1,3-Butadiene	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
F	85	1,3-Butadiene	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
F	85	1,3-Butadiene	Mouse	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
F	85	1,3-Butadiene	Mouse	Harderian gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		0	1
F	85	1,3-Butadiene	Mouse	Preputial gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		0	1
F	86	Coal gasification	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	86	Coal gasification	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	87	Coal-tar distillation	Human	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	87	Coal-tar distillation	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	88	Coal-tar pitch	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	88	Coal-tar pitch	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	89	Coke production	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	89	Coke production	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	89	Coke production	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	89	Coke production	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	90	Ethylene oxide	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		1	0
F	90	Ethylene oxide	Rat	Peritoneum	Mesothelium	Mesothelium	12	Mesothelium	3	1		1	0
F	90	Ethylene oxide	Rat	Brain	Brain and spinal cord (CNS)	CNS	20	Nervous system and eye	6	1		1	0
F	90	Ethylene oxide	Rat	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		1	0
F	90	Ethylene oxide	Human	Not specified						1		1	0
F	91	Formaldehyde	Rat	Nasal cavity	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	1		0	1
F	91	Formaldehyde	Human	Nasopharynx	Nasopharynx	Nasopharynx	2	Upper aerodigestive tract	1	1		0	1
F	91	Formaldehyde	Human	Leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	1		0	1
F	92	Iron and steel founding (occupational exposure during)	Human	Lung	Lung	Lung	10	Respiratory system	2	0	1	0	1
F	93	Isopropyl alcohol manufacture using strong acids	Human	Nasal cavity	Nasal cavity and paranasal sinuses	Nasal cavity	1	Upper aerodigestive tract	1	0	1	0	1
F	94	Magenta production	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	1	0	1
F	95	4,4'-Methylenebis(2-chloroaniline) (MOCA)	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		1	0
F	95	4,4'-Methylenebis(2-chloroaniline) (MOCA)	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		1	0
F	95	4,4'-Methylenebis(2-chloroaniline) (MOCA)	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		1	0
F	95	4,4'-Methylenebis(2-chloroaniline) (MOCA)	Human	Not specified						1		1	0
F	96	Mineral oils, untreated or mildly treated	Human	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	96	Mineral oils, untreated or mildly treated	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	97	2-Naphthylamine	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	97	2-Naphthylamine	Dog	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	97	2-Naphthylamine	Hamster	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	97	2-Naphthylamine	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	97	2-Naphthylamine	Monkey	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	97	2-Naphthylamine	Rat	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	98	*ortho*-Toluidine	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	98	*ortho*-Toluidine	Rat	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	1		0	1
F	98	*ortho*-Toluidine	Rat	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	98	*ortho*-Toluidine	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
F	99	Painter, occupational exposure	Human	Lung	Lung	Lung	10	Respiratory system	2	0	1	0	1
F	99	Painter, occupational exposure	Human	Mesothelioma	Mesothelium	Mesothelium	12	Mesothelium	3	0	1	0	1
F	99	Painter, occupational exposure	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	1	0	1
F	100	2,3,4,7,8-Pentachlorodibenzofuran	Human	Not specified						0	7	1	0
F	101	Rubber manufacturing industry	Human	Lung	Lung	Lung	10	Respiratory system	2	0	1	0	1
F	101	Rubber manufacturing industry	Human	Stomach	Stomach	Stomach	15	Digestive tract	4	0	1	0	1
F	101	Rubber manufacturing industry	Human	Urinary bladder	Urothelium (renal pelvis, ureter, urinary bladder)	Urothelium	27	Urothelium	9	0	1	0	1
F	101	Rubber manufacturing industry	Human	Leukaemia	Haematopoietic tissue	Haematopoietic tissue	28	Lymphoid and haematopoietic tissues	10	0	1	0	1
F	101	Rubber manufacturing industry	Human	Lymphoma	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	0	1	0	1
F	102	Shale oils	Human	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	102	Shale oils	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1

Suplemental Table 2. Database of Animal and Human Tumour Sites for 111 Distinct Group-1 Agents through Volume 109 of the IARC Monographs													
Volume	Agent Number	Agent Name	Species	Site	Anatomical Site	Anatomical Site Label	Anatomical Site Number	Organ System	Organ System Number	Animal Tumour Site Specified	Reason for Lack of Animal Data*	Mechanistic Upgrade	Human Tumour Site Specified
F	103	Soot (as found in occupational exposure of chimney sweeps)	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	103	Soot (as found in occupational exposure of chimney sweeps)	Human	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	103	Soot (as found in occupational exposure of chimney sweeps)	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	104	Sulfur mustard	Human	Lung	Lung	Lung	10	Respiratory system	2	0	6	0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Rat	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Lymphoid tissue	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Thymus	Lymphoid tissue	Lymphoid tissue	29	Lymphoid and haematopoietic tissues	10	1		0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Skin	Skin and adnexae	Skin and adnexae	30	Skin	11	1		0	1
F	105	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Human	All cancers combined	All cancers combined	All cancers combined	43	Other groupings	15	1		0	1
F	106	Vinyl chloride	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
F	106	Vinyl chloride	Human	Hepatocellular carcinoma	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	106	Vinyl chloride	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
F	106	Vinyl chloride	Mouse	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
F	106	Vinyl chloride	Rat	Soft tissue	Soft connective tissue	Soft connective tissue	32	Connective tissues	12	1		0	1
F	106	Vinyl chloride	Human	Angiosarcoma of the liver	Blood vasculature (endothelium)	Blood vasculature	33	Connective tissues	12	1		0	1
F	106	Vinyl chloride	Mouse	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
F	106	Vinyl chloride	Rat	Mammary gland	Breast	Breast	35	Female breast, female reproductive organs and reproductive tract	13	1		0	1
F	106	Vinyl chloride	Rat	Zymbal gland	Exocrine glands NOS	Exocrine glands NOS	47	Other groupings	15	1		0	1
105	107	Engine Exhaust, diesel	Human	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
105	107	Engine Exhaust, diesel	Rat	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
106	108	Trichloroethylene	Mouse	Lung	Lung	Lung	10	Respiratory system	2	1		0	1
106	108	Trichloroethylene	Mouse	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
106	108	Trichloroethylene	Human	Kidney	Kidney	Kidney	26	Kidney	8	1		0	1
106	108	Trichloroethylene	Rat	Kidney	Kidney	Kidney	26	Kidney	8	1		0	1
107	109	Polychlorinated biphenyls	Rat	Oral cavity	Oral cavity	Oral cavity	3	Upper aerodigestive tract	1	1		0	1
107	109	Polychlorinated biphenyls	Rat	Liver	Liver parenchyma and bile ducts	Liver	17	Digestive organs	5	1		0	1
107	109	Polychlorinated biphenyls	Human	Skin (melanoma)	Cutaneous melanocytes	Cutaneous melanocytes	31	Skin	11	1		0	1
109	110	Outdoor air pollution	Human	Lung	Lung	Lung	10	Respiratory system	2	0	7	0	1
109	111	Particulate matter in outdoor air pollution	Human	Lung	Lung	Lung	10	Respiratory system	2	0	7	0	1
***Reasons for Lack of Animal Data: 1 - Occupational exposure not replicable in laboratory; 2 - Used in combination with no data on mixture; 3 - Animal models problematic due to species-specificity 4 - Animal tests inadequate; 5 - No animal data available; 6 - Limited evidence in animals ; 7 - Sufficient evidence in animals, but no site specified**													

Supplemental Table 3. Data Dictionary for the Anatomically-based Tumour Site Concordance Database

Data Element	Description	Coding
Volume	IARC Monographs Volume from which the data were abstracted	100A, 100B, 100C, 100D, 100E, 100F, 105, 106, 107, 109
Agent Number	Number assigned to agents listed in alphabetical order (see Table 1)	1, 2,…,111
Agent Name	Name of the agent as listed in the IARC Monographs	
Species	Species from which the data were derived	Human, Rat, Mouse, Hamster, Dog, Monkey, Baboon
Site	The tumour site, as abstracted from the IARC Monographs (see Table 1)	
Anatomical Site	Coding of the tumour site into an anatomical site based on The Organ and Tumour Site Nomenclature Table	See Table 3
Anatomical Site Number	Number assigned to anatomical tumour site	1, 2,…, 47(see Table 4)
Organ System	Organ and tissue system to which the anatomical tumour site belongs	See Table 3
Organ System Number	Number assigned to the organ and tissue system	1, 2,…,15 (see Table 4)
Animal Data Available	Indicator variable indicating the availability of	0- No animal data available 1- Animal data available
Reason for Lack of Animal Data	Reason for lack of sufficient evidence of carcinogenicity in animals	1-Occupational exposures are complex and likely could not be reliably replicated in the laboratory 2- Used in combination; no data available on mixture 3- Animal tests were conducted by are considered inadequate

		4-The use of animal models is problematic due to species-specificity and other limitations 5- No animal data available
Mechanistic Upgrade	Indicator variable to identify agents assigned to Group-1 on the basis of a mechanistic upgrade	0- No mechanistic upgrade 1- Mechanistic upgrade
Tumour Site Specified	Indicator variable to confirm the determination of a specific tumour site by the WG	0- No tumour site specified 1- Tumour site(s) specified

Supplemental Table 4. Numerical Coding of Anatomically-based Tumour Sites and Organ and Tissue Systems

Anatomical Site	Anatomical Site Number
Upper Aerodigestive Tract (1)	
Nasal cavity and paranasal sinuses	1
Nasopharynx	2
Oral cavity	3
Pharynx	4
Tongue	5
Tonsil	6
Salivary gland	7
Respiratory System (2)	
Trachea	8
Larynx	9
Lung	10
Lower respiratory tract	11
Mesothelium (3)	
Mesothelium	12
Digestive Tract (4)	
Digestive tract, unspecified	13
Oesophagus	14
Stomach	15
Intestine (including colon and rectum)	16
Digestive Organs (5)	
Liver parenchyma and bile ducts	17
Pancreas NOS	18
Gall bladder	19
Nervous System and Eye (6)	

Brain and spinal cord (CNS)	20
Cranial and peripheral nerves	21
Eye	22
Endocrine System (7)	
Thyroid, follicular epithelium	23
Adrenal gland (medulla, cortex, NOS)	24
Pituitary	25
Kidney (8)	
Kidney (renal cortex, renal medulla, kidney NOS)	26
Urothelium (9)	
Urothelium (renal pelvis or ureter or urinary bladder)	27
Lymphoid and Haematopoietic Tissues (10)	
Haematopoietic tissue	28
Lymphoid tissue	29
Skin (11)	
Skin and adnexae	30
Cutaneous melanocytes	31
Connective Tissues (12)	
Soft connective tissue	32
Blood vasculature (endothelium)	33
Hard connective tissue (bone, cartilage)	34
Female Breast, Female Reproductive Organs and Reproductive Tract (13)	
Breast	35
Ovary	36
Uterine cervix	37
Uterus	38
Vulva/vagina	39
Male Reproductive System (14)	

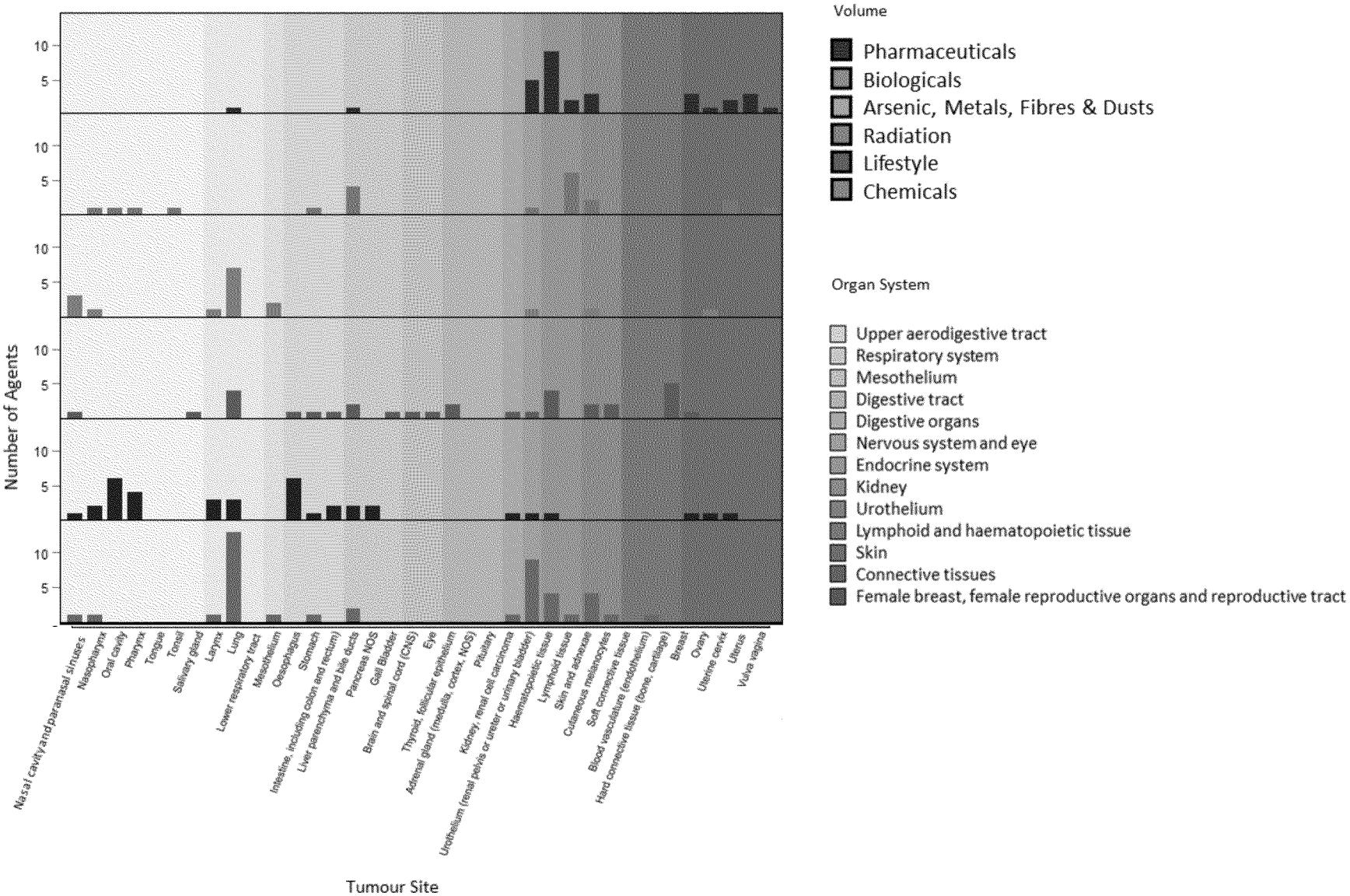
Testis, germ cells	40
Testis, specialized gonadal stroma	41
Prostate	42
Other Groupings (15)	
All cancers combined	43
All solid cancers	44
Solid cancers, aside from lung	45
Multiple or unspecified sites	46
Exocrine glands NOS	47

Supplemental Table 5. Group-1 Agents With at Least One Tumour Site Specified in Humans and in Animals (60 agents)				
Volume	Agent	Species	Tissue Site	Organ and Tissue System
A	Aristolochic acid, plants containing	Rat	Stomach	Digestive tract
A	Aristolochic acid, plants containing	Human	Urothelium	Urothelium
A	Aristolochic acid, plants containing	Rat	Urothelium	Urothelium
A	Aristolochic acid, plants containing	Human	Urothelium	Urothelium
A	Azathioprine	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
A	Azathioprine	Human	Lymphoid tissue	Lymphoid and haematopoietic tissues
A	Azathioprine	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
A	Azathioprine	Human	Skin and adnexae	Skin
A	Chlorambucil	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
A	Chlorambucil	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
A	Cyclophosphamide	Mouse	Lung	Respiratory system
A	Cyclophosphamide	Human	Urothelium	Urothelium
A	Cyclophosphamide	Rat	Urothelium	Urothelium
A	Cyclophosphamide	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
A	Cyclophosphamide	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
A	Cyclophosphamide	Mouse	Breast	Female breast, female reproductive organs and reproductive tract
A	Diethylstilbestrol	Hamster	Kidney	Kidney
A	Diethylstilbestrol	Human	Breast	Female breast, female reproductive organs and reproductive tract
A	Diethylstilbestrol	Human	Cervix	Female breast, female reproductive organs and reproductive tract
A	Diethylstilbestrol	Mouse	Cervix	Female breast, female reproductive organs and reproductive tract
A	Diethylstilbestrol	Mouse	Uterus	Female breast, female reproductive organs and reproductive tract
A	Diethylstilbestrol	Human	Vulva/vagina	Female breast, female reproductive organs and reproductive tract
A	Estrogen-only menopausal therapy	Hamster	Kidney	Kidney
A	Estrogen-only menopausal therapy	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
A	Estrogen-only menopausal therapy	Mouse	Breast	Female breast, female reproductive organs and reproductive tract
A	Estrogen-only menopausal therapy	Rat	Breast	Female breast, female reproductive organs and reproductive tract
A	Estrogen-only menopausal therapy	Human	Ovary	Female breast, female reproductive organs and reproductive tract
A	Estrogen-only menopausal therapy	Mouse	Cervix	Female breast, female reproductive organs and reproductive tract
A	Estrogen-only menopausal therapy	Human	Uterus	Female breast, female reproductive organs and reproductive tract
A	Estrogen-only menopausal therapy	Mouse	Uterus	Female breast, female reproductive organs and reproductive tract
A	Estrogen-progestogen oral contraceptives (combined)	Human	Liver	Digestive organs
A	Estrogen-progestogen oral contraceptives (combined)	Human	Breast	Female breast, female reproductive organs and reproductive tract
A	Estrogen-progestogen oral contraceptives (combined)	Human	Cervix	Female breast, female reproductive organs and reproductive tract
A	Estrogen-progestogen oral contraceptives (combined)	Rat	Breast	Female breast, female reproductive organs and reproductive tract
A	Methoxsalen in combination with UVA	Mouse	Skin and adnexae	Skin
A	Methoxsalen in combination with UVA	Human	Skin and adnexae	Skin
A	Phenacetin	Mouse	Kidney	Kidney
A	Phenacetin	Rat	Kidney	Kidney
A	Phenacetin	Human	Urothelium	Urothelium
A	Phenacetin	Rat	Urothelium	Urothelium
A	Phenacetin	Human	Urothelium	Urothelium
A	Tamoxifen	Rat	Liver	Digestive organs
A	Tamoxifen	Human	Uterus	Female breast, female reproductive organs and reproductive tract
A	Thiotepa	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
A	Thiotepa	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
B	Helicobacter pylori (infection with)	Mouse	Stomach	Digestive tract
B	Helicobacter pylori (infection with)	Human	Stomach	Digestive tract
B	Helicobacter pylori (infection with)	Human	Lymphoid tissue	Lymphoid and haematopoietic tissues
C	Arsenic and inorganic arsenic compounds	Human	Lung	Respiratory system
C	Arsenic and inorganic arsenic compounds	Mouse	Lung	Respiratory system
C	Arsenic and inorganic arsenic compounds	Mouse	Liver	Digestive organs
C	Arsenic and inorganic arsenic compounds	Human	Urothelium	Urothelium
C	Arsenic and inorganic arsenic compounds	Rat	Urothelium	Urothelium
C	Arsenic and inorganic arsenic compounds	Human	Skin and adnexae	Skin
C	Asbestos (all forms)	Human	Larynx	Respiratory system
C	Asbestos (all forms)	Human	Lung	Respiratory system
C	Asbestos (all forms)	Rat	Lung	Respiratory system
C	Asbestos (all forms)	Human	Mesothelium	Mesothelium
C	Asbestos (all forms)	Baboon	Mesothelium	Mesothelium
C	Asbestos (all forms)	Hamster	Mesothelium	Mesothelium
C	Asbestos (all forms)	Rat	Mesothelium	Mesothelium
C	Asbestos (all forms)	Human	Ovary	Female breast, female reproductive organs and reproductive tract
C	Beryllium and beryllium compounds	Human	Lung	Respiratory system
C	Beryllium and beryllium compounds	Rat	Lung	Respiratory system
C	Cadmium and cadmium compounds	Human	Lung	Respiratory system
C	Cadmium and cadmium compounds	Rat	Lung	Respiratory system
C	Cadmium and cadmium compounds	Rat	Soft connective tissue	Connective tissues
C	Chromium (VI) compounds	Rat	Oral cavity	Upper aerodigestive tract
C	Chromium (VI) compounds	Rat	Tongue	Upper aerodigestive tract
C	Chromium (VI) compounds	Human	Lung	Respiratory system
C	Chromium (VI) compounds	Rat	Lung	Respiratory system
C	Chromium (VI) compounds	Mouse	Intestine	Digestive tract
C	Chromium (VI) compounds	Mouse	Intestine	Digestive tract
C	Chromium (VI) compounds	Mouse	Intestine	Digestive tract
C	Chromium (VI) compounds	Mouse	Intestine	Digestive tract
C	Chromium (VI) compounds	Rat	Soft connective tissue	Connective tissues
C	Erionite	Human	Mesothelium	Mesothelium
C	Erionite	Rat	Mesothelium	Mesothelium
C	Nickel compounds	Human	Nasal cavity	Upper aerodigestive tract
C	Nickel compounds	Human	Lung	Respiratory system
C	Nickel compounds	Rat	Lung	Respiratory system

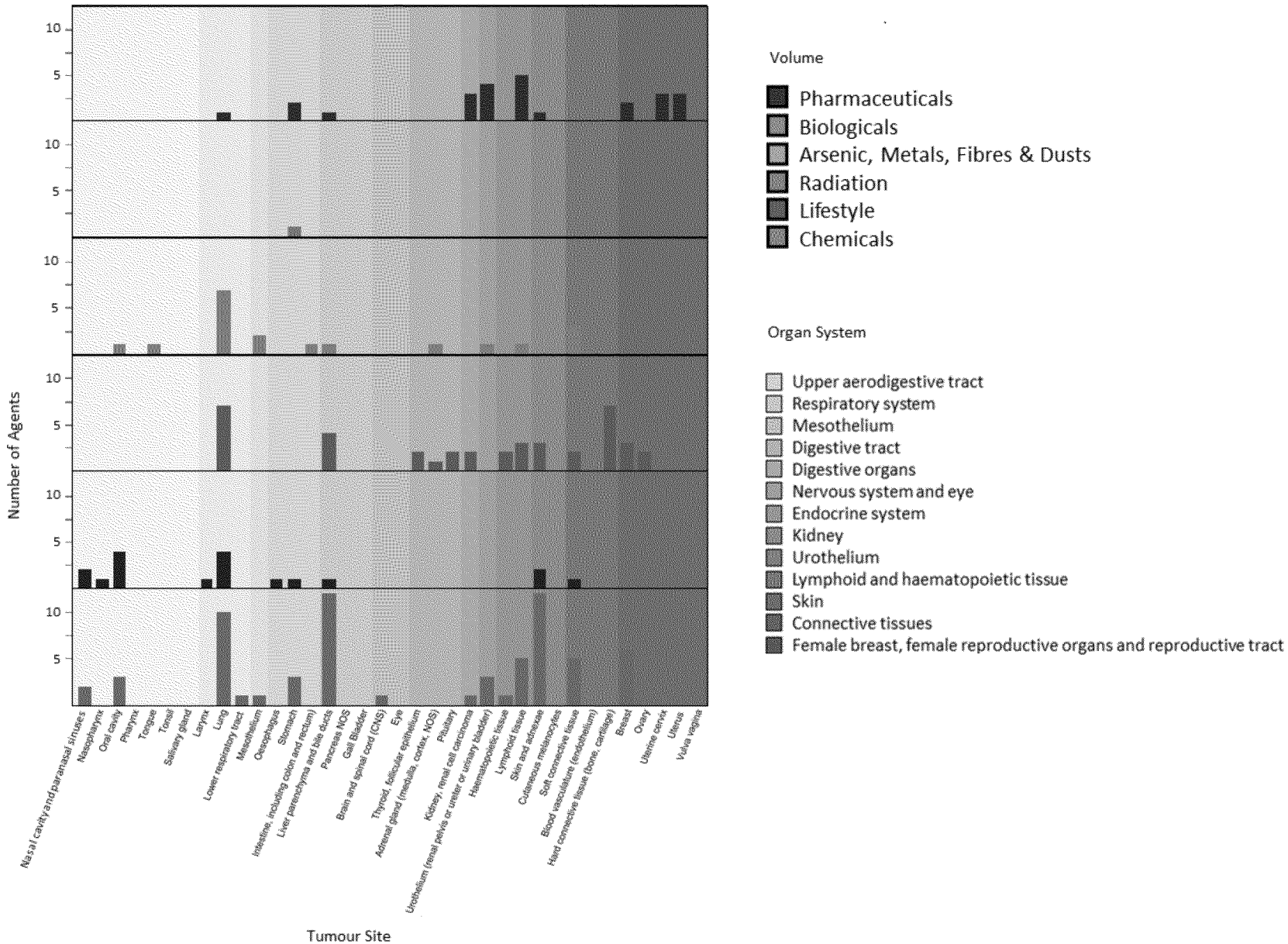
Supplemental Table 5. Group-1 Agents With at Least One Tumour Site Specified in Humans and in Animals (60 agents)				
Volume	Agent	Species	Tissue Site	Organ and Tissue System
C	Nickel compounds	Rat	Adrenal gland	Endocrine system
C	Nickel compounds	Hamster	Soft connective tissue	Connective tissues
C	Nickel compounds	Mouse	Soft connective tissue	Connective tissues
C	Nickel compounds	Rat	Soft connective tissue	Connective tissues
C	Silica dust, crystalline, in the form of quartz or cristobalite	Human	Lung	Respiratory system
C	Silica dust, crystalline, in the form of quartz or cristobalite	Rat	Lung	Respiratory system
C	Silica dust, crystalline, in the form of quartz or cristobalite	Rat	Lymphoid tissue	Lymphoid and haematopoietic tissues
D	Fission products including Sr-90	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
D	Fission products including Sr-90	Dog	Hard connective tissue	Connective tissues
D	Fission products including Sr-90	Mouse	Hard connective tissue	Connective tissues
D	Fission products including Sr-90	Human	All solid cancers	Other groupings
D	Haematite mining with exposure to radon (underground)	Human	Lung	Respiratory system
D	Haematite mining with exposure to radon (underground)	Rat	Lung	Respiratory system
D	Pu-239	Dog	Lung	Respiratory system
D	Pu-239	Human	Lung	Respiratory system
D	Pu-239	Rat	Lung	Respiratory system
D	Pu-239	Dog	Liver	Digestive organs
D	Pu-239	Human	Liver	Digestive organs
D	Pu-239	Human	Hard connective tissue	Connective tissues
D	Pu-239	Dog	Hard connective tissue	Connective tissues
D	Pu-239	Mouse	Hard connective tissue	Connective tissues
D	Pu-239	Rat	Hard connective tissue	Connective tissues
D	Radioiodines, including I-131	Human	Thyroid	Endocrine system
D	Radioiodines, including I-131	Mouse	Thyroid	Endocrine system
D	Radioiodines, including I-131	Rat	Thyroid	Endocrine system
D	Ra-224 and its decay products	Human	Hard connective tissue	Connective tissues
D	Ra-224 and its decay products	Dog	Hard connective tissue	Connective tissues
D	Ra-224 and its decay products	Mouse	Hard connective tissue	Connective tissues
D	Ra-226 and its decay products	Human	Nasal cavity	Upper aerodigestive tract
D	Ra-226 and its decay products	Human	Hard connective tissue	Connective tissues
D	Ra-226 and its decay products	Human	Hard connective tissue	Connective tissues
D	Ra-226 and its decay products	Dog	Hard connective tissue	Connective tissues
D	Ra-226 and its decay products	Mouse	Hard connective tissue	Connective tissues
D	Ra-228 and its decay products	Human	Hard connective tissue	Connective tissues
D	Ra-228 and its decay products	Dog	Hard connective tissue	Connective tissues
D	Rn-222 and its decay products	Human	Lung	Respiratory system
D	Rn-222 and its decay products	Rat	Lung	Respiratory system
D	Solar radiation	Mouse	Skin and adnexae	Skin
D	Solar radiation	Rat	Skin and adnexae	Skin
D	Solar radiation	Human	Skin and adnexae	Skin
D	Solar radiation	Human	Cutaneous melanocytes	Skin
D	Th-232 (as Thorotrast)	Human	Liver	Digestive organs
D	Th-232 (as Thorotrast)	Hamster	Liver	Digestive organs
D	Th-232 (as Thorotrast)	Human	Liver	Digestive organs
D	Th-232 (as Thorotrast)	Rat	Liver	Digestive organs
D	Th-232 (as Thorotrast)	Human	Gall bladder	Digestive organs
D	Th-232 (as Thorotrast)	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
D	UV-emitting tanning devices	Human	Eye	Nervous system and eye
D	UV-emitting tanning devices	Mouse	Skin and adnexae	Skin
D	UV-emitting tanning devices	Human	Cutaneous melanocytes	Skin
D	X- and Gamma radiation	Human	Salivary gland	Upper aerodigestive tract
D	X- and Gamma radiation	Human	Lung	Respiratory system
D	X- and Gamma radiation	Mouse	Lung	Respiratory system
D	X- and Gamma radiation	Human	Oesophagus	Digestive tract
D	X- and Gamma radiation	Human	Stomach	Digestive tract
D	X- and Gamma radiation	Human	Intestine	Digestive tract
D	X- and Gamma radiation	Mouse	Liver	Digestive organs
D	X- and Gamma radiation	Human	CNS	Nervous system and eye
D	X- and Gamma radiation	Human	Thyroid	Endocrine system
D	X- and Gamma radiation	Rat	Thyroid	Endocrine system
D	X- and Gamma radiation	Mouse	Pituitary	Endocrine system
D	X- and Gamma radiation	Human	Kidney	Kidney
D	X- and Gamma radiation	Monkey	Kidney	Kidney
D	X- and Gamma radiation	Human	Urothelium	Urothelium
D	X- and Gamma radiation	Mouse	Haematopoietic tissue	Lymphoid and haematopoietic tissues
D	X- and Gamma radiation	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
D	X- and Gamma radiation	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
D	X- and Gamma radiation	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
D	X- and Gamma radiation	Human	Skin and adnexae	Skin
D	X- and Gamma radiation	Mouse	Soft connective tissue	Connective tissues
D	X- and Gamma radiation	Human	Hard connective tissue	Connective tissues
D	X- and Gamma radiation	Human	Breast	Female breast, female reproductive organs and reproductive tract
D	X- and Gamma radiation	Mouse	Breast	Female breast, female reproductive organs and reproductive tract
D	X- and Gamma radiation	Rat	Breast	Female breast, female reproductive organs and reproductive tract
D	X- and Gamma radiation	Mouse	Ovary	Female breast, female reproductive organs and reproductive tract
D	X- and Gamma radiation	Mouse	Exocrine glands NOS	Other groupings
E	Alcoholic beverages	Human	Oral cavity	Upper aerodigestive tract
E	Alcoholic beverages	Rat	Oral cavity	Upper aerodigestive tract
E	Alcoholic beverages	Human	Pharynx	Upper aerodigestive tract
E	Alcoholic beverages	Human	Larynx	Respiratory system
E	Alcoholic beverages	Human	Oesophagus	Digestive tract

Supplemental Table 5. Group-1 Agents With at Least One Tumour Site Specified in Humans and in Animals (60 agents)				
Volume	Agent	Species	Tissue Site	Organ and Tissue System
E	Alcoholic beverages	Human	Intestine	Digestive tract
E	Alcoholic beverages	Human	Liver	Digestive organs
E	Alcoholic beverages	Human	Breast	Female breast, female reproductive organs and reproductive tract
E	Betel quid without tobacco	Human	Oral cavity	Upper aerodigestive tract
E	Betel quid without tobacco	Human	Oesophagus	Digestive tract
E	Betel quid without tobacco	Hamster	Stomach	Digestive tract
E	Coal, indoor emissions from household combusion of	Human	Lung	Respiratory system
E	Coal, indoor emissions from household combusion of	Mouse	Lung	Respiratory system
E	Coal, indoor emissions from household combusion of	Mouse	Skin and adnexae	Skin
E	Salted fish, chinese style	Rat	Nasal cavity	Upper aerodigestive tract
E	Salted fish, chinese style	Rat	Nasal cavity	Upper aerodigestive tract
E	Salted fish, chinese style	Rat	Nasopharynx	Upper aerodigestive tract
E	Salted fish, chinese style	Human	Nasopharynx	Upper aerodigestive tract
E	Second-hand tobacco smoke	Human	Lung	Respiratory system
E	Second-hand tobacco smoke	Mouse	Lung	Respiratory system
E	Tobacco smoking	Human	Nasal cavity	Upper aerodigestive tract
E	Tobacco smoking	Human	Nasal cavity	Upper aerodigestive tract
E	Tobacco smoking	Human	Nasopharynx	Upper aerodigestive tract
E	Tobacco smoking	Human	Oral cavity	Upper aerodigestive tract
E	Tobacco smoking	Human	Pharynx	Upper aerodigestive tract
E	Tobacco smoking	Human	Larynx	Respiratory system
E	Tobacco smoking	Human	Lung	Respiratory system
E	Tobacco smoking	Hamster	Larynx	Respiratory system
E	Tobacco smoking	Mouse	Lung	Respiratory system
E	Tobacco smoking	Rat	Lung	Respiratory system
E	Tobacco smoking	Human	Oesophagus	Digestive tract
E	Tobacco smoking	Human	Stomach	Digestive tract
E	Tobacco smoking	Human	Intestine	Digestive tract
E	Tobacco smoking	Human	Liver	Digestive organs
E	Tobacco smoking	Human	Liver	Digestive organs
E	Tobacco smoking	Human	Pancreas	Digestive organs
E	Tobacco smoking	Human	Kidney	Kidney
E	Tobacco smoking	Human	Urothelium	Urothelium
E	Tobacco smoking	Human	Urothelium	Urothelium
E	Tobacco smoking	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
E	Tobacco smoking	Mouse	Skin and adnexae	Skin
E	Tobacco smoking	Human	Ovary	Female breast, female reproductive organs and reproductive tract
E	Tobacco smoking	Human	Cervix	Female breast, female reproductive organs and reproductive tract
E	Tobacco, smokeless	Rat	Oral cavity	Upper aerodigestive tract
E	Tobacco, smokeless	Human	Oral cavity	Upper aerodigestive tract
E	Tobacco, smokeless	Rat	Oral cavity	Upper aerodigestive tract
E	Tobacco, smokeless	Human	Oesophagus	Digestive tract
E	Tobacco, smokeless	Human	Pancreas	Digestive organs
F	Aflatoxins	Human	Liver	Digestive organs
F	Aflatoxins	Rat	Liver	Digestive organs
F	4-Aminobiphenyl	Mouse	Liver	Digestive organs
F	4-Aminobiphenyl	Dog	Urothelium	Urothelium
F	4-Aminobiphenyl	Human	Urothelium	Urothelium
F	4-Aminobiphenyl	Mouse	Soft connective tissue	Connective tissues
F	Benzene	Rat	Oral cavity	Upper aerodigestive tract
F	Benzene	Mouse	Lung	Respiratory system
F	Benzene	Rat	Stomach	Digestive tract
F	Benzene	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
F	Benzene	Mouse	Haematopoietic tissue	Lymphoid and haematopoietic tissues
F	Benzene	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
F	Benzene	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
F	Benzene	Rat	Skin and adnexae	Skin
F	Benzene	Mouse	Breast	Female breast, female reproductive organs and reproductive tract
F	Benzene	Mouse	Exocrine glands NOS	Other groupings
F	Benzene	Mouse	Exocrine glands NOS	Other groupings
F	Benzene	Rat	Exocrine glands NOS	Other groupings
F	Benzidine	Mouse	Liver	Digestive organs
F	Benzidine	Human	Urothelium	Urothelium
F	Benzidine	Rat	Breast	Female breast, female reproductive organs and reproductive tract
F	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Rat	Nasal cavity	Upper aerodigestive tract
F	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Human	Lung	Respiratory system
F	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Mouse	Skin and adnexae	Skin
F	Bis(chloromethyl)ether; chloromethyl methyl ether (technical-grade)	Mouse	Soft connective tissue	Connective tissues
F	1,3-Butadiene	Mouse	Lung	Respiratory system
F	1,3-Butadiene	Mouse	Stomach	Digestive tract
F	1,3-Butadiene	Mouse	Liver	Digestive organs
F	1,3-Butadiene	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
F	1,3-Butadiene	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
F	1,3-Butadiene	Mouse	Soft connective tissue	Connective tissues
F	1,3-Butadiene	Mouse	Breast	Female breast, female reproductive organs and reproductive tract
F	1,3-Butadiene	Mouse	Exocrine glands NOS	Other groupings
F	1,3-Butadiene	Mouse	Exocrine glands NOS	Other groupings
F	Coal gasification	Human	Lung	Respiratory system
F	Coal gasification	Mouse	Skin and adnexae	Skin
F	Coal-tar distillation	Human	Skin and adnexae	Skin
F	Coal-tar distillation	Mouse	Skin and adnexae	Skin

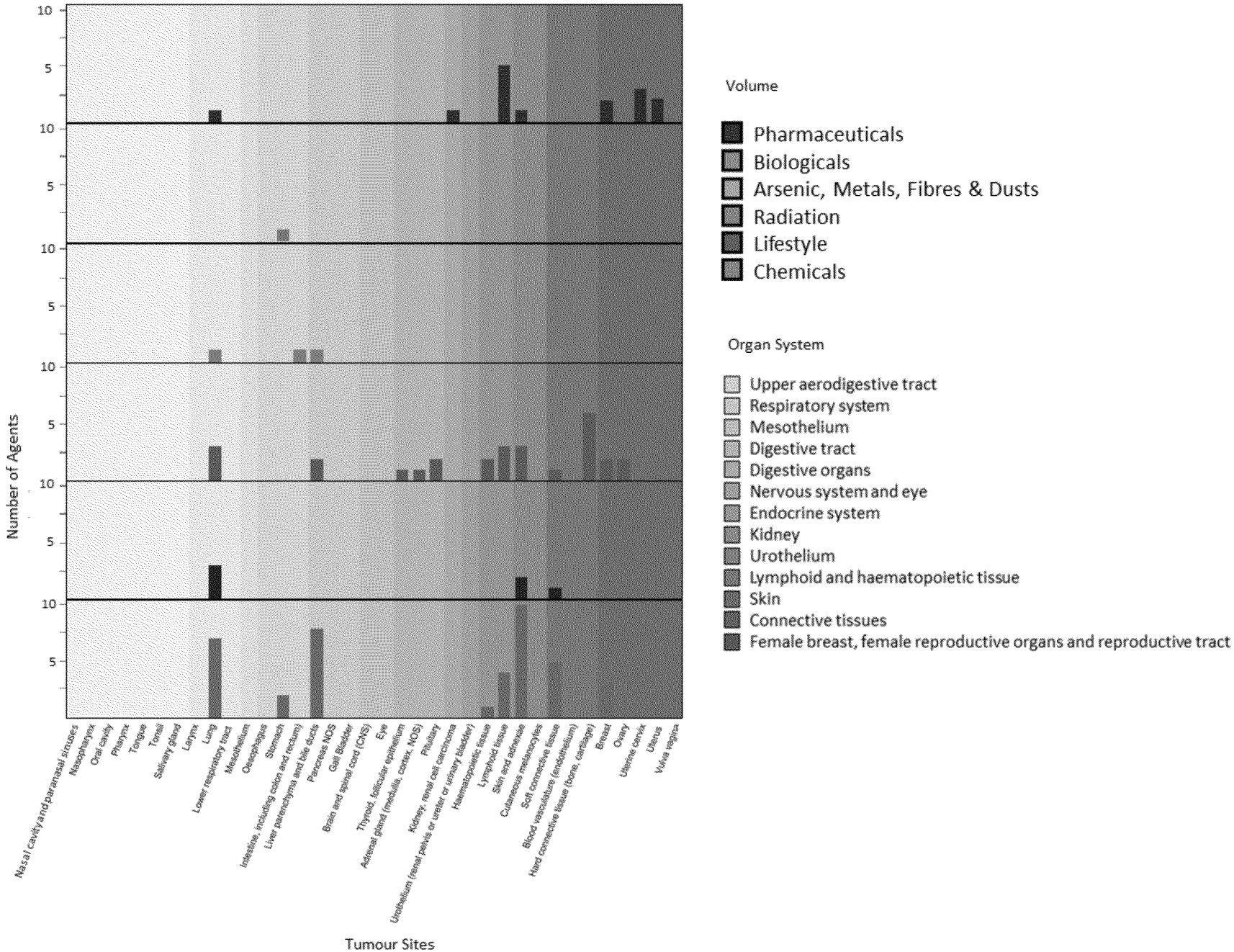
Supplemental Table 5. Group-1 Agents With at Least One Tumour Site Specified in Humans and in Animals (60 agents)				
Volume	Agent	Species	Tissue Site	Organ and Tissue System
F	Coal-tar pitch	Human	Lung	Respiratory system
F	Coal-tar pitch	Mouse	Skin and adnexae	Skin
F	Coke production	Human	Lung	Respiratory system
F	Coke production	Mouse	Lung	Respiratory system
F	Coke production	Rat	Lung	Respiratory system
F	Coke production	Mouse	Skin and adnexae	Skin
F	Formaldehyde	Rat	Nasal cavity	Upper aerodigestive tract
F	Formaldehyde	Human	Nasopharynx	Upper aerodigestive tract
F	Formaldehyde	Human	Haematopoietic tissue	Lymphoid and haematopoietic tissues
F	Mineral oils, untreated or mildly treated	Human	Skin and adnexae	Skin
F	Mineral oils, untreated or mildly treated	Mouse	Skin and adnexae	Skin
F	2-Naphthylamine	Mouse	Liver	Digestive organs
F	2-Naphthylamine	Dog	Urothelium	Urothelium
F	2-Naphthylamine	Hamster	Urothelium	Urothelium
F	2-Naphthylamine	Human	Urothelium	Urothelium
F	2-Naphthylamine	Monkey	Urothelium	Urothelium
F	2-Naphthylamine	Rat	Urothelium	Urothelium
F	ortho-Toluidine	Human	Urothelium	Urothelium
F	ortho-Toluidine	Rat	Urothelium	Urothelium
F	ortho-Toluidine	Rat	Skin and adnexae	Skin
F	ortho-Toluidine	Mouse	Soft connective tissue	Connective tissues
F	Shale oils	Human	Skin and adnexae	Skin
F	Shale oils	Mouse	Skin and adnexae	Skin
F	Soot (as found in occupational exposure of chimney sweeps)	Human	Lung	Respiratory system
F	Soot (as found in occupational exposure of chimney sweeps)	Human	Skin and adnexae	Skin
F	Soot (as found in occupational exposure of chimney sweeps)	Mouse	Skin and adnexae	Skin
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Rat	Oral cavity	Upper aerodigestive tract
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Rat	Lung	Respiratory system
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Liver	Digestive organs
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Rat	Liver	Digestive organs
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Lymphoid tissue	Lymphoid and haematopoietic tissues
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Mouse	Skin and adnexae	Skin
F	2,3,7,8-Tetrachlorodibenzo-para-dioxin	Human	All cancers combined	Other groupings
F	Vinyl chloride	Mouse	Lung	Respiratory system
F	Vinyl chloride	Human	Liver	Digestive organs
F	Vinyl chloride	Rat	Liver	Digestive organs
F	Vinyl chloride	Mouse	Soft connective tissue	Connective tissues
F	Vinyl chloride	Rat	Soft connective tissue	Connective tissues
F	Vinyl chloride	Human	Blood vasculature	Connective tissues
F	Vinyl chloride	Mouse	Breast	Female breast, female reproductive organs and reproductive tract
F	Vinyl chloride	Rat	Breast	Female breast, female reproductive organs and reproductive tract
F	Vinyl chloride	Rat	Exocrine glands NOS	Other groupings
F	Engine Exhaust, diesel	Human	Lung	Respiratory system
F	Engine Exhaust, diesel	Rat	Lung	Respiratory system
F	Trichloroethylene	Mouse	Lung	Respiratory system
F	Trichloroethylene	Mouse	Liver	Digestive organs
F	Trichloroethylene	Human	Kidney	Kidney
F	Trichloroethylene	Rat	Kidney	Kidney
F	Polychlorinated biphenyls	Rat	Oral cavity	Upper aerodigestive tract
F	Polychlorinated biphenyls	Rat	Liver	Digestive organs
F	Polychlorinated biphenyls	Human	Cutaneous melanocytes	Skin



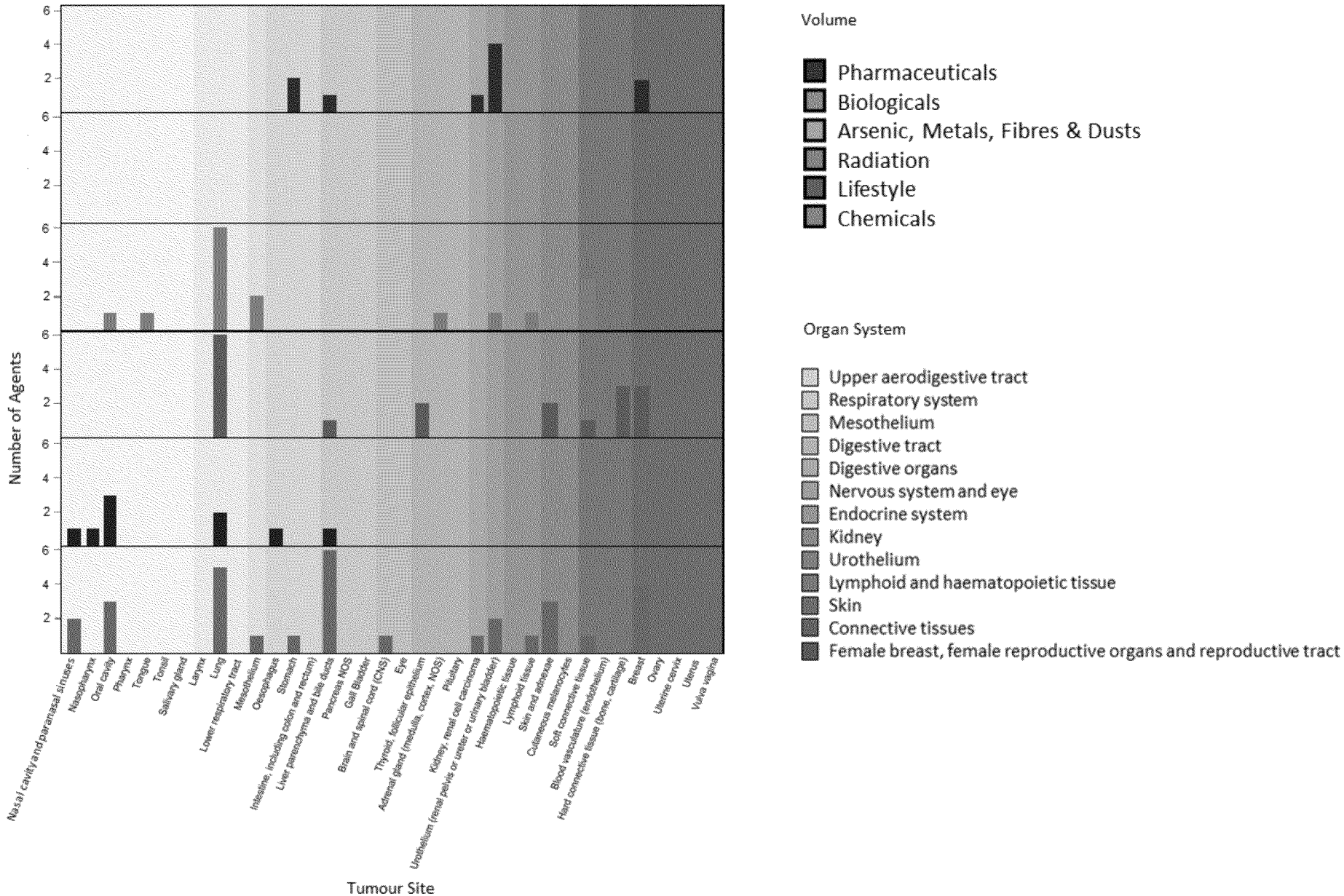
Supplemental Figure 1: Number of Agents Inducing Tumours in Humans in Each of 39 Tumour Sites by Type of Agent



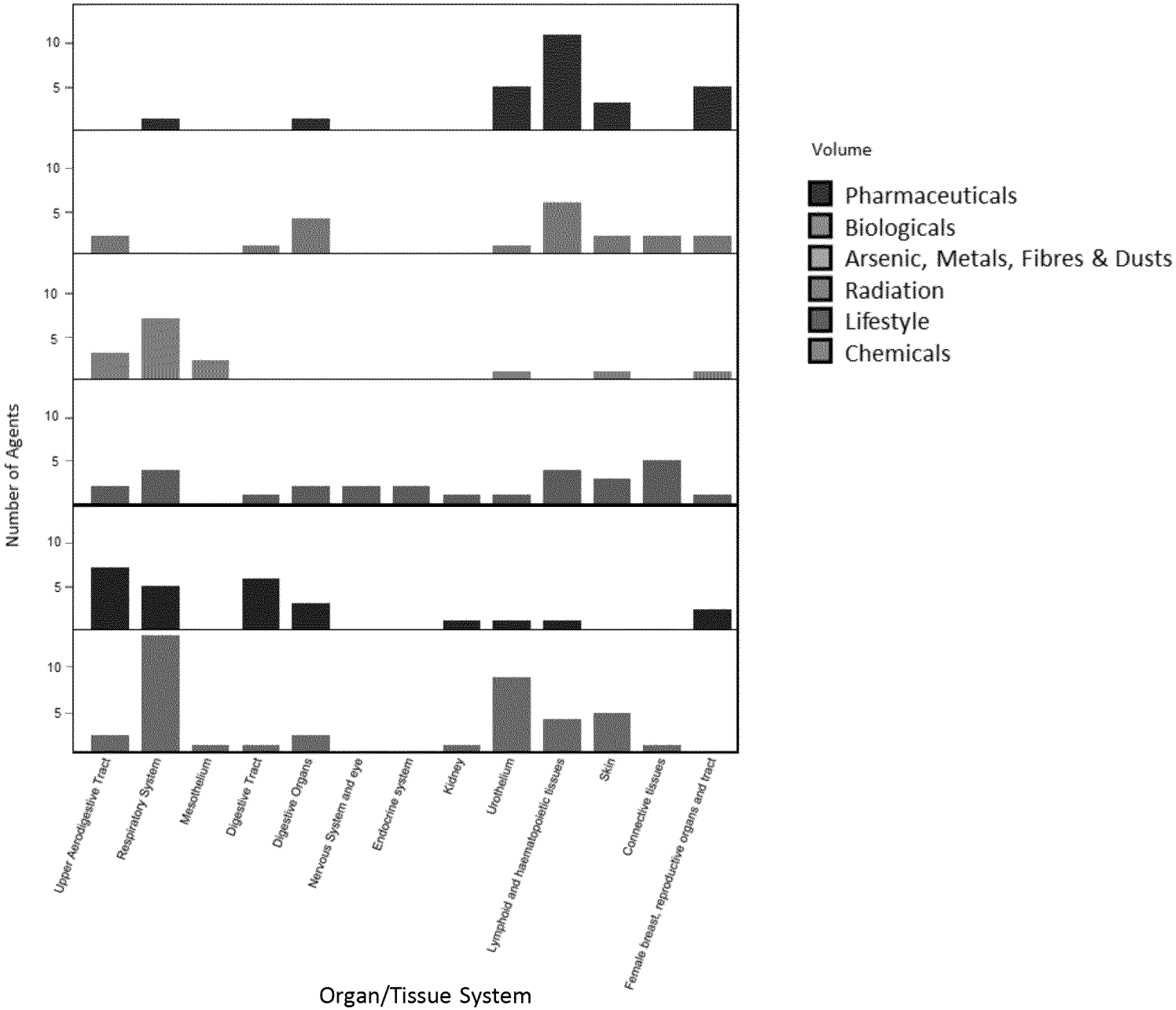
Supplemental Figure 2: Number of Agents Inducing Tumours in Animals in Each of 39 Tumour Sites by Type of Agent



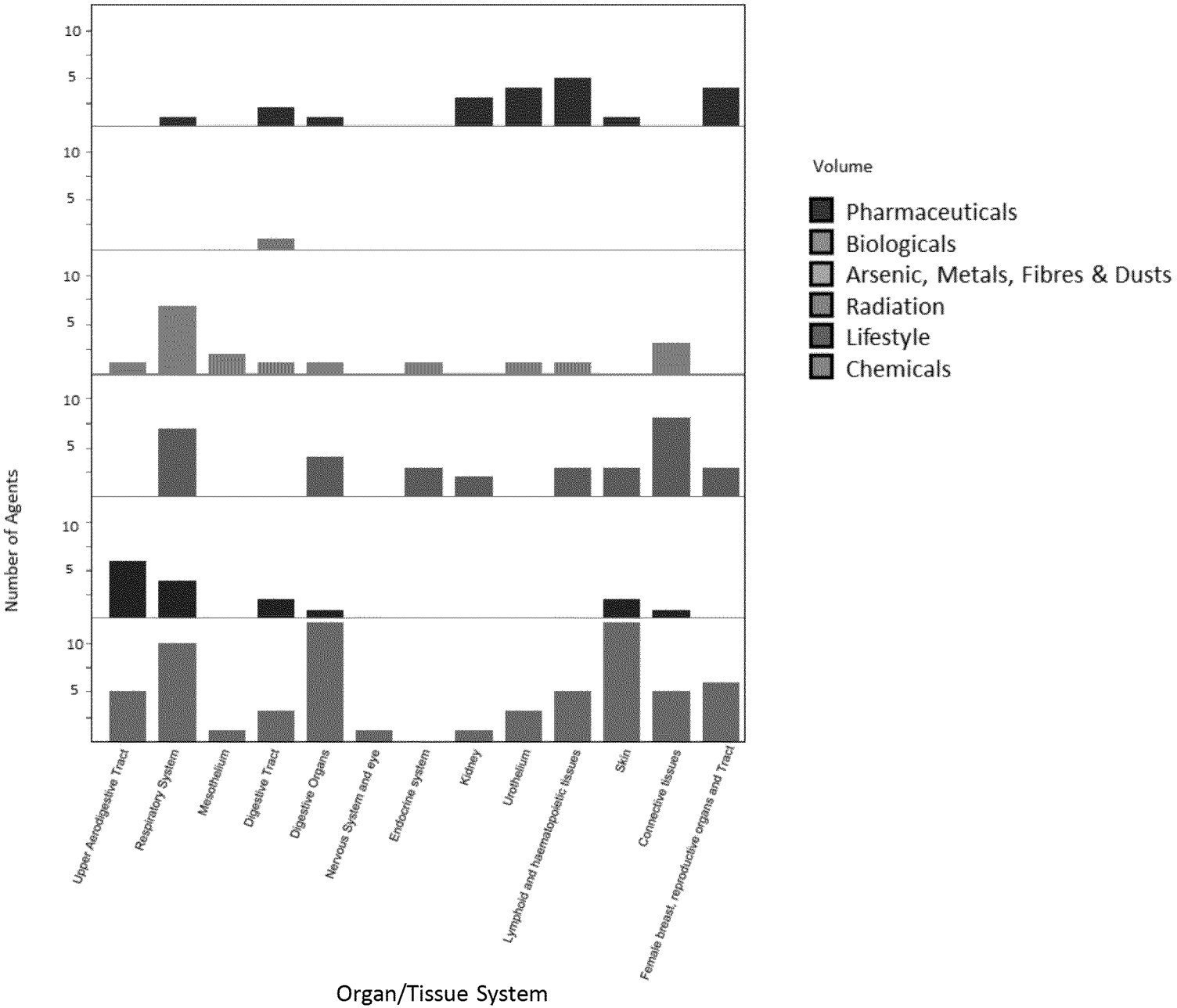
Supplemental Figure 3: Number of Agents Inducing Tumours in Mice in Each of 39 Tumour Sites by Type of Agent



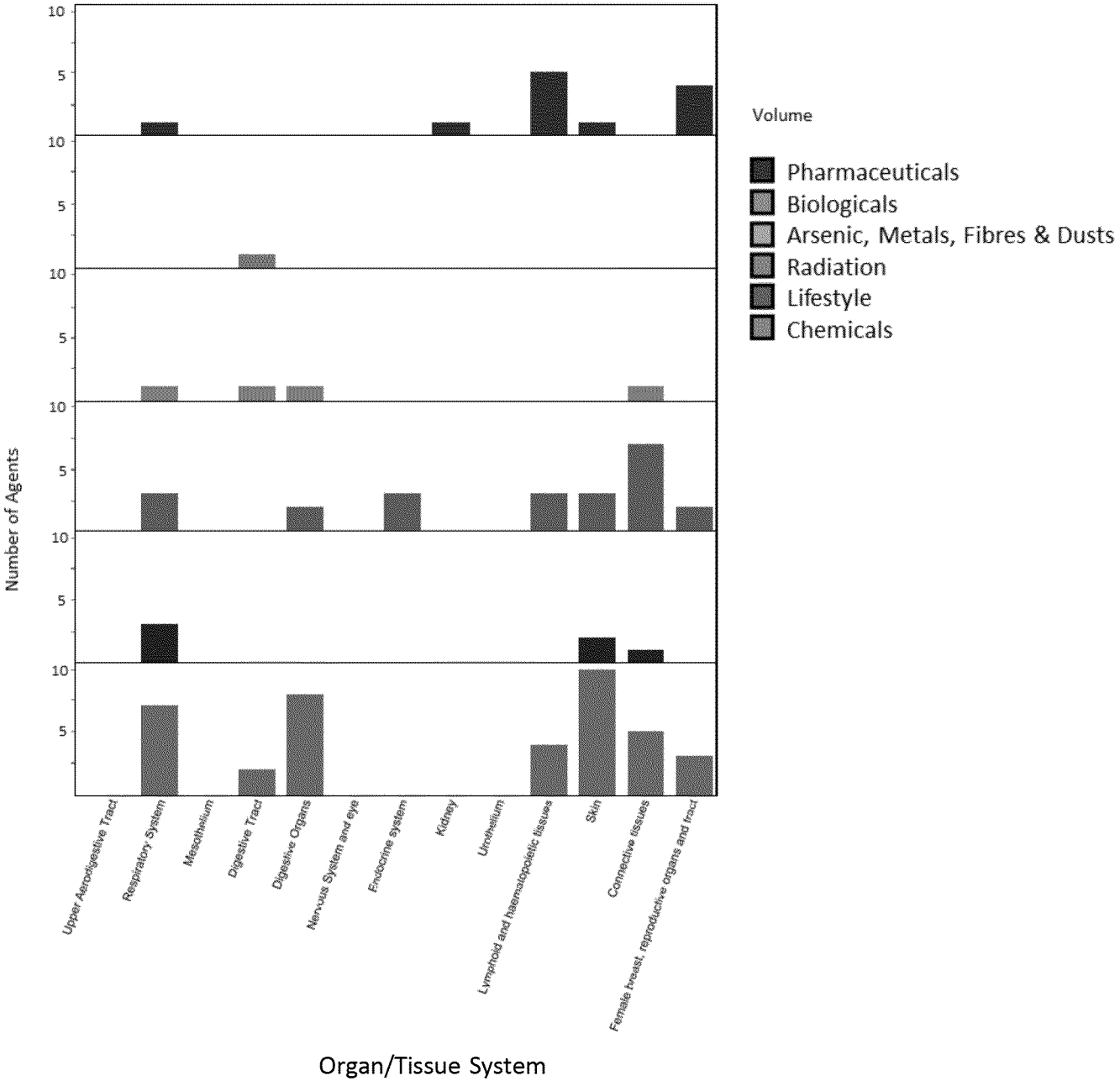
Supplemental Figure 4: Number of Agents Inducing Tumours in Rats in Each of 39 Tumour Sites by Type of Agent



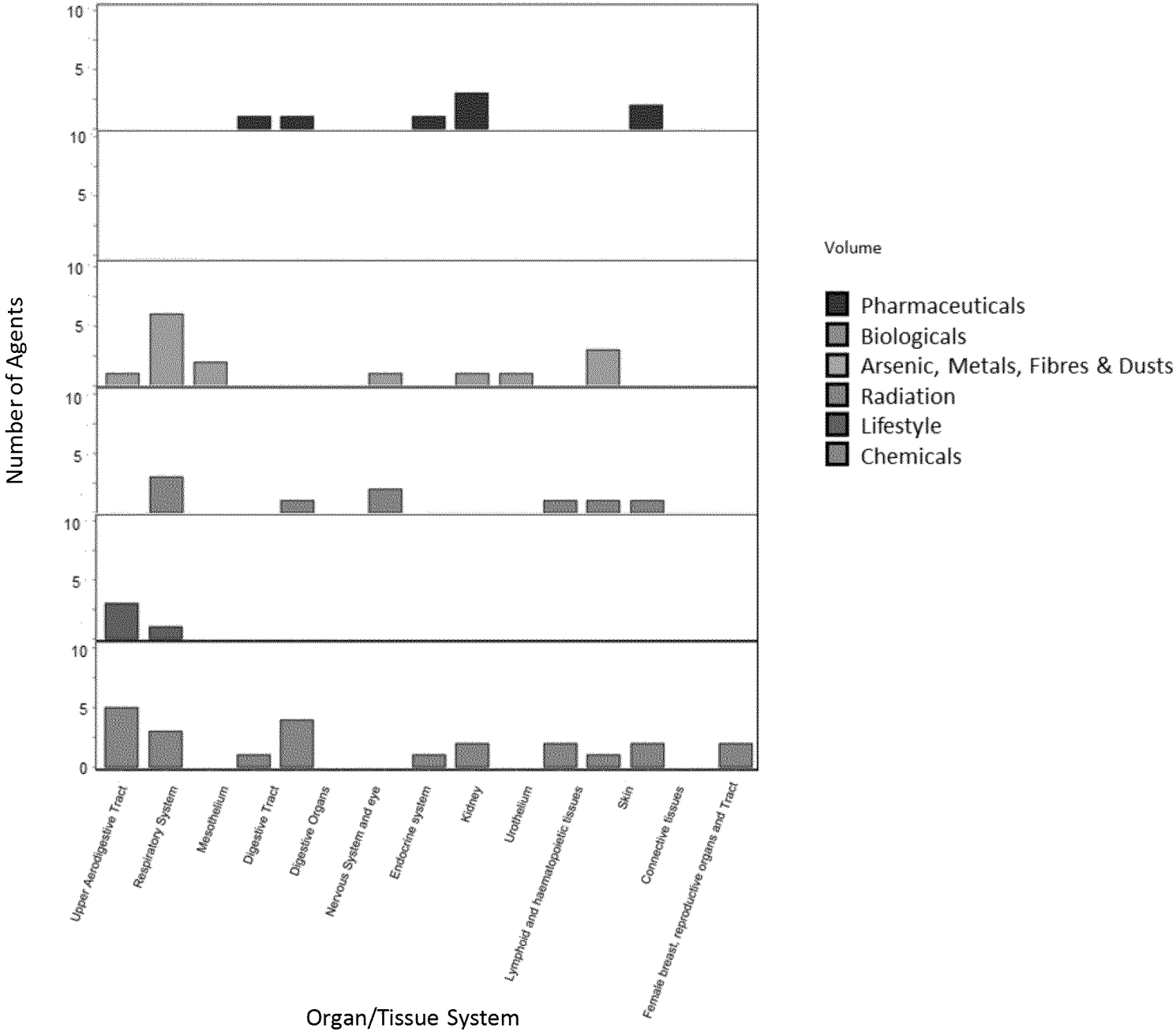
Supplemental Figure 5: Number of Agents Inducing Tumours in Humans in Each of 15 Organ/Tissue Systems by Type of Agent



Supplemental Figure 6: Number of Agents Inducing Tumours in Animals in Each of 15 Organ/Tissue Systems by Type of Agent



Supplemental Figure 7: Number of Agents Inducing Tumours in Mice in Each of 15 Organ/Tissue Systems by Type of Agent



Supplemental Figure 8: Number of Agents Inducing Tumours in Rats in Each of 15 Organ/Tissue Systems by Type of Agent

Concordance between Animal and Human Tumours: An Analysis of 111 Agents Known to Cause Cancer in Humans

Supplemental Material I: Statistical Measures of Concordance between Animal and Human Tumours

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on behalf of the IARC Working Group on 'Tumour-site Concordance and Mechanisms of Carcinogenesis' which convened in Lyon April/November 2012

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Krewski et al. (2016) conducted a comprehensive analysis of the concordance between tumours seen in animals and humans for 111 distinct Group-1 agents identified in the IARC Monographs programme through Volume 109, based on information abstracted from the IARC Monographs by Grosse et al. (2016). Concordance analysis was based on the 60 agents with sufficient evidence of carcinogenicity both in humans and in animals, with at least one tumour site specified for humans and at least one tumour site specified for animals. For simplicity of presentation, analysis of concordance were based on the overlap between tumour sites expressed in animals and humans (Krewski et al., 2016, Table 7, Figure 9).

Concordance between animal and human tumour sites is based on the overlap between animal and human tumour sites, as shown in Supplemental Table 6 (all animals) and Supplemental Table 7 (mice and rats). Let N_h, N_a, and N_b denote the number of agents demonstrating a particular tumour site in humans, animals, or both humans and animals, respectively. The total number of agents demonstrating tumours at this site is then $N_t=N_h+N_a-N_b$. Concordance is measured by the percentage overlap, calculated as (N_b/N_t)x100%. These results are shown in the column headed 'overlap' in Supplemental Tables 6 and 7. [The 'overlap' results in Supplemental Table 6 are the basis of the evaluation of concordance in Table 7 of Krewski et al. (2016)]

The WG was also interested in the overlap between agents demonstrating tumours in animals at a particular site with agents demonstrating tumours in humans at that site, calculated as (N_b/N_h)x100%. These results are shown in the column headed 'animal/human overlap' in Supplemental Tables 6 and 7, and reflect the percentage of agents demonstrating tumours at the site of interest in humans that have also been seen to cause tumours at that site in animals. [The 'animal/human overlap' results in

Supplemental Table 6 are the basis of the analysis of overlap between animal and human tumours in Panel A of Figure 9 in Krewski et al. (2016).]

Conversely, the 'human/animal overlap' column in Supplementary Tables 6 and 7, calculated as (N_b/N_a)x100%, reflects the percentage of agents demonstrating tumours at the site of interest in animals that have also been seen to cause tumours at that site in humans. [The 'human/animal overlap' results in Supplemental Table 6 are the basis of the analysis of overlap between human and animal tumours in Panel B of Figure 9 in Krewski et al. (2016).]

More formal statistical analyses of concordance may be based on a comparison of animal and human tumours summarized in the form of the following 2x2 table.

	Humans		
Animals	Positive	Negative	Total
Positive	N_{11}	N_{12}	$N_{1.}$
Negative	N_{21}	N_{22}	$N_{2.}$
Total	$N_{.1}$	$N_{.1}$	N_t

Here, N_{11} denotes the number of agents for which the tumour site of interest was observed in both animals and humans, N_{22} denotes the number of agents for which the tumour site was seen in neither animals nor humans, N_{21} denotes the number of agents positive in humans and negative in animals, and N_{12} denotes the number of agents positive in animals and negative in humans. The total number of agents is given by $N_t = N_{11} + N_{22} + N_{12} + N_{21}$.

A simple, intuitive measure of overall concordance used by Gold et al. (1989) is the proportion positive in both species, (N_{11}/N_t), plus the proportion negative in both species, (N_{22}/N_t), defined by

$$\rho = ((N_{11}+N_{22})/N_t).$$

The value of ρ ranges from 0 to 1, where ρ=0 and ρ=1 reflect perfect discordance and perfect concordance, respectively. Concordance can also be measured using the kappa (κ) statistic discussed by Viera & Garrett (2005), defined by

$$\kappa = (N_o-N_e)/(N_t-N_e),$$

where N_o and N_e denote the observed and expected total counts along the diagonal of the 2 x 2 matrix, with $N_o = N_{11}+N_{22}$ and $N_e = (N_{1.}N_{.1}/N_t) + (N_{2.}N_{.2}/N_t)$. This statistic measures concordance as slight (0.01-0.20), fair (0.21-0.40), moderate (0.41-0.60), substantial (0.61-0.80), and almost perfect (0.81-0.99). Values of $\kappa < 0$ correspond to less than chance agreement (Viera & Garrett, 2005). Since these two concordance measures are related by the formula

$$\kappa = (N_t\rho - N_e)/(N_t-N_e),$$

they provide equivalent information on concordance, albeit on a different scale of measurement.

Although the above statistical measures of concordance were considered by the Working Group (WG), the simpler measures of concordance in Supplemental Table 6 (all animals) and Supplemental Table 7 (mice and rats) were used as the basis for evaluating concordance between animal and human tumour sin the present analysis.

References

Gold,L.S., Bernstein,L., Magaw,R., & Slone,T.H. (1989) Interspecies extrapolation in carcinogenesis: prediction between rats and mice. *Environ.Health Perspect.*, **81**, 211-219.

Krewski et al. (2016). Concordance between Animal and Human Tumours: An Analysis of 111 Agents Known to Cause Cancer in Humans. [This volume.]

Viera, A.J. & Garrett, J.M. (2005). Understanding interobserver agreement: the Kappa statistic. *Family Medicine* 37: 360-363.

List of Tables

Supplemental Table 6. Concordance between Tumours seen in Humans and Animals for 60 Group-1 Agents by Organ and Tissue System/Tumour Site

Organ and Tissue System (Organ System No.)[1] *Tissue Site (Anatomical Site No.)* [1]	Humans	Animals[2]	Both	Overlap (%)[3]	Animal/Human Overlap (%)[4]	Human/Animal Overlap (%)[5]
Upper Aerodigestive Tract (1)	9	9	4	28.6	44.4	44.4
Nasal cavity and paranasal sinuses (1)	3	3	0	0.0	0.0	0.0
Nasopharynx (2)	3	1	1	33.3	33.3	100.0
Oral cavity (3)	4	6	2	25.0	50.0	33.3
Pharynx (4)	2	0	0	N/A	N/A	N/A
Tongue (5)	0	1	0	N/A	N/A	N/A
Salivary gland (7)	1	0	0	N/A	N/A	N/A
Respiratory System (2)	21	22	16	59.3	76.2	72.7
Larynx (9)	3	1	1	33.3	33.3	100.0
Lung (10)	20	22	16	61.5	80.0	72.7
Mesothelium (3)	2	2	2	100.0	100.0	100.0
Mesothelium (12)	2	2	2	100.0	100.0	100.0
Digestive Tract (4)	6	6	2	20.0	33.3	33.3
Oesophagus (14)	5	0	0	N/A	N/A	N/A
Stomach (15)	3	5	1	14.3	33.3	20.0
Intestine (including colon and rectum) (16)	3	1	0	0.0	0.0	0.0
Digestive Organs (5)	8	14	4	22.2	50.0	28.6
Liver parenchyma and bile ducts (17)	7	14	4	23.5	57.1	28.6
Pancreas NOS (18)	2	0	0	N/A	N/A	N/A
Gall bladder (19)	1	0	0	N/A	N/A	N/A
Nervous System and Eye (6)	2	0	0	N/A	N/A	N/A
Brain and spinal cord (CNS) (20)	1	0	0	N/A	N/A	N/A
Eye (22)	1	0	0	N/A	N/A	N/A
Endocrine System (7)	2	3	2	66.7	100.0	66.7
Thyroid, follicular epithelium (23)	2	2	2	100.0	100.0	100.0
Adrenal gland (medulla, cortex, NOS) (24)	0	1	0	N/A	N/A	N/A
Pituitary (25)	0	1	0	N/A	N/A	N/A
Kidney (8)	3	5	2	33.3	66.7	40.0
Kidney (renal cortex, renal medulla, kidney NOS) (26)	3	5	2	33.3	66.7	40.0
Urothelium (9)	10	7	7	70.0	70.0	100.0
Urothelium (renal pelvis or ureter or urinary bladder) (27)	10	7	7	70.0	70.0	100.0
Lymphoid and Haematopoietic Tissues (10)	12	10	7	46.7	58.3	70.0
Haematopoietic tissue (28)	10	2	2	20.0	20.0	100.0
Lymphoid tissue (29)	2	10	1	9.1	50.0	10.0
Skin (11)	11	16	7	35.0	63.6	43.8
Skin and adnexae (30)	9	16	6	31.6	66.7	37.5
Cutaneous melanocytes (31)	3	0	0	N/A	N/A	N/A
Connective Tissues (12)	6	14	6	42.9	100.0	42.9
Soft connective tissue (32)	0	9	0	N/A	N/A	N/A
Blood vasculature (endothelium) (33)	1	0	0	N/A	N/A	N/A
Hard connective tissue (bone, cartilage) (34)	5	5	4	66.7	80.0	80.0
Female Breast, Female Reproductive Organs and Reproductive Tract (13)	8	9	4	30.8	50.0	44.4
Breast (35)	4	7	1	10.0	25.0	14.3
Ovary (36)	3	1	0	0.0	0.0	0.0
Uterine cervix (37)	3	3	2	50.0	66.7	66.7
Uterus (38)	2	3	1	25.0	50.0	33.3
Vulva/vagina (39)	1	0	0	N/A	N/A	N/A
Other Groupings (15)	2	4	0	0.0	0.0	0.0
All cancers combined (43)	1	0	0	N/A	N/A	N/A
All solid cancers (44)	1	0	0	N/A	N/A	N/A
Exocrine glands NOS (47)	0	4	0	N/A	N/A	N/A

[1] Systems/sites in the anatomcially based tumour nomenclature system (see Supplemental Tables 1 and 4) lacking sufficient evidence in both humans and animals not shown. (For example, there was insufficient evidence of tumours of the male reportuctive tract in both humans and animals.)

[2] 'Animals' includes mice, rats, monkeys, dogs, and hamsters

[3] Percentage overlap calculated as $(N_b/(N_h+N_a-N_b))$x100%, where N_h, N_a, and N_b denote the number of agents with sufficient evidence in humans, animals, or both humans and animals, respectively.

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N/A: Calculation of overlap not possible when no agents demonstrate the tumour site of interest in either humans or animals (or both).

Supplemental Table 7. Concordance between Tumours seen in Humans and Rodents for 60 Group-1 Agents by Organ and Tissue System/Tumour Site

Organ and Tissue System (Organ System No.)[1] *Tissue Site (Anatomical Site No.)*[1]	Humans	Rodents[2]	Both	Overlap (%)[3]	Animal/Human Overlap (%)[4]	Human/Animal Overlap (%)[5]
Nasal cavity and paranasal sinuses (1)	3	3	0	0.0	0.0	0.0
Nasopharynx (2)	3	1	1	33.3	33.3	100.0
Oral cavity (3)	4	6	2	25.0	50.0	33.3
Pharynx (4)	2	0	0	N/A	N/A	N/A
Tongue (5)	0	1	0	N/A	N/A	N/A
Salivary gland (7)	1	0	0	N/A	N/A	N/A
Respiratory System (2)	21	22	16	59.3	76.2	72.7
Larynx (9)	3	0	0	0.0	0.0	N/A
Lung (10)	20	22	16	61.5	80.0	72.7
Mesothelium (3)	2	2	2	100.0	100.0	100.0
Mesothelium (12)	2	2	2	100.0	100.0	100.0
Digestive Tract (4)	6	5	1	10.0	16.7	20.0
Oesophagus (14)	5	0	0	N/A	N/A	N/A
Stomach (15)	3	4	1	16.7	33.3	25.0
Intestine (including colon and rectum) (16)	3	1	0	0.0	0.0	0.0
Digestive Organs (5)	8	13	3	16.7	37.5	23.1
Liver parenchyma and bile ducts (17)	7	13	3	17.6	42.9	23.1
Pancreas NOS (18)	2	0	0	N/A	N/A	N/A
Gall bladder (19)	1	0	0	N/A	N/A	N/A
Nervous System and Eye (6)	2	0	0	N/A	N/A	N/A
Brain and spinal cord (CNS) (20)	1	0	0	N/A	N/A	N/A
Eye (22)	1	0	0	N/A	N/A	N/A
Endocrine System (7)	2	3	2	66.7	100.0	66.7
Thyroid, follicular epithelium (23)	2	2	2	100.0	100.0	100.0
Adrenal gland (medulla, cortex, NOS) (24)	0	1	0	N/A	N/A	N/A
Pituitary (25)	0	1	0	N/A	N/A	N/A
Kidney (8)	3	2	1	25.0	33.3	50.0
Kidney (renal cortex, renal medulla, kidney NOS) (26)	3	2	1	25.0	33.3	50.0
Urothelium (9)	10	6	6	60.0	60.0	100.0
Urothelium (renal pelvis or ureter or urinary bladder) (27)	10	6	6	60.0	60.0	100.0
Lymphoid and Haematopoietic Tissues (10)	12	10	7	46.7	58.3	70.0
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Hard connective tissue (bone, cartilage) (34)	5	4	3	50.0	60.0	75.0
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All cancers combined (43)	1	0	0	N/A	N/A	N/A
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Cc: Cogliano, Vincent[cogliano.vincent@epa.gov]; dkrewski@uottawa.ca[dkrewski@uottawa.ca]
From: Bernard Stewart
Sent: Tue 7/12/2016 4:30:52 AM
Subject: RE: Consensus statement Vol100WS

Dear all.

I am completely happy to have no change made concerning designation of the group engaged in Mechanism and Concordance deliberations. Rather than reflecting in any way on this particular group, I thought I was making a simple technical correction.

I had the impression that groups convened to make evaluations in the context of a particular volume of Monographs were 'Working Groups'. I had the impression, based on Advisory Groups in relation to Priorities for 2015-19 and Quantitative risk characterization, that groups convened for purposes other than making Monograph evaluations were designated as Advisory Groups.

Beyond those considerations, I was not seeking to reflect on the authority or character of the present Group. So, no problem with leaving terminology as proposed.

Regards

Bernard.

From: Kurt Straif [mailto:StraifK@iarc.fr]
Sent: Tuesday, 12 July 2016 2:23 AM
To: Robert Baan <BaanR@visitors.iarc.fr>; Bernard Stewart <Bernard.Stewart@health.nsw.gov.au>; Vincent Cogliano <cogliano.vincent@gmail.com>
Cc: Vincent Cogliano <cogliano.vincent@epa.gov>; Daniel Krewski <dkrewski@uottawa.ca>
Subject: RE: Consensus statement Vol100WS

Dear all,

I am not in favour of post-hoc calling this an AG, I support Roberts approach,

Kurt

From: Robert Baan
Sent: 11 July 2016 15:43
To: Bernard Stewart <Bernard.Stewart@health.nsw.gov.au>; Vincent Cogliano <cogliano.vincent@gmail.com>; Kurt Straif <StraifK@iarc.fr>
Cc: Vincent Cogliano <cogliano.vincent@epa.gov>; Daniel Krewski <dkrewski@uottawa.ca>
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I myself have been using the term 'Workshop participants'. Please advice.

I also drafted some text by way of Introduction to the consensus document.

I value comments,

Robert

From: Bernard Stewart <Bernard.Stewart@health.nsw.gov.au>
Sent: Monday, July 11, 2016 10:32 AM
To: Vincent Cogliano; Kurt Straif; Robert Baan
Cc: Vincent Cogliano
Subject: RE: Consensus statement Vol100WS

Greetings to all from 'down under' with Sydney gripped by winter; at 6am it was 7°C.

I take this opportunity to join others and offer my own congratulations to you, Vincent, in creating a meaningful statement.

It seemed prudent to delay my own input till other matters had been addressed. In the attached, I adopted all previous track changes in order to have a manageable text into which I have inserted a few suggestions. Obviously adopt, modify or discard as thought best.

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And Portugal did it in extra time.

Warmest regards

Bernard.

From: Vincent Cogliano [mailto:cogliano.vincent@gmail.com]
Sent: Sunday, 10 July 2016 6:35 AM
To: Kurt Straif <StraifK@iarc.fr>; BaanR@visitors.iarc.fr; Bernard Stewart <Bernard.Stewart@health.nsw.gov.au>
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ALLEZ LES BLEUS !!!

Vincent

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Date: July 8, 2016 at 10:15:10 EDT
To: Robert Baan <BaanR@visitors.iarc.fr>, "Cogliano, Vincent" <cogliano.vincent@epa.gov>
Cc: Bernard Stewart <Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU>
Subject: RE: Consensus statement Vol100WS

Fine with me,

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PS As always, I'm for the underdogs, Portugal!

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Dear Kurt, Bernard, Vincent,

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Bon weekend!

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From: Kurt Straif
Sent: Wednesday, July 6, 2016 10:04 AM
To: Cogliano, Vincent
Cc: Bernard Stewart; Robert Baan
Subject: RE: Consensus statement Vol100WS

Dear Vincent,

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Please see some additional edits and comments – I think we are zeroing in on a clean draft to be shared with the v100+ WG.

Perhaps this should best come from Robert?

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From: Cogliano, Vincent [mailto:cogliano.vincent@epa.gov]
Sent: 05 July 2016 15:49
To: Robert Baan <BaanR@visitors.iarc.fr>
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To: Cogliano, Vincent <cogliano.vincent@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>
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Views expressed in this message are those of the individual sender, and are not necessarily the views of NSW Health or any of its entities.

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Cc: Kurt Straif[StraifK@iarc.fr]; Bernard Stewart[Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU]
From: Daniel Krewski
Sent: Sun 7/10/2016 5:55:21 PM
Subject: RE: Consensus statement Vol100WS

Vincent, I've read through the draft consensus statement, and very much like the way you've kept the draft consensus at a sufficiently high level, that should serve to promote endorsement by the WG, but also sufficiently detailed so as to provide useful guidance to future Monograph Working Groups on enhanced reporting of their findings.

I also like the examples you have included in the draft, such as noting the absence of malignant melanoma in rats and mice in support of (dis)concordance between animal and human tumour sites.

The endorsement of the anatomically based tumour site concordance system to permit future comparisons between animal and human tumour sites will be welcomed by those who worked with Jerry Rice though multiple iterations of this system to achieve consensus.

Only one minor editorial suggestion on Consensus Statement 3: suggest change 'in 15 organ systems' to 'in 15 organ and tissue systems', as not all of the systems are strictly speaking organ systems.

I'm in Lyon all this week, and would be happy to participate in further discussion on this excellent draft consensus statement if that would be helpful . . .

Dan K.

From: Cogliano, Vincent [mailto:cogliano.vincent@epa.gov]
Sent: July-05-16 9:49 AM
To: Robert Baan <BaanR@visitors.iarc.fr>
Cc: Kurt Straif <StraifK@iarc.fr>; Bernard Stewart <Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU>; Daniel Krewski <dkrewski@uottawa.ca>
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Cc: Cogliano, Vincent[cogliano.vincent@epa.gov]
From: Kurt Straif
Sent: Sat 7/9/2016 8:54:00 PM
Subject: RE: Consensus statement Vol100WS

Thank you, Vincent!

Allez les Portugais,

Kurt

From: Vincent Cogliano [mailto:cogliano.vincent@gmail.com]
Sent: 09 July 2016 22:35
To: Kurt Straif <StraifK@iarc.fr>; Robert Baan <BaanR@visitors.iarc.fr>; Bernard.Stewart@sesiahs.health.nsw.gov.au Stewart <Bernard.Stewart@sesiahs.health.nsw.gov.au>
Cc: Vincent Cogliano <cogliano.vincent@epa.gov>
Subject: Re: Consensus statement Vol100WS

Hello everyone--I agree with Robert's plan. Yes/No, then Go! Attached are some more edits based on the additional comments sent last week by Kurt. I'm OK with all comments and changes, so you can convert the attached redline to a clean copy, then send to the Working Group. It might be best for it to come from Robert. He'll get better compliance than if it came from anyone else.

ALLEZ LES BLEUS !!!

Vincent

formally approved use.

To: Robert Baan[BaanR@visitors.iarc.fr]; Cogliano, Vincent[cogliano.vincent@epa.gov]
Cc: Bernard Stewart[Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU]
From: Kurt Straif
Sent: Fri 7/8/2016 2:15:10 PM
Subject: RE: Consensus statement Vol100WS

Fine with me,

Kurt

PS As always, I'm for the underdogs, Portugal!

From: Robert Baan
Sent: 08 July 2016 16:06
To: Kurt Straif <StraifK@iarc.fr>; Cogliano, Vincent <cogliano.vincent@epa.gov>
Cc: Bernard Stewart <Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU>
Subject: Consensus statement Vol100WS

Dear Kurt, Bernard, Vincent,

Dan Krewski has kept the 30-June deadline for submitting the final version of his chapters.

I will do my best to send the Concordance and Mechanistic Analyses, Yann's Concordance Data Set, and the Consensus Statement to all the participants this weekend, asking their approval. As we cannot engage in lengthy discussions about comments from 30+ participants, I propose that we ask for a Yes/No answer.

May I assume that you generally agree with this plan.

Bon weekend!

Robert

ALLEZ LES BLEUS!!

(there is a chance that France will win the European Soccer Championship this coming Sunday!)

From: Kurt Straif
Sent: Wednesday, July 6, 2016 10:04 AM
To: Cogliano, Vincent
Cc: Bernard Stewart; Robert Baan
Subject: RE: Consensus statement Vol100WS

Dear Vincent,

Thank you for swift turn-around of the revised summary conclusions.

Please see some additional edits and comments – I think we are zeroing in on a clean draft to be shared with the v100+ WG.

Perhaps this should best come from Robert?

Kurt

From: Cogliano, Vincent [mailto:cogliano.vincent@epa.gov]
Sent: 05 July 2016 15:49
To: Robert Baan <BaanR@visitors.iarc.fr>
Cc: Kurt Straif <StraifK@iarc.fr>; Bernard Stewart <Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU>; dkrewski@uottawa.ca
Subject: RE: Consensus statement Vol100WS

Dear Robert et al—Attached is a revised set of possible consensus statements. Several have been revised, and there are three new statements.

I stayed away from factual descriptive statements that are covered well in Dan's papers (for example, lung cancer is the most common site and genotoxicity by far the most common key characteristic). Dan's papers cover these points well, and it saves the consensus statement for overarching principles and insights from the Advisory Group.

There are also responses to Kurt's queries in comments on his comments.

Thanks again, everyone, and I hope we can wrap this up soon in a couple of calls.

Vincent

From: Robert Baan [mailto:BaanR@visitors.iarc.fr]
Sent: Thursday, June 23, 2016 10:00 AM
To: Cogliano, Vincent <cogliano.vincent@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>
Cc: Kurt Straif <StraifK@iarc.fr>; Bernard Stewart <Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU>; dkrewski@uottawa.ca
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I hope you can give this priority on your 'to-do' list.

Best wishes,

Robert

To: Kurt Straif[StraifK@iarc.fr]; Cogliano, Vincent[cogliano.vincent@epa.gov]
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To: Cogliano, Vincent <cogliano.vincent@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>
Cc: Kurt Straif <StraifK@iarc.fr>; Bernard Stewart <Bernard.Stewart@SESIAHS.HEALTH.NSW.GOV.AU>; dkrewski@uottawa.ca
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Best wishes,

Robert

To: Kurt Straif[StraifK@iarc.fr]
Cc: pinfante@starpower.net[pinfante@starpower.net]; Cogliano, Vincent[cogliano.vincent@epa.gov]
From: Goldstein, Bernard D
Sent: Mon 6/6/2016 1:19:59 PM
Subject: RE: Is there a forthcoming IARC meeting on benzene??

In that case I'm back to the original argument which is made in our poster. The overreliance on epidemiology mirrors IARC's initial delay in designating benzene as Group 1 based on the AML evidence, and does not conform to the newer IARC approach to increase reliance on mechanistic information.

Eager to talk to you about this and hope you have some time in the next few days. If I am awake after the long plane trip I hope to get to the reception tomorrow night

Bernie

From: Kurt Straif [mailto:StraifK@iarc.fr]
Sent: Monday, June 6, 2016 8:30 AM
To: Goldstein, Bernard D <bdgold@pitt.edu>
Cc: pinfante@starpower.net; Cogliano, Vincent <cogliano.vincent@epa.gov>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

This evidence can be considered and in fact has been considered in Vol 100F, but it does not elevate the cancer-site specific evidence for NHL, in your scenario this would stay at "limited" with the overall evaluation upgraded to Group 1 based on mechanistic grounds, see ethylene oxide for a similar example,

Kurt

From: Goldstein, Bernard D [mailto:bdgold@pitt.edu]
Sent: 06 June 2016 14:22
To: Kurt Straif <StraifK@iarc.fr>
Cc: pinfante@starpower.net; Cogliano, Vincent <cogliano.vincent@epa.gov>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Hi Kurt

I understand. So let me be direct.

1. Assume there were no evidence about AML,

2. Assume benzene was to be evaluated by IARC for the first time solely on whether it caused NHL,

3. In coming to its decision IARC would be able to consider the 7 studies showing lymphoma in benzene-exposed lab animals and the evidence from many studies of a genotoxic mechanism affecting circulating lymphocytes in exposed humans

4. But because benzene is already accorded Group 1 status due to its known causation of AML, this evidence cannot be considered – even though benzene's known ability to cause AML through a genotoxic mechanism affecting the common precursor to both myelocytes and lymphocytes strengthens the evidence that it causes NHL

This sounds more like a legalistic argument than one which represents the mission of IARC which you have done so much to further

Bernie

From: Kurt Straif [mailto:StraifK@iarc.fr]
Sent: Monday, June 6, 2016 3:43 AM
To: Goldstein, Bernard D <bdgold@pitt.edu>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Hi Bernard,

It is important to distinguish between a mechanistic up- (or down-)grade and a change in evaluation that may come with a re-evaluation.

Mechanistic upgrades are for overall evaluations – not separately for each cancer site (keep in mind that IARC Monographs are for hazard identification). Further, the current benzene classification in group 1 is also supported by strong mechanistic evidence (in addition to the sufficient evidence from cancer epidemiology and cancer bioassays). Therefore, what would be needed to raise NHL (or subsets) is sufficient evidence from cancer epidemiology, and Jelle Vlaanderen et al concluded in their meta-analysis "the evidence for an association with NHL is less clear".

Kurt

From: Goldstein, Bernard D [mailto:bdgold@pitt.edu]
Sent: 06 June 2016 01:03
To: Kurt Straif <StraifK@iarc.fr>
Cc: pinfante@starpower.net; Cogliano, Vincent <cogliano.vincent@epa.gov>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Hi Kurt

Thanks for the helpful reply. If I understand you correctly, if a chemical that had never been previously considered had exactly the same findings as benzene/NHL, then IARC could include the very strong mechanistic and animal data in deliberations related to assigning the compound to Group 1; but as IARC has already assigned benzene to Group 1, the mechanistic and animal data cannot be considered when IARC deliberates about benzene and NHL??

I see the basic issue as related to the theme of the conference, which is the role of IARC in cancer prevention. Perhaps it is an EU/US difference, but in the US, and elsewhere, there is a greater reliance on post-hoc litigation as a means to put industry in a preventive mode. IARC's apparent failure to use the totality of evidence related to benzene and NHL makes it harder for plaintiffs to successfully sue industry. Similarly, government priority setting for control of industry emissions is often dependent on risk assessment, which for benzene would now include estimates of its impact on ANLL but probably not NHL.

While I greatly admire European precautionary approaches to known carcinogens, the US style of adversary regulation also has merits. A recent study from England comparing EU and US success in controlling refinery benzene emissions showed not only that the US did much better, but that Germany, which arguably has the most adversarial US-style regulatory approach did best among EU countries and the UK, considered to be the epitome of EU consensus-based approaches, did the worst

http://www.academia.edu/12066779/Environmental_leadership_Comparing_regulatory_outcomes_and_industria

I hope I have misinterpreted your note. But if I have this right, there is a hole that IARC needs to close if it is to fulfill its mission of providing cancer hazard identification information on which prevention is based

Looking forward to seeing you in Lyon

Bernie

Bernard D. Goldstein, MD

Professor Emeritus and Dean Emeritus

University of Pittsburgh Graduate School of Public Health

130 Desoto St; Rm A-710

Pittsburgh PA 15261

Office: 412 648 9994

Cell: 412 417 9611

From: Kurt Straif [mailto:StraifK@iarc.fr]
Sent: Sunday, June 5, 2016 5:52 PM
To: Goldstein, Bernard D <bdgold@pitt.edu>
Cc: pinfante@starpower.net; Cogliano, Vincent <cogliano.vincent@epa.gov>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Hi Bernie,

Immediately after the 8-days and nights Monographs meeting I left for duty travel and have now tried to re-organize myself regarding all the other priorities.

Please see my comments inserted below.

Looking forward to welcome you to the conference,

Kurt

From: Goldstein, Bernard D [mailto:bdgold@pitt.edu]
Sent: 27 May 2016 17:59
To: Kurt Straif <StraifK@iarc.fr>; straif@iarc.fr
Cc: pinfante@starpower.net; Cogliano, Vincent <cogliano.vincent@epa.gov>; Hudak, Juliann Marie <jmh206@pitt.edu>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Hi Kurt

I've attached our planned poster. The key points we make supplement the valuable exchange that Peter and you and your colleagues made in print. Our basic argument is that irrespective of whether the epidemiological evidence raises to the level of sufficiency, benzene should be considered to be a known cause of NHL. Our major points are:

1. Benzene should be considered a known cause of NHL based on current IARC rules which state: IARC now considers a chemical to be a Group 1 carcinogen when there is less than sufficient evidence in humans but sufficient evidence in animals and "**strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity"** (my emphasis). While we can argue about whether the epi data is "sufficient" there can be no question about lymphoma in animals (I count seven studies and Peter counts ten). Further, with a superabundance of laboratory data on genotoxicity, and with lymphocyte chromosomal abnormalities routinely reported in the circulating lymphocytes of exposed workers there can be no question about the presence of a genotoxic mechanism relevant to humans

Mechanistic upgrades are for the overall evaluation (eg Group 1), not on a cancer-site specific level which is based on the cancer epidemiology.

(similarly, Tobacco smoking is not a group 1 for some specified 20 cancer sites and a group 4 for cancers of the endometrium).

2. The outcome of the 2009 IARC deliberations on benzene and NHL is hauntingly similar to the 1974 IARC review of benzene and AML in its overdependence on cohort-based epidemiology.

3. In 1974 there was a legitimate scientific argument about whether lymphocytic and myelocytic cells arose from the same stem cell. That argument has been settled in favor of a single precursor cell which is clearly affected by benzene in causing AML. Further, benzene has a promiscuous effect in causing multiple chromosomal abnormalities, again consistent with a causal role in NHL

4. Most disappointing is that the modification of the IARC process to include mechanistic information, on which you and Vincent (whom I have copied) and your colleagues worked so hard and so eloquently, has apparently failed in this case.

I do strongly suggest that benzene and NHL be subject to an IARC review. And I know that Peter feels strongly, as I do, in suggesting a review of workers exposed to gasoline. This is an important global issue, particularly in view of the large number of exposed workers and because it brings up some of the knotty mixture issues in relation to a known human carcinogen.

Gasoline had not been nominated for the 2014 AG on Future Priorities. I would suggest that you submit a nomination (now open at any given time, see bottom of page at http://monographs.iarc.fr/ENG/Meetings/index.php) in making your case why this needs to be re-evaluated.

Looking forward to seeing you in Lyon

Bernie

From: Kurt Straif [mailto:StraifK@iarc.fr]
Sent: Monday, May 2, 2016 5:51 AM
To: Goldstein, Bernard D <bdgold@pitt.edu>; straif@iarc.fr
Cc: pinfante@starpower.net
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Dear Bernie,

I look forward to welcoming you to the IARC conference – we all expect this will be a great meeting with lots of new science that impacts on public health and a great opportunity to welcome many friends to Lyon.

I am curious to read and discuss your poster. A new benzene Monograph has not yet been firmly scheduled.

Best wishes,

Kurt

From: Goldstein, Bernard D [mailto:bdgold@pitt.edu]
Sent: 30 April 2016 19:17

To: straif@iarc.fr
Cc: pinfante@starpower.net
Subject: Is there a forthcoming IARC meeting on benzene??

Hi Kurt

Hope all is well with you and your colleagues. As you probably know, Peter Infante and I have a poster presentation at the 50th Anniversary meeting on benzene and NHL in June. We argue that the delay in the recognition of benzene as a known cause of NHL mirrors the initial delay in the recognition of benzene as a known cause of ANLL, and fails to take into account the mechanistic evidence.

I recall there was talk of a future IARC meeting in which benzene would again be reviewed with a focus on NHL and other non-ANLL cancers. I could not find any mention of such a meeting on the IARC website. I am preparing the poster now, and if such a meeting is being scheduled by IARC I would welcome including such a statement within the poster material

Best personal regards – and I look forward to seeing you in June

Bernie

Bernard D. Goldstein, MD

Emeritus Professor and Emeritus Dean

Graduate School of Public Health

University of Pittsburgh

Rm A710 Crabtree Hall

130 De Soto St

Pittsburgh, PA 15261

Phone 412 648 9994

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To: Cogliano, Vincent[cogliano.vincent@epa.gov]; Gaudin Nicolas[gaudin@iarc.fr]
From: Kurt Straif
Sent: Thur 6/2/2016 3:46:25 PM
Subject: RE: Lancet Oncology editorial

We had the same bad surprise, we'll inquire

Kurt
From mobile

-------- Original message --------
From: "Cogliano, Vincent"
Date:02/06/2016 15:38 (GMT+01:00)
To: Kurt Straif ,Gaudin Nicolas
Subject: Fwd: Lancet Oncology editorial

Hi Kurt and Nicolas—How did this happen with TLO? ... Leaving today for Paris and looking forward to talking with you all after arriving in Lyon on Tuesday ... Warm regards, Vincent

Begin forwarded message:

From: "Flowers, Lynn" <Flowers.Lynn@epa.gov>
Date: June 2, 2016 at 08:00:20 EDT
To: "Ross, Mary" <Ross.Mary@epa.gov>, "Vogel, Dana" <Vogel.Dana@epa.gov>, "Lowit, Anna" <Lowit.Anna@epa.gov>, "Vandenberg, John" <Vandenberg.John@epa.gov>, "Cogliano, Vincent" <cogliano.vincent@epa.gov>, "McQueen, Jacqueline" <McQueen.Jacqueline@epa.gov>, "Fegley, Robert" <Fegley.Robert@epa.gov>, "Hauchman, Fred" <hauchman.fred@epa.gov>, "Kavlock, Robert" <Kavlock.Robert@epa.gov>, "Gwinn, Maureen" <gwinn.maureen@epa.gov>, "Deener, Kathleen" <Deener.Kathleen@epa.gov>, "Burke, Thomas" <Burke.Thomas@epa.gov>, "Bahadori, Tina" <Bahadori.Tina@epa.gov>, "Housenger, Jack" <Housenger.Jack@epa.gov>
Subject: Lancet Oncology editorial - When is a carcinogen not a carcinogen (talc and glyphosate)

Just came out today. Interesting read.

Lynn Flowers, PhD, DABT

Senior Science Advisor

Office of Science Policy

US EPA

Washington, DC

202-564-6293

To: Cogliano, Vincent[cogliano.vincent@epa.gov]
From: Fritz, Jason
Sent: Thur 6/2/2016 2:44:35 PM
Subject: RE: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

That sounds great, thanks Vince!

She's got friends from language school in Germany, Poland and Ibiza as well, so we'll have to see how to arrange visiting at least some of them, or they may track us down.

jf

From: Cogliano, Vincent
Sent: Thursday, June 02, 2016 10:38 AM
To: Fritz, Jason <Fritz.Jason@epa.gov>
Subject: Re: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

But we can't afford to lose you until I retire ... Seriously, though, they'll keep you busy, but you'll have late dinners and Sunday free. As she's comfortable getting around, she'll have no trouble finding interesting things to do while you work, and the train makes day trips, even to Paris, possible.

On Jun 2, 2016, at 10:30, Fritz, Jason <Fritz.Jason@epa.gov> wrote:

Thanks Vince!

And too late for my wife falling in love with Lyon, I think…she's fluent in French and German, and loves pretty much all of central and Northern Europe…☺

jf

From: Cogliano, Vincent
Sent: Thursday, June 02, 2016 10:28 AM
To: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>
Cc: Fritz, Jason <Fritz.Jason@epa.gov>; D'Amico, Louis <DAmico.Louis@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>; Subramaniam, Ravi <Subramaniam.Ravi@epa.gov>
Subject: Re: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

Yes, congratulations! If you bring your wife, don't let her fall in love with Lyon.

On Jun 2, 2016, at 09:46, Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov> wrote:

Congrats Jason! Well deserved!

Best regards,

Andrew

From: Fritz, Jason
Sent: Thursday, June 02, 2016 9:15 AM
To: D'Amico, Louis <DAmico.Louis@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Subramaniam, Ravi <Subramaniam.Ravi@epa.gov>
Subject: FW: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

My official invitation to participate on the IARC monograph vol118 next year, FYI.

Thanks,

Jason

From: IARC Monograph 118 [mailto:monograph118@iarc.fr]
Sent: Thursday, June 02, 2016 8:12 AM
To: Fritz, Jason <Fritz.Jason@epa.gov>
Subject: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

Official Invitation

***IARC Monographs* on the Evaluation of Carcinogenic Risks to Humans**

Volume 118 – 'Welding, Welding Fumes and Some Related Chemicals'

21-28 March 2017

Lyon, France

Dear Dr Fritz,

Following our prior correspondence by e-mail, we are pleased to officially invite you to participate in the *IARC Monographs* Working Group for volume 118. The Working Group will meet at the International Agency for Research on Cancer (IARC) in Lyon, France, from Tuesday 21 March 2017 9am through Tuesday 28 March 2017 6pm (Saturday included). **Your participation for the full duration of the meeting is required.**

You will receive a writing assignment shortly. Experience has shown that **on-time completion** of writing assignments and pre-meeting peer-reviews are key to the efficiency of the meeting and the ultimate quality of the *Monographs*. Accordingly, **we expect all participants to comply with the following schedule:**

01.11.2016 **Preliminary drafts and references due to IARC**

22.11.2016 **Peer-reviews due to IARC**

14.02.2017 **Revised drafts and references due to IARC**

During the 8-day *Monograph* meeting, you will be expected to take an active part in peer-reviewing and revising all drafts, and discussing and finalizing the evaluations. The entire volume is the joint product of the Working Group and there are no individually authored sections.

Please note that much of the work during the meeting is done electronically, so it is most helpful if you bring a computer. If this is not possible, please let us know.

We thank you for completing IARC's Declaration of Interests, which we will ask you to update at the *Monograph* meeting. As a condition of your participation, description of any pertinent interests will be disclosed at the meeting and in the published Volume 118.

IARC will publish a summary of the meeting in *The Lancet Oncology* on behalf of the Working Group. You will be requested to complete the conflict-of-interest form used by *The Lancet Oncology*, and their editor will disclose conflicting interests alongside IARC's summary of the meeting.

Attached please find a Code of Conduct for IARC Experts document as well as a Confidentiality Undertaking form. **Please sign and return the Confidentiality Undertaking document to monograph118@iarc.fr as soon as possible.**

In the spirit of transparency, IARC will post the names of participants on the *Monographs* programme website in advance of the meeting. It is important that there be **no interference from interested parties with the Working Group**, before or during the meeting. Accordingly, we ask you not to discuss the subject matter with anyone with a conflicting interest and to let us know if anyone attempts to lobby you, send you written materials, or make any offer that may be linked to your participation.

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- Per diem: 170 € per night during the authorized travel period (reduced to 50% during overnight flights);

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We look forward to working with you and welcoming you to Lyon.

Yours sincerely,

Neela Guha, PhD

Responsible Officer for the meeting

Kurt Straif, MD, PhD

Head, IARC Monographs Section

International Agency for Research on Cancer/Centre International de Recherche sur le Cancer

150, cours Albert Thomas

F-69372 Lyon Cedex 08

France

Tel: 33-4-72.73.83.67

Fax: 33-4-72.73.83.19

monograph118@iarc.fr

http://monographs.iarc.fr/

To: Cogliano, Vincent[cogliano.vincent@epa.gov]
From: Fritz, Jason
Sent: Thur 6/2/2016 2:30:32 PM
Subject: RE: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

Thanks Vince!

And too late for my wife falling in love with Lyon, I think…she's fluent in French and German, and loves pretty much all of central and Northern Europe…☺

jf

From: Cogliano, Vincent
Sent: Thursday, June 02, 2016 10:28 AM
To: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>
Cc: Fritz, Jason <Fritz.Jason@epa.gov>; D'Amico, Louis <DAmico.Louis@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>; Subramaniam, Ravi <Subramaniam.Ravi@epa.gov>
Subject: Re: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

Yes, congratulations! If you bring your wife, don't let her fall in love with Lyon.

On Jun 2, 2016, at 09:46, Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov> wrote:

Congrats Jason! Well deserved!

Best regards,

Andrew

From: Fritz, Jason
Sent: Thursday, June 02, 2016 9:15 AM
To: D'Amico, Louis <DAmico.Louis@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Subramaniam, Ravi <Subramaniam.Ravi@epa.gov>
Subject: FW: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

My official invitation to participate on the IARC monograph vol118 next year, FYI.

Thanks,

Jason

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Sent: Thursday, June 02, 2016 8:12 AM
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Responsible Officer for the meeting

Kurt Straif, MD, PhD

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Except for insurance coverage provided for accidents and loss of, or damage to, baggage and personal effects during travel, WHO will not be responsible for any loss, accident, damage or injury suffered by an expert, or any person claiming under such expert, arising in or out of his/her participation in this activity. WHO will not be responsible for any claims which are not covered, or which exceed the coverage provided, under WHO's insurance coverage. Experts serve in their individual capacities as scientists and not as representatives of their government or any organization with which they are affiliated. It is understood that the execution of this work does not create any employer-employee relationship between yourself and the World Health Organization, of which IARC is a part. Furthermore, experts are required to disclose all circumstances that could give rise to a potential conflict of interest as a result of their membership in the expert committee, advisory group or other activity, in accordance with the procedures established by the Director-General for that purpose.

To: Fritz, Jason[Fritz.Jason@epa.gov]; D'Amico, Louis[DAmico.Louis@epa.gov]; Cogliano, Vincent[cogliano.vincent@epa.gov]; Perovich, Gina[Perovich.Gina@epa.gov]
Cc: Subramaniam, Ravi[Subramaniam.Ravi@epa.gov]
From: Hotchkiss, Andrew
Sent: Thur 6/2/2016 1:46:39 PM
Subject: RE: Official Invitation: IARC Monographs Vol. 118, IARC, Lyon, 21-28 March 2017

Congrats Jason! Well deserved!

Best regards,

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Tel: 33-4-72.73.83.67

Fax: 33-4-72.73.83.19

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To: Fritz, Jason[Fritz.Jason@epa.gov]; Salazar, Keith[Salazar.Keith@epa.gov]
Cc: Hotchkiss, Andrew[Hotchkiss.Andrew@epa.gov]; Shams, Dahnish[Shams.Dahnish@epa.gov]; Cogliano, Vincent[cogliano.vincent@epa.gov]; Jones, Samantha[Jones.Samantha@epa.gov]; Perovich, Gina[Perovich.Gina@epa.gov]
From: Soto, Vicki
Sent: Wed 6/1/2016 7:42:45 PM
Subject: RE: PLEASE REVIEW ASAP - NAS meeting today

Sorry – being systematic and starting at the beginning and working through☺ Thanks Andrew!

From: Fritz, Jason
Sent: Wednesday, June 01, 2016 3:42 PM
To: Soto, Vicki <Soto.Vicki@epa.gov>; Salazar, Keith <Salazar.Keith@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Shams, Dahnish <Shams.Dahnish@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>
Subject: RE: PLEASE REVIEW ASAP - NAS meeting today

Yes- Andrew already caught that, please see the most recent email in the chain ☺

jf

From: Soto, Vicki
Sent: Wednesday, June 01, 2016 3:41 PM
To: Fritz, Jason <Fritz.Jason@epa.gov>; Salazar, Keith <Salazar.Keith@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Shams, Dahnish <Shams.Dahnish@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>
Subject: RE: PLEASE REVIEW ASAP - NAS meeting today

Jason sorry, I'm just getting to this. Shouldn't it be …a decreased rate of acetaldehyde….?

From: Fritz, Jason
Sent: Wednesday, June 01, 2016 1:03 PM
To: Salazar, Keith <Salazar.Keith@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Shams, Dahnish

<Shams.Dahnish@epa.gov>; Soto, Vicki <Soto.Vicki@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>
Subject: RE: PLEASE REVIEW ASAP - NAS meeting today

In response to some of the comments from Ray, for the title of science topic 2, I would suggest something like:

"The potential for increased susceptibility to toxic effects resulting from a decreased rate acetaldehyde clearance in the liver"

Happy to hear any other thoughts/comments/suggestions.

jf

From: Soto, Vicki
Sent: Wednesday, June 01, 2016 9:41 AM
To: Fritz, Jason <Fritz.Jason@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Salazar, Keith <Salazar.Keith@epa.gov>; Shams, Dahnish <Shams.Dahnish@epa.gov>
Subject: RE: PLEASE REVIEW ASAP - NAS meeting today

All – here is the table updated with Jason's edits. Any other changes? I'd like to send this to NAS ASAP.

Science Topic 1 **Liver tumor modes of action**	Science Topic 2 **Susceptibility associated with slow clearance of acetaldehyde in the liver**	Science Topic 3 **Use of 2-stage carcinogenicity bioassays**
Need familiarity with animal data. Need expertise in liver carcinogenesis with knowledge of nuclear receptor-mediated (e.g., PPAR, PXR, CAR) –cancer	Familiarity with animal data, with a focus on direct translational relevance. Must have knowledge in chemicals that are metabolized to acetaldehyde in or rapidly delivered to the liver(e.g., ethanol, ETBE).	Familiarity with animal data. Expertise in 2-stage initiation-promotion carcinogenicity assays in rodents, specifically including liver tumorigenesis in rats (knowledge of thyroid,

mechanisms or modes of action, and acetaldehyde-mediated genotoxicity. For this topic should have both sides representing the PPAR MOA hypothesis as it relates to human relevance of rodent liver cancer (i.e., Klaunig vs. Guyton).	Need familiarity with increased susceptibility of acetaldehyde due to polymorphisms in acetaldehyde metabolic enzymes in human populations (e.g., familiarity with epidemiological data). Need expertise in toxicity of chemicals that are metabolized to acetaldehyde in the liver in animals and humans with reduced metabolism due to genotypic variation.	colon, forestomach and kidney tumorigenesis desirable, but secondary) and how it pertains to determining human cancer hazards or risk.

From: Fritz, Jason
Sent: Wednesday, June 01, 2016 9:28 AM
To: Soto, Vicki <Soto.Vicki@epa.gov>; Cogliano, Vincent <cogliano.vincent@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Salazar, Keith <Salazar.Keith@epa.gov>; Shams, Dahnish <Shams.Dahnish@epa.gov>
Subject: RE: PLEASE REVIEW ASAP - NAS meeting today

I'd say for ALL science topics, familiarity with animal data is a perquisite (although if it is clearer to say so for each topic, that seems fine too). Topic 2, more than any, would also benefit from a cogent discussion of what is known about this topic the human population.

Science experts as contact suggestions (by no means complete, this is just as far as I've gotten):

- Topic 1: Liver tumors MOA
  - Kathryn Guyton (IARC, Lyon, France)
  - Jim Klaunig (Indiana University)
  - Udayan Apte (University of Kansas Medical Center)
- Topic 2: Susceptibility…
  - Dennis Petersen (University of Colorado Anzchutz Medical Campus)
  - James Roede (University of Colorado Anzchutz Medical Campus)

- Vasilis Vasiliou (Yale)
- Kris Fritz (University of Colorado Anzchutz Medical Campus)
- Colin Shearn (University of Colorado Anzchutz Medical Campus)
- Richard Dietrich (?)

•□□□□□□□□ Topic 3: 2-stage bioassays

- Shibutani, M. (Tokyo University of Agriculture and Technology)
- Mitsumari, K. (Tokyo University of Agriculture and Technology)
- Gary Stoner (Emeritus, Ohio State University)
- Mark Miller (NCI, Division of Cancer Prevention)

Also, I would make the current topic 3 "2-stage bioassays…" as topic #2, and move the current topic 2 "Susceptibility" to be the new topic 3, since it will focus more on differences resulting from metabolism, and will not necessarily be focused on cancer.

jf

From: Soto, Vicki
Sent: Wednesday, June 01, 2016 7:37 AM
To: Cogliano, Vincent <cogliano.vincent@epa.gov>; Perovich, Gina <Perovich.Gina@epa.gov>; Jones, Samantha <Jones.Samantha@epa.gov>
Cc: Hotchkiss, Andrew <Hotchkiss.Andrew@epa.gov>; Salazar, Keith <Salazar.Keith@epa.gov>; Fritz, Jason <Fritz.Jason@epa.gov>; Shams, Dahnish <Shams.Dahnish@epa.gov>
Subject: PLEASE REVIEW ASAP - NAS meeting today

Good morning,

I'd like to forward this to NAS in advance of our meeting today. It combines the information that Keith provided to me about the science topics and expertise needed. Please review and let me

know if there are any "stoppers" to me sending this. We can always update this later if necessary, I just want NAS to have some initial information. Right now all they know is that it is ETBE.

Thanks

Vicki

Science Topic 1 **Liver tumor modes of action**	Science Topic 2 **Susceptibility associated with slow clearance of acetaldehyde in the liver**	Science Topic 3 **Use of 2-stage carcinogenicity bioassays**
Need familiarity with animal data. ~~General knowledge is sufficient for nuclear hormone receptor-mediated carcinogenesis MOAs~~. ~~Expert must have knowledge in chemicals that are metabolized to acetaldehyde (e.g., ethanol, ETBE). Need familiarity with EPA cancer guidelines.~~ Need expertise in liver carcinogenesis with knowledge of nuclear receptor-mediated (e.g., PPAR, PXR, CAR) –cancer mechanisms or modes of action, and acetaldehyde-mediated genotoxicity. For this topic should have both sides representing the PPAR MOA hypothesis as it relates to human relevance of rodent liver cancer (i.e., Klaunig vs. Guyton).	Familiarity with animal data, with a focus on direct translational relevance. Must have knowledge in chemicals that are metabolized to acetaldehyde in or rapidly delivered to the liver(e.g., ethanol, ETBE). Need familiarity with increased susceptibility of acetaldehyde due to ~~genotypic variation~~ polymorphisms in acetaldehyde metabolic enzymes in human populations (e.g., familiarity with epidemiological data). Need expertise in ~~geno~~toxicity of chemicals that are metabolized to acetaldehyde in the liver in animals and humans with reduced metabolism due to genotypic variation.	Familiarity with animal data. ~~Experts need familiarity with EPA cancer guidelines.~~ Expertise in 2-stage initiation-promotion carcinogenicity assays in rodents, specifically including liver tumorigenesis in rats (knowledge of thyroid, colon, forestomach and kidney tumorigenesis desirable, but secondary) and how it pertains to determining human cancer hazards or risk ~~cancer weight of evidence descriptor~~.

To: David Forman[FormanD@visitors.iarc.fr]
Cc: Cogliano, Vincent[cogliano.vincent@epa.gov]; Kurt Straif[StraifK@iarc.fr]; pinfante@starpower.net[pinfante@starpower.net]; Hudak, Juliann Marie[jmh206@pitt.edu]; Carruth, Russellyn[carruth@pitt.edu]
From: Goldstein, Bernard D
Sent: Wed 6/1/2016 10:46:01 AM
Subject: RE: Not available for poster presentation on Friday

Dear Dr Forman

Many thanks for this clarification

Bernard D. Goldstein, MD

Professor Emeritus and Dean Emeritus

University of Pittsburgh Graduate School of Public Health

130 Desoto St; Rm A-710

Pittsburgh PA 15261

Office: 412 648 9994

Cell: 412 417 9611

From: David Forman [mailto:FormanD@visitors.iarc.fr]
Sent: Wednesday, June 1, 2016 5:57 AM
To: Goldstein, Bernard D <bdgold@pitt.edu>
Cc: Iarc Conference 2016 <iarc-conference2016@iarc.fr>; Aurelie Viotto <ViottoA@iarc.fr>
Subject: RE: Not available for poster presentation on Friday

Dear Dr Goldstein

Apologies firstly for the difficulties you have experienced in communication with our Secretariat regarding the timing of your poster presentation. I am, however, pleased to say your poster (and all those in the category "Mechanisms in Carcinogen Evaluation") will be presented in the Thursday lunch break as originally notified. That it was listed in the online program for Friday presentation was due to a mistake in the construction of the program which has now been rectified. So apologies for this as well. Had you not identified this problem to us, we would not have been aware of the error in the program so I am extremely grateful for you bringing it to our attention.

We look forward to seeing you in Lyon next week.

With best wishes

David Forman

Dr David Forman

Chair, Local Organising Committee, 50th Anniversary Conference & Senior Visiting Scientist

International Agency for Research on Cancer

150, cours Albert Thomas

F-69372 Lyon Cedex 08 France

Tel.: (+33) (0)6 33 38 2576

E-mail: formand@visitors.iarc.fr

www.iarc.fr/conference2016

From: Goldstein, Bernard D [mailto:bdgold@pitt.edu]
Sent: 01 June 2016 03:01
To: Iarc Conference 2016 <iarc-conference2016@iarc.fr>
Subject: Not available for poster presentation on Friday

Dear IARC

The original IARC meeting agenda showed posters on Thursday but not on Friday. I am leaving Friday midday to meet my wife who is flying to Britain. BUT the agenda that finally was transmitted to me lists my poster as being on Friday afternoon. My attempts to get information by phone from the Secretariat have been unsuccessful beyond being told, if I understand it correctly, that there were so many posters that they needed to add a Friday session. But they have been unable to give me the name of anyone to speak to about switching my poster to Thursday

Please let me know as soon as possible whether I can give my poster on Thursday rather than Friday

Thank you

Bernard D. Goldstein, MD

Professor Emeritus and Dean Emeritus

University of Pittsburgh Graduate School of Public Health

130 Desoto St; Rm A-710

Pittsburgh PA 15261

Office: 412 648 9994

Cell: 412 417 9611

To: Kurt Straif[StraifK@iarc.fr]
Cc: pinfante@starpower.net[pinfante@starpower.net]; Cogliano, Vincent[cogliano.vincent@epa.gov]; Hudak, Juliann Marie[jmh206@pitt.edu]
From: Goldstein, Bernard D
Sent: Tue 5/31/2016 3:49:35 PM
Subject: Help needed asap

Hi Kurt

Sorry to bother you when you are busy. But I have an immediate problem and cannot get the information needed from the Secretariat of the IARC meeting.

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Sent: Friday, May 27, 2016 2:37 PM
To: Goldstein, Bernard D <bdgold@pitt.edu>
Cc: pinfante@starpower.net; Cogliano, Vincent <cogliano.vincent@epa.gov>; Hudak, Juliann Marie <jmh206@pitt.edu>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

We are in the midst of the hot phase of a Monographs meeting, will respond asap

Kurt

From: Goldstein, Bernard D [mailto:bdgold@pitt.edu]
Sent: 27 May 2016 17:59
To: Kurt Straif <StraifK@iarc.fr>; straif@iarc.fr
Cc: pinfante@starpower.net; Cogliano, Vincent <cogliano.vincent@epa.gov>; Hudak, Juliann Marie <jmh206@pitt.edu>
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Hi Kurt

I've attached our planned poster. The key points we make supplement the valuable exchange that Peter and you and your colleagues made in print. Our basic argument is that irrespective of whether the epidemiological evidence raises to the level of sufficiency, benzene should be considered to be a known cause of NHL. Our major points are:

1. Benzene should be considered a known cause of NHL based on current IARC rules which state: IARC now considers a chemical to be a Group 1 carcinogen when there is less than sufficient evidence in humans but sufficient evidence in animals and "**strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity**" (my emphasis). While we can argue about whether the epi data is "sufficient" there can be no question about lymphoma in animals (I count seven studies and Peter counts ten). Further, with a superabundance of laboratory data on genotoxicity, and with lymphocyte chromosomal abnormalities routinely reported in the circulating lymphocytes of exposed workers there can be no question about the presence of a genotoxic mechanism relevant to humans

2. The outcome of the 2009 IARC deliberations on benzene and NHL is hauntingly similar to the 1974 IARC review of benzene and AML in its overdependence on cohort-based epidemiology.

3. In 1974 there was a legitimate scientific argument about whether lymphocytic and myelocytic cells arose from the same stem cell. That argument has been settled in favor of a single precursor cell which is clearly affected by benzene in causing AML. Further, benzene has a promiscuous effect in causing multiple chromosomal abnormalities, again consistent with a causal role in NHL

4. Most disappointing is that the modification of the IARC process to include mechanistic information, on which you and Vincent (whom I have copied) and your colleagues worked so hard and so eloquently, has apparently failed in this case.

I do strongly suggest that benzene and NHL be subject to an IARC review. And I know that Peter feels strongly, as I do, in suggesting a review of workers exposed to gasoline. This is an important global issue, particularly in view of the large number of exposed workers and because it brings up some of the knotty mixture issues in relation to a known human carcinogen.

Looking forward to seeing you in Lyon

Bernie

From: Kurt Straif [mailto:StraifK@iarc.fr]
Sent: Monday, May 2, 2016 5:51 AM
To: Goldstein, Bernard D <bdgold@pitt.edu>; straif@iarc.fr
Cc: pinfante@starpower.net
Subject: RE: Is there a forthcoming IARC meeting on benzene??

Dear Bernie,

I look forward to welcoming you to the IARC conference – we all expect this will be a great meeting with lots of new science that impacts on public health and a great opportunity to welcome many friends to Lyon.

I am curious to read and discuss your poster. A new benzene Monograph has not yet been firmly scheduled.

Best wishes,

Kurt

From: Goldstein, Bernard D [mailto:bdgold@pitt.edu]
Sent: 30 April 2016 19:17
To: straif@iarc.fr
Cc: pinfante@starpower.net
Subject: Is there a forthcoming IARC meeting on benzene??

Hi Kurt

Hope all is well with you and your colleagues. As you probably know, Peter Infante and I have a poster presentation at the 50th Anniversary meeting on benzene and NHL in June. We argue that the delay in the recognition of benzene as a known cause of NHL mirrors the initial delay in the recognition of benzene as a known cause of ANLL, and fails to take into account the mechanistic evidence.

I recall there was talk of a future IARC meeting in which benzene would again be reviewed with a focus on NHL and other non-ANLL cancers. I could not find any mention of such a meeting on the IARC website. I am preparing the poster now, and if such a meeting is being scheduled by IARC I would welcome including such a statement within the poster material

Best personal regards – and I look forward to seeing you in June

Bernie

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