



# La monografia sui PCB: presentazione

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# Outline

- A few words about the Monographs
- What are PCBs and where do we find them?
- Available evidence: types of studies, exposure assessment
- Association between exposure to PCB and NHL for each type of study
- Summary of the evidence and evaluation

# The *IARC Monographs*

- ❖ Systematic review and evaluation of available literature on carcinogenicity of agents
- ❖ Used by government agencies for regulations and recommendations
- ❖ Serve as a reference for scientific community

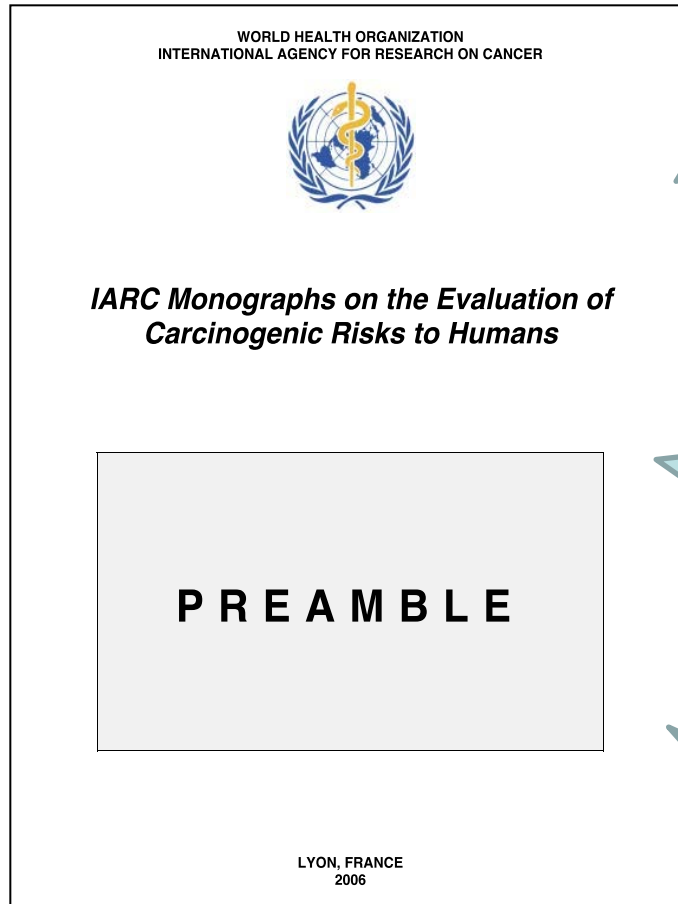
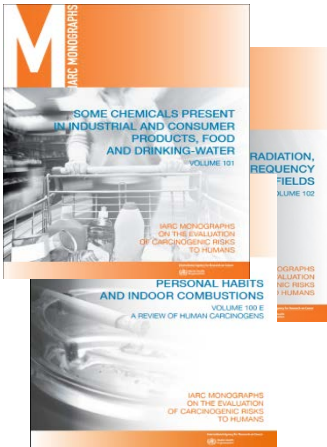
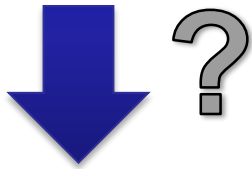
# The *IARC Monographs* programme

- Over 40 years of publication
- Almost 1000 agents evaluated
- Over 100 known carcinogens
- Over 1200 scientists
- About 350'000 references



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# How are the evaluations conducted?

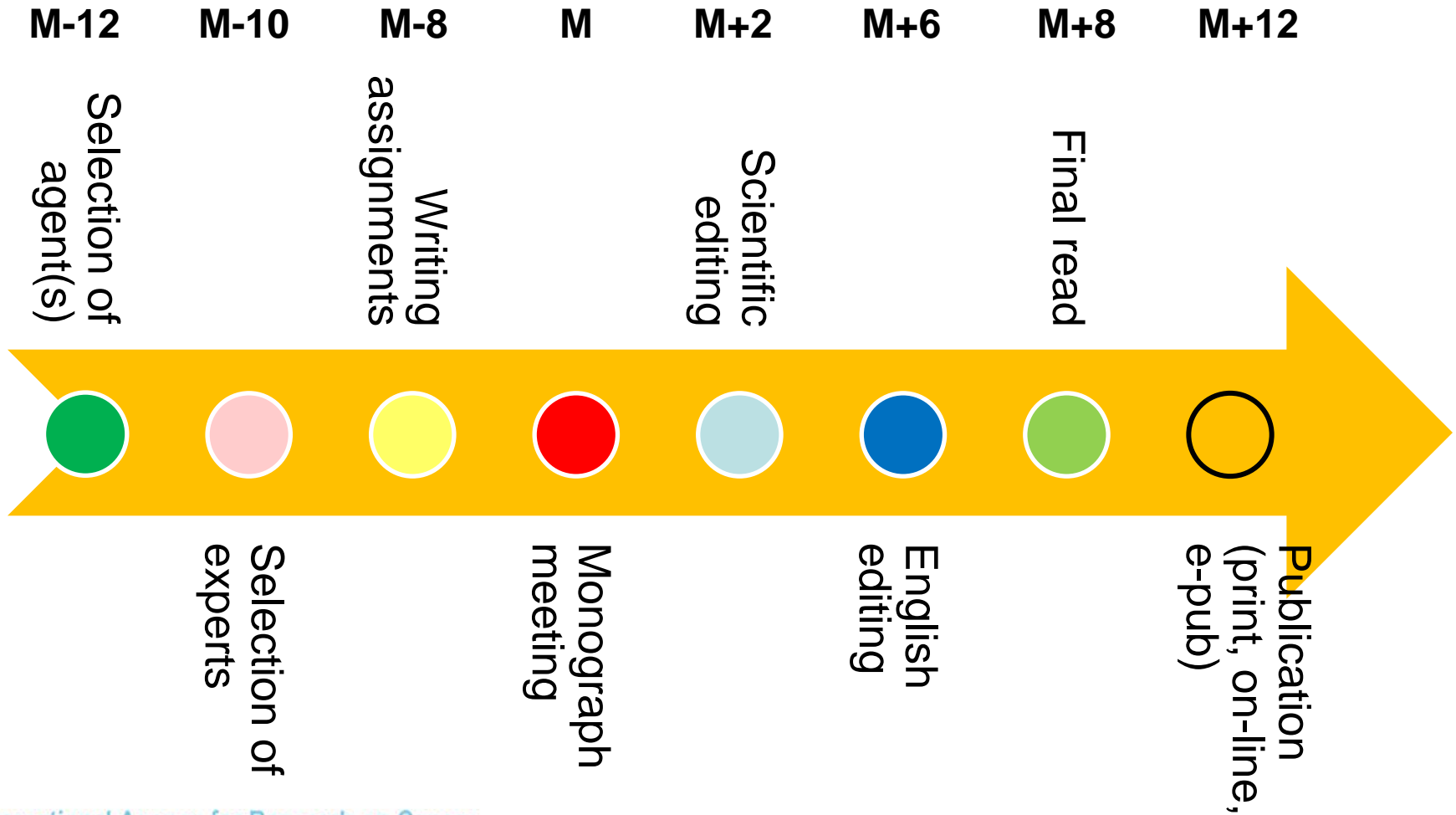


Procedural guidelines for participant selection, conflict of interest, stakeholder involvement & meeting conduct

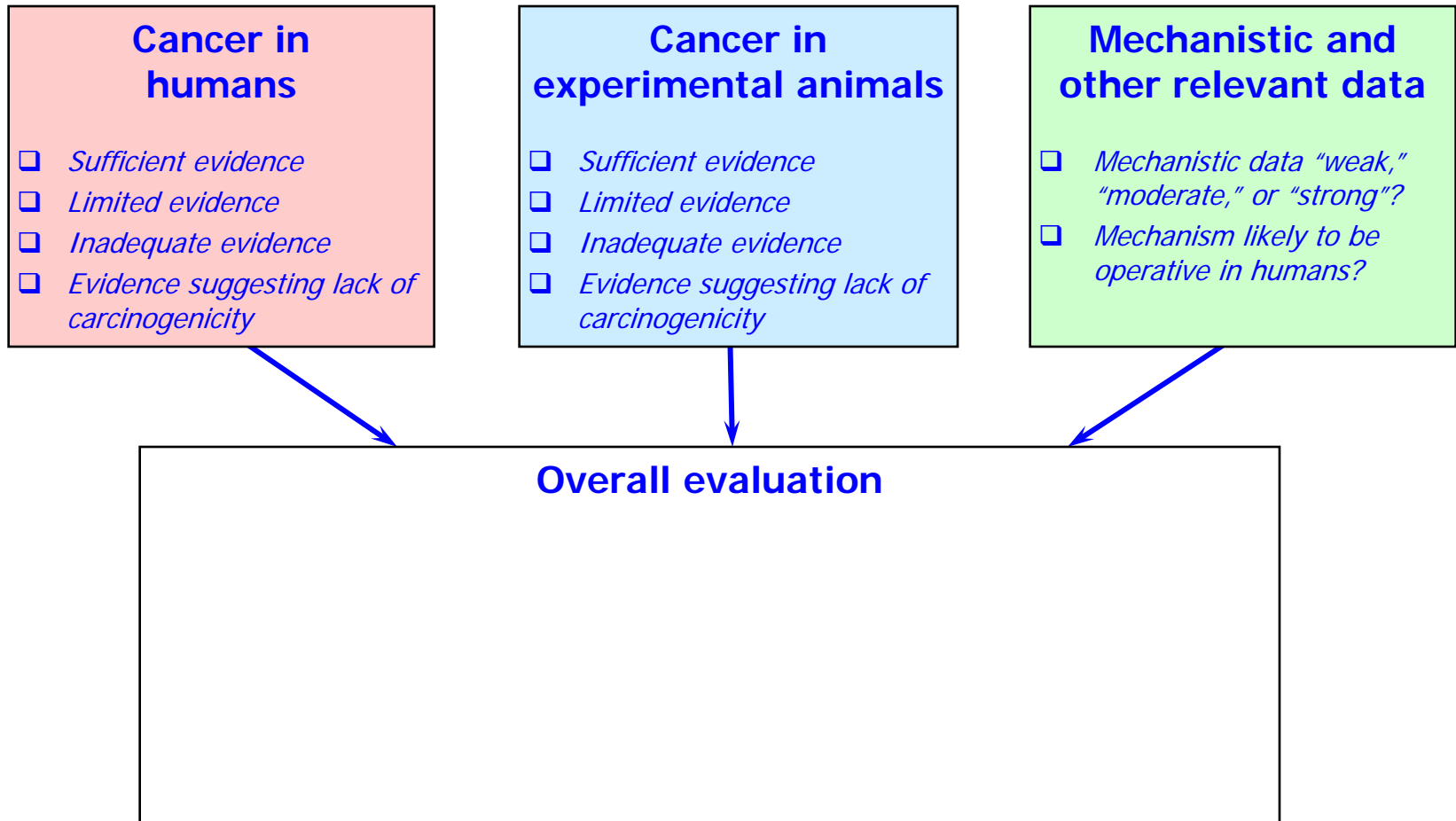
Separate criteria for review of human, animal and mechanistic evidence

Decision process for overall evaluations

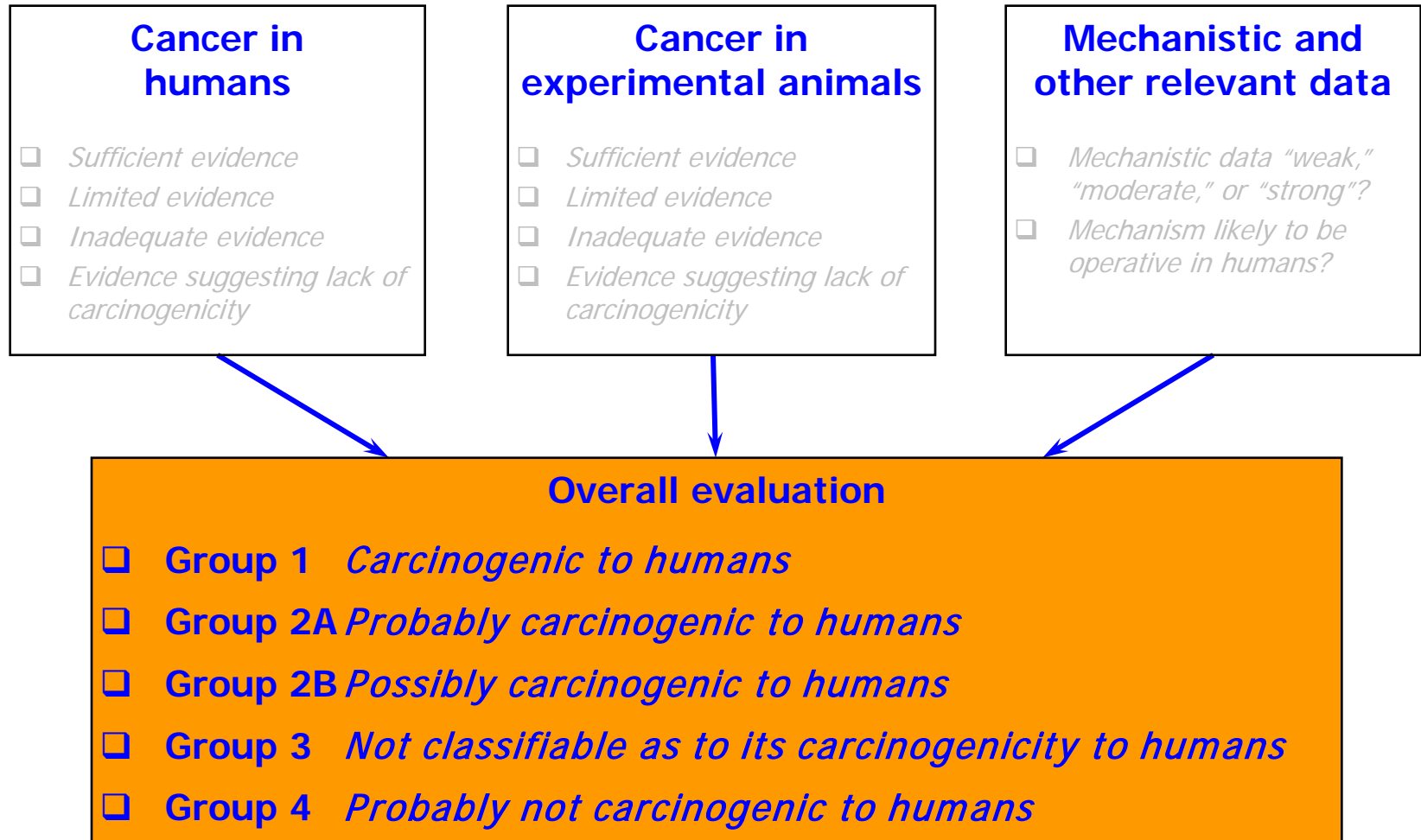
# The *IARC Monographs* process



# Cancer hazard identification based on the weight of the evidence (I)



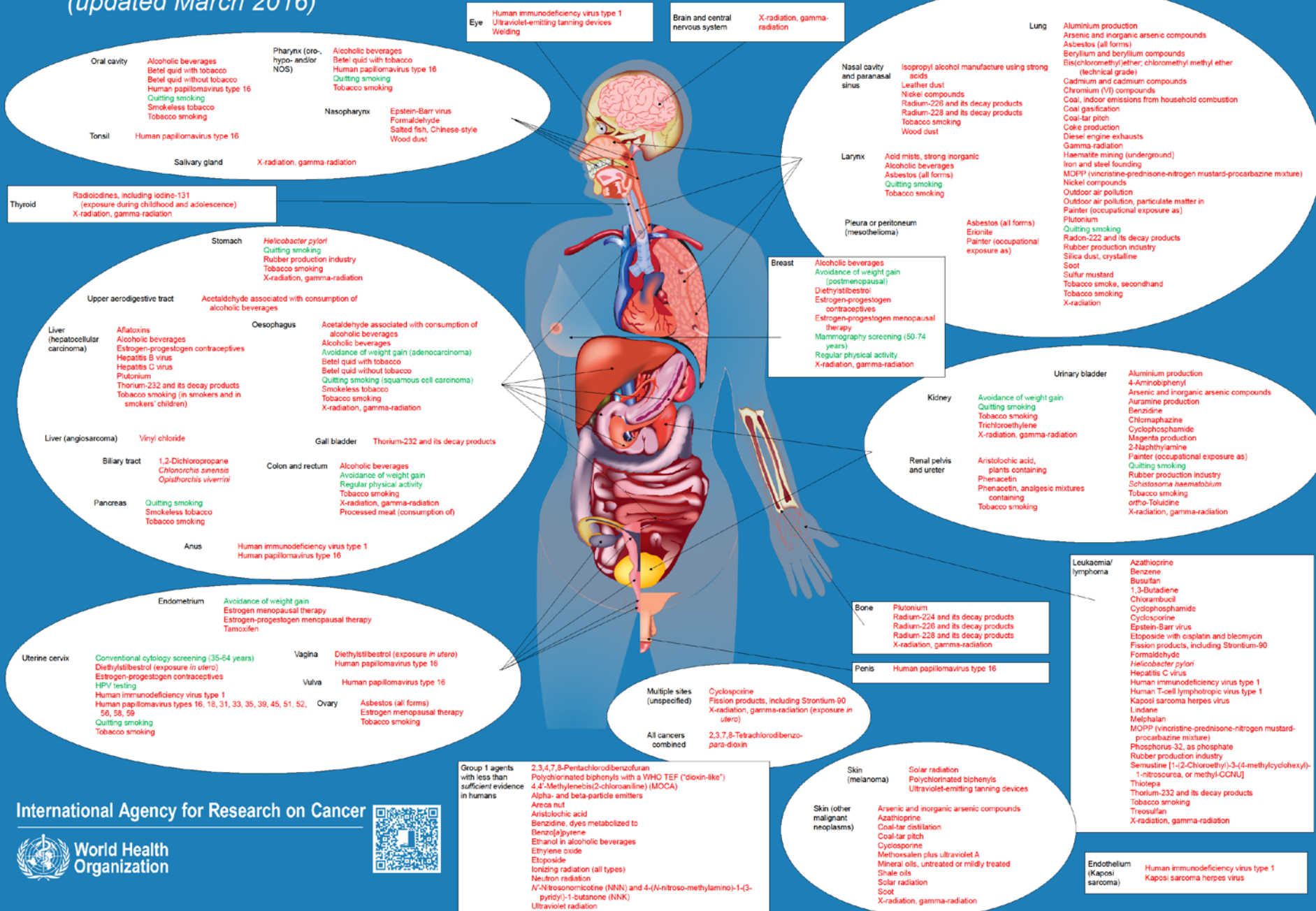
# Cancer hazard identification based on the weight of the evidence (II)



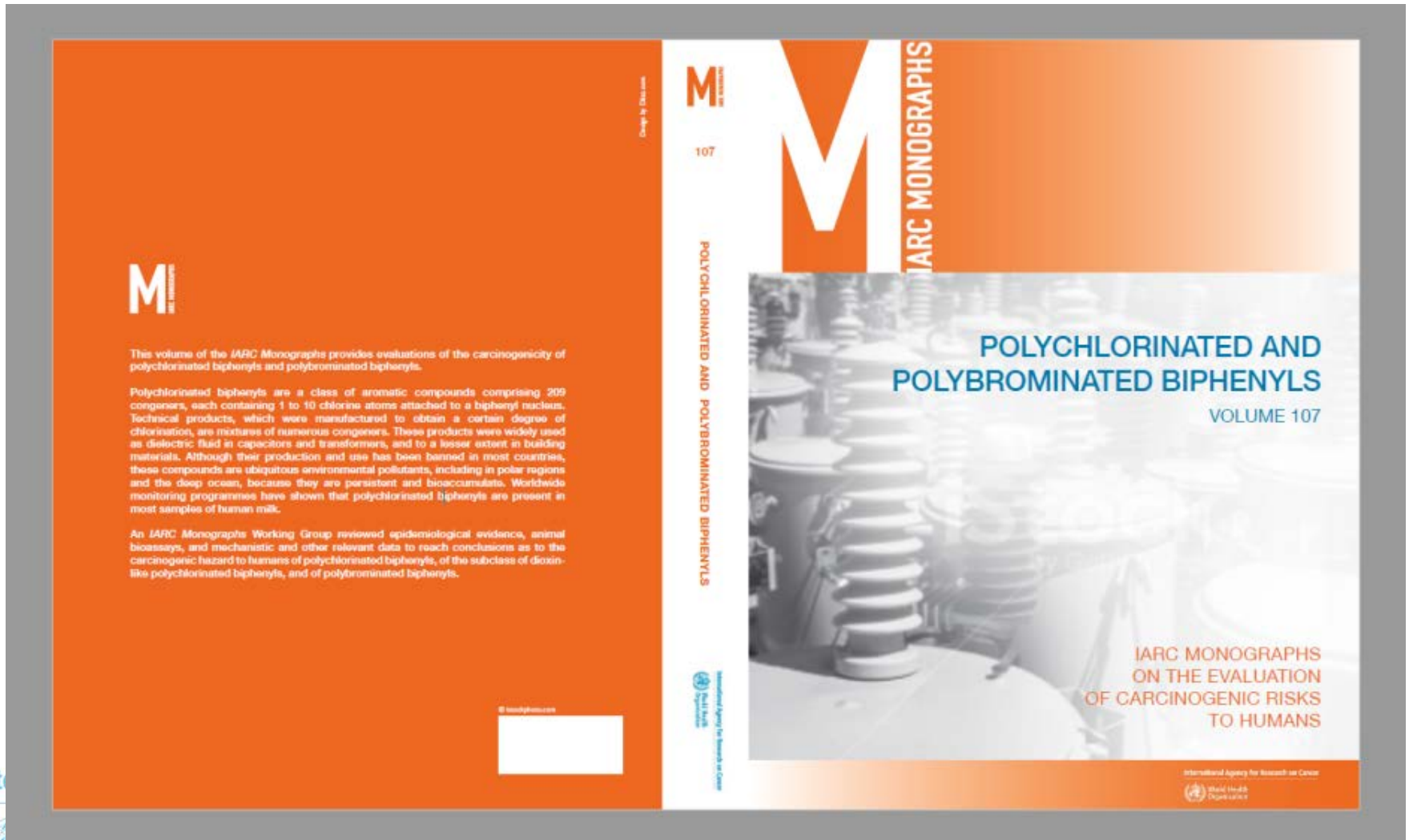


# IARC Monographs of Carcinogenic Risks to Humans and Handbooks of Cancer Prevention

(updated March 2016)



# IARC Monograph Vol. 107

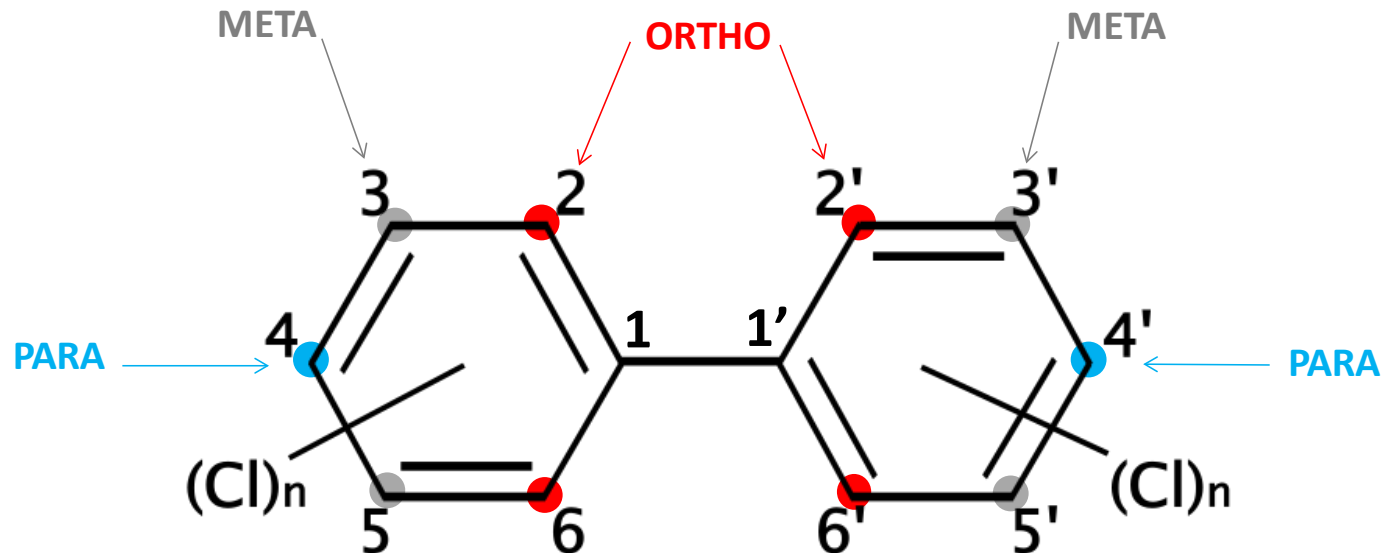


# Final evaluations

CAS No	Agent	Group
001336-36-3	Polychlorinated biphenyls	1
	Polychlorinated biphenyls, dioxin-like, with a Toxicity Equivalency Factor (TEF) according to WHO (PCBs 77, 81, 105, 114, 118, 123, 126, 156, 157, 167, 169, 189) (NB: Overall evaluation upgraded to Group 1 with strong supporting evidence from other relevant data)	1
059536-65-1	Polybrominated biphenyls (NB: Overall evaluation upgraded to Group 2A with supporting evidence from other relevant data, namely mechanistic similarity with polychlorinated biphenyls classified in Group 1)	2A

# PCBs: polychlorinated biphenyls

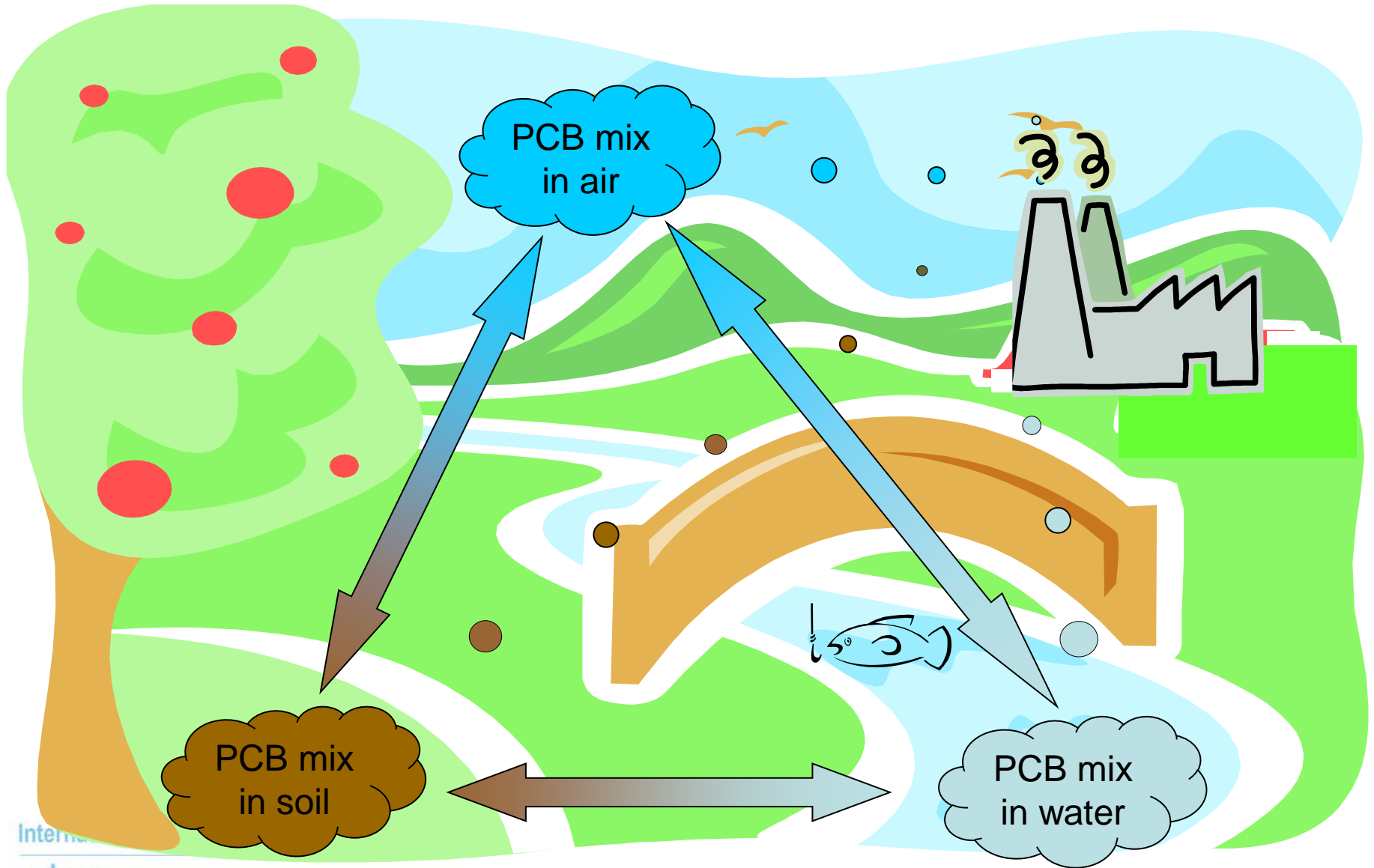
- 1 to 5 Cl atoms on either part of the biphenyl ring



# A family of 209 congeners

Chlorine position on each ring	2	3	4	2,3	2,4	2,5	2,6	3,4	3,5	2,3,4	2,3,5	2,3,6	2,4,5	2,4,6	3,4,5	2,3,4,5	2,3,4,6	2,3,5,6	2,3,4,5,6
None	1	2	3	5	7	9	10	12	14	21	23	24	29	30	38	61	62	65	116
2'	4	6	8	16	17	18	19	33	34	41	43	45	48	50	76	86	88	93	142
3'		11	13	20	25	26	27	35	36	55	57	59	67	69	78	106	108	112	160
4'			15	22	28	31	32	37	39	60	63	64	74	75	81	114	115	117	166
2',3'				40	42	44	45	56	58	82	83	84	97	98	122	129	131	134	173
2',4'					47	49	51	66	68	85	90	91	99	100	123	137	139	147	181
2',5'						52	53	70	72	87	92	95	101	103	124	141	144	151	185
2',6'							54	71	73	89	94	96	102	104	125	143	145	152	186
3',4'								77	79	105	109	110	118	119	126	156	158	163	190
3',5'									80	107	111	113	120	121	127	159	161	165	192
2',3',4'										128	130	132	138	140	157	170	171	177	195
2',3',5'											133	135	146	148	162	172	175	178	198
2',3',6'												136	149	150	164	174	176	179	200
2',4',5'													153	154	167	180	183	187	203
2',4',6'														155	168	182	184	188	204
3',4',5'															169	189	191	193	205
2',3',4',5'																194	196	199	206
2',3',4',6'																	197	201	207
2',3',5',6'																		202	208
2',3',4',5',6'																			209

# Transport of PCBs between media



# Where do we find them?

- In the environment
  - Discharge from industrial waste (recycling waste) & accidental release
  - Chemical composition of product changes with time, T°, UV, media (air, water, soil, sediment)
  - We are never exposed to the same compounds as those found in the industrial products.
- Entering our body
  - Workers: dermal, inhalation
  - General population: ingestion (food), inhalation
- In the body
  - Stored in the fat of the animals/humans
  - Remains in the body up to 20 years

# Exposure to PCBs and NHL: types of available studies

## Cohorts

- Cohorts of occupational exposure
- Cohorts of accidental exposure (*Yusho, Yucheng*)
- Cohorts of high dietary exposure (fishermen's wives)
- Cohorts general population, nested case-control studies

## Case-controls

- Non-Hodgkin lymphoma



# Exposure to PCBs and NHL: assessment and level of exposure

## Cohort studies

- Cohorts of occupational exposure : type of employment (duration), department (some with high exposure), expert assessment, or job-exposure matrix (cumulative exposure)
- Cohorts of accidental exposure (*Yusho*, *Yucheng*): mass poisoning at the population level (area of highest contamination compared to neighbouring area of low contamination)
- Cohorts of high dietary intake: consumption of fatty fish, comparing area of high contamination to area of low contamination
- General population cohorts (nested case-control studies): blood or adipose tissue samples

**Case-control studies:** blood or adipose tissue samples

# PCBs and NHL: Occupational cohort studies

- 5 cohorts in the **capacitor** manufacture industry (3 in the USA, 1 each in Italy and Sweden)
- 2 cohorts of **transformer** manufacturing and repair workers (1 in the USA, 1 in Canada)
- **Mortality**: Statistically significant increase in the study in Italy and in study in transformer workers; non-significant increases in the other studies
- **Dose-response**: no effect in the 4 studies that assess different levels of exposure

# PCBs and NHL: acute exposure by food contamination

- Two episodes of mass poisoning in Japan in 1970 (*Yusho*) and in Taiwan, China in 1980 (*Yusheng*)
- For each incident, large cohort studies with 4 follow-up each
- Number of deaths from NHL above expected in men in the *Yucheng* cohorts
- No such effect observed in the *Yusho* patients
- BUT: the exposure profile of the two episode was very different (more toxic PCDFs in *Yucheng* than in *Yusho*, which could have caused the observed increase)

# PCBs and NHL: high dietary intake

- Cohorts of high dietary exposure, conducted in populations who had high fish consumption, the wives of fishermen in northern Europe or following accidental spill in river
- No association was observed in the study that assessed the relationship between exposures to PCBs and NHL

# PCBs and NHL: Cohorts in the general population

- Nested case-control studies among subsamples of large cohorts in the general population
- Blood samples collected at recruitment
- More appropriate to study rare cancers or subtypes (few cases)
- Covariates adjusted for: BMI, smoking, height, ....
- Exposure to PCBs and to other confounding factors is not always well assessed
- Statistically significant trends in risk with sum of PCBs in 3 out of 5 studies
- Positive association with specific congeners in several studies

# PCBs and NHL: case-control studies

## Case-controls

- Numerous case-controls studies conducted in Australia, Italy, Sweden, Canada, 3-country study, USA
- 6 large good-quality studies
- Measure of plasma concentrations of sum of PCBs
- Positive trends in 4 of these studies
- NHL subtypes: association with follicular lymphoma, but not large B-cell lymphoma in 3 studies

# Do PCBs cause Non-Hodgkin lymphoma in humans?

- Occupational studies show positive results (1 study in Italy)
  - Increased mortality in *Yusho* cohort, not in *Yucheng* cohort
  - In nested case-control studies with blood PCBs levels, significant trends in risk with sum of congeners in 3 studies and/or specific congeners in several studies
  - Also some negative results in large studies
- Evidence for non-Hodgkin lymphoma is *limited*  
(*bias and confounding excluded; chance not excluded*)

# The *IARC Monographs* Section



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