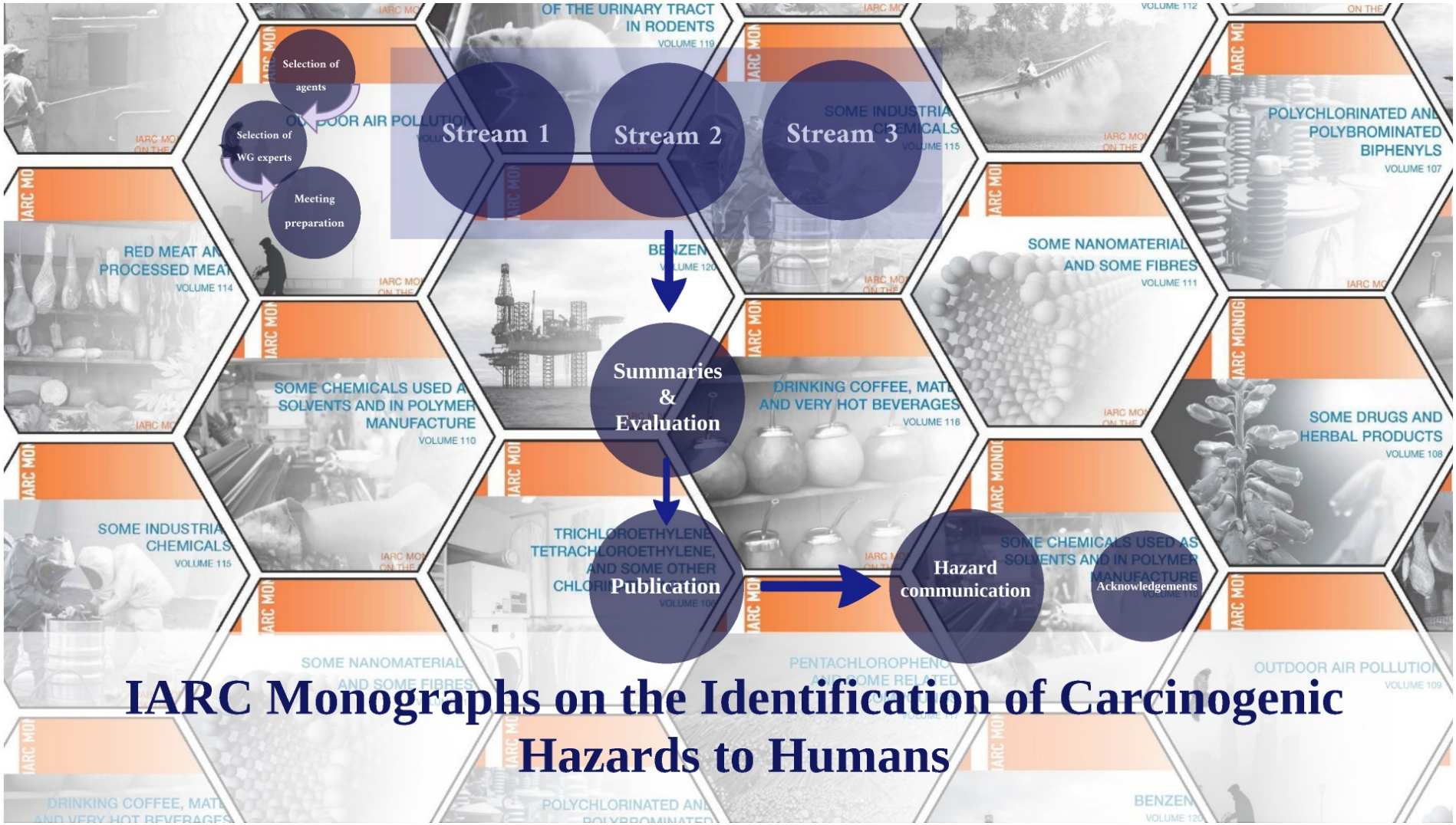


IARC Monographs on the Identification of Carcinogenic Hazards to Humans


From nominations to evaluations
• Nominations: by scientists, government agencies, the public (since 2003)
• Identifying priorities: Advisory Group every 5 years
• Selection and timing of evaluations: IARC, following consultation with WHO
Priorities
Public engagement

THE LANCET
Oncology

NEWS | ONLINE FIRST

Advisory Group recommendations on priorities for the IARC Monographs

IARC Monographs Priorities Group † • Show footnotes

Published: April 17, 2019 • DOI: https://doi.org/10.1016/S1470-2045(19)30246-3 •

References

Article Info

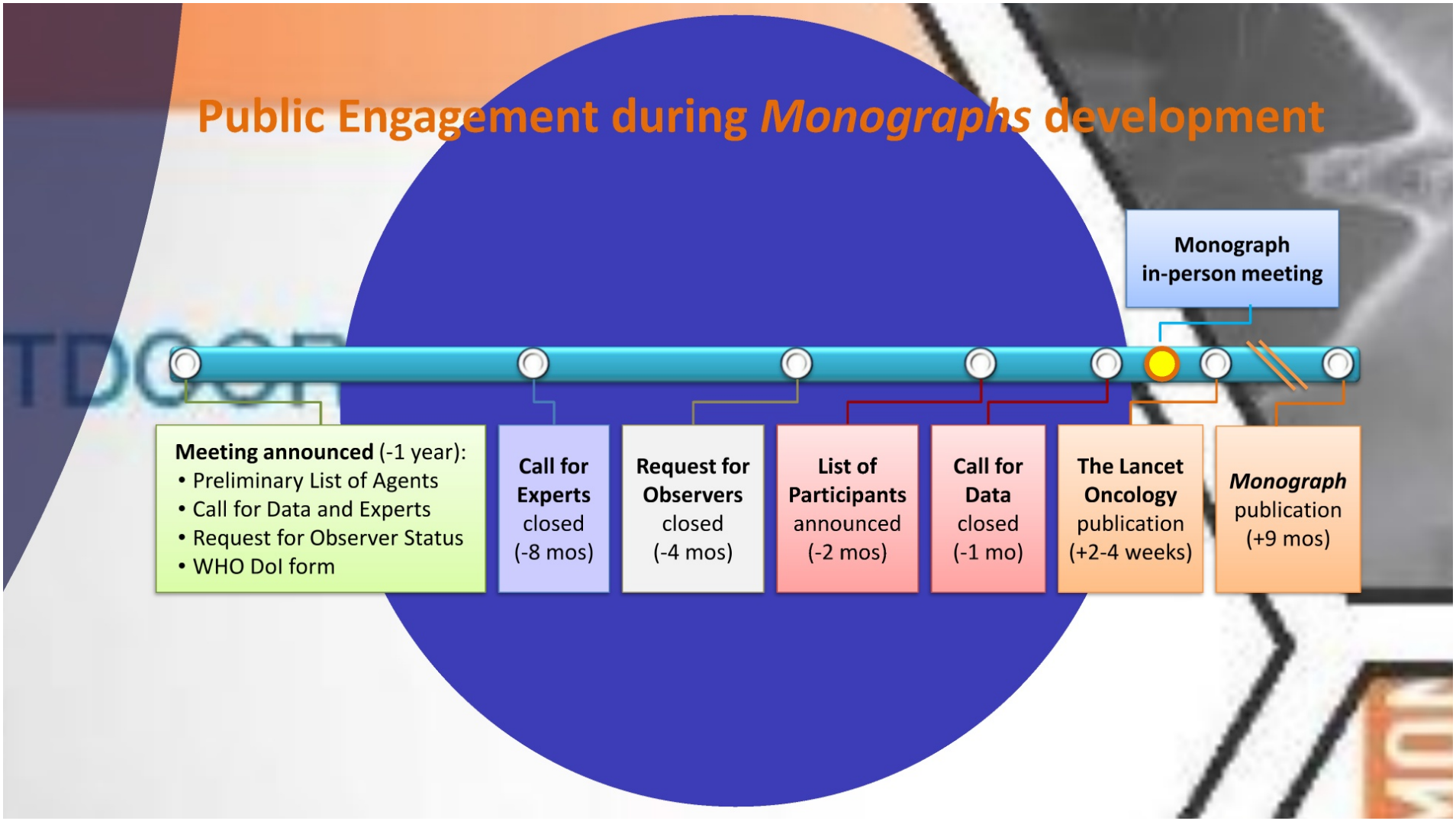
An Advisory Group of 29 scientists from 18 countries met in March, 2019, to recommend priorities for the International Agency for Research on Cancer (IARC) Monographs programme during 2020–24. IARC periodically convenes such advisory groups to ensure that the Monographs evaluations reflect the current state of scientific evidence relevant to carcinogenicity.[1] A detailed report of the Advisory Group will be published subsequently.[2]

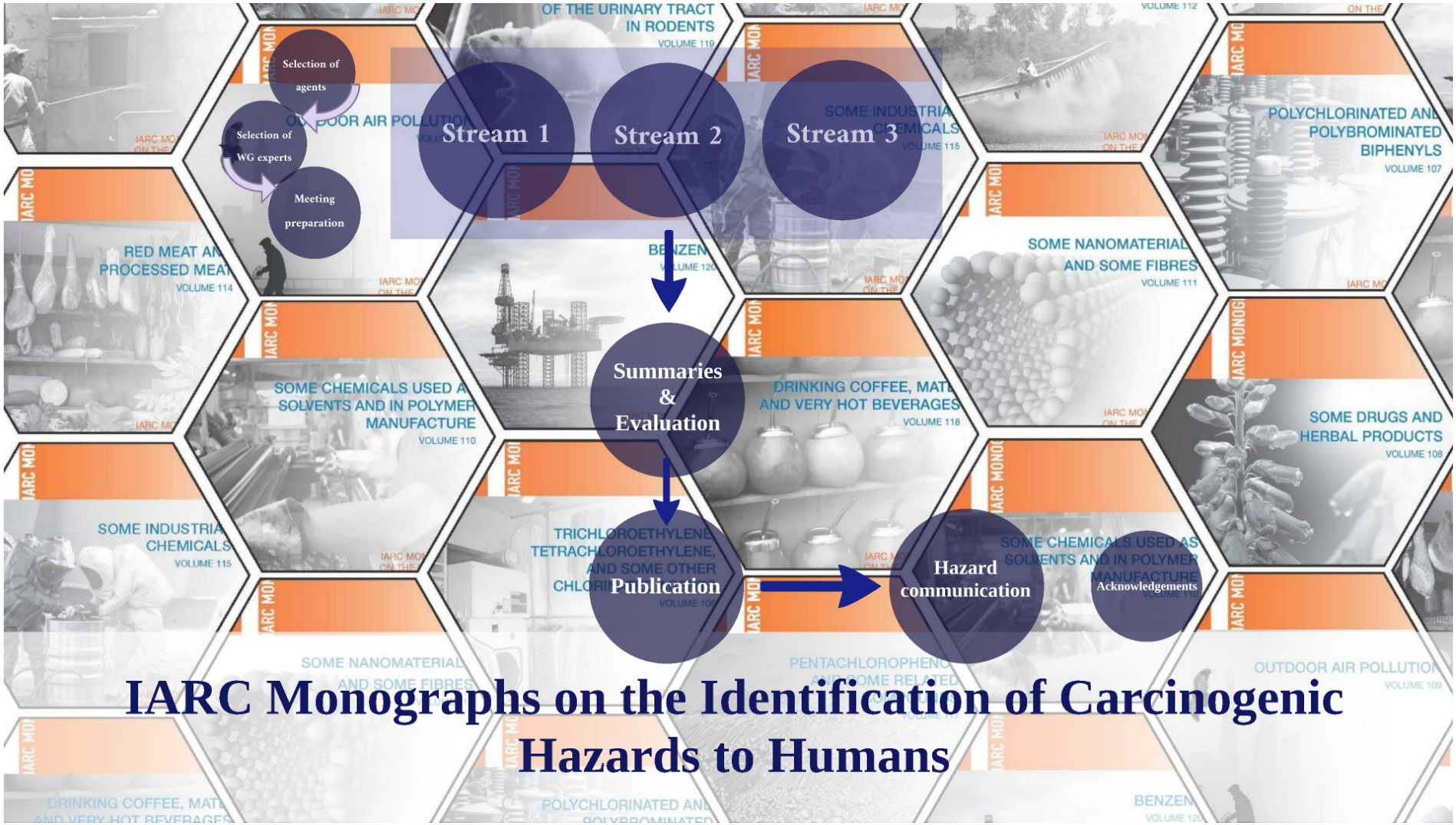

TDOOR
109

	Rationale
Agents not previously evaluated by IARC Monographs	
Haloacetic acids (and other disinfection byproducts)	Relevant human cancer, bioassay, and mechanistic evidence
Metalworking fluids	Relevant human cancer and bioassay evidence
Cannabis smoking, fertility treatment, glucocorticoids, *Salmonella typhi*, sedentary behaviour*, tetracyclines and other photosensitising drugs	Relevant human cancer and mechanistic evidence
Cupferron, gasoline oxygenated additives, gentian violet, glycidamide, malachite green and leucomalachite green, oxymetholone, pentabromodiphenyl ethers, vinclozolin	Relevant bioassay and mechanistic evidence
Breast implants, dietary salt intake*, neonatal phototherapy*, poor oral hygiene*	Relevant human cancer evidence
Aspartame	Relevant bioassay evidence
Arecoline, carbon disulphide, electronic nicotine delivery systems and nicotine*, human cytomegalovirus, parabens	Relevant mechanistic evidence
Agents previously evaluated by IARC Monographs†	
Automotive gasoline (leaded and unleaded), carbaryl, malaria	New human cancer, bioassay, and mechanistic evidence to warrant re-evaluation of the classification
Acrylamide*, acrylonitrile, some anthracyclines, coal dust, combustion of biomass, domestic talc products, firefighting exposure, metallic nickel, some pyrethroids (ie, permethrin, cypermethrin, deltamethrin)	New human cancer and mechanistic evidence to warrant re-evaluation of the classification
Aniline, acrolein, methyl eugenol and isoeugenol*, multi-walled carbon nanotubes*, non-ionising radiation (radiofrequency)*, some perfluorinated compounds (eg, perfluorooctanoic acid)	New bioassay and mechanistic evidence to warrant re-evaluation of the classification
Ostrogen:oestradiol and oestrogen-progestogens‡, hydrochlorothiazide, Merkel cell polyomavirus, perchloroethylene, very hot foods and beverages	New human cancer evidence to warrant re-evaluation of the classification
1,1,1-trichloroethane, weapons-grade alloy (tungsten, nickel, and cobalt)	New bioassay evidence to warrant re-evaluation of the classification
Acetaldehyde, bisphenol A*, cobalt and cobalt compounds, crotonaldehyde, cyclopeptide cyanotoxins, fumonisin B_1, inorganic lead compounds, isoprene, o-anisidine	New mechanistic evidence to warrant re-evaluation of the classification

Evidence of human exposure was identified for all agents. *Advised to conduct in latter half of 5-year period. †See current International Agency for Research on Cancer (IARC) list of classifications, volumes 1–123. ‡Group 1 carcinogen; new evidence of cancer in humans indicates possible causal associations for additional tumour sites (see Section 3 of Preamble to the IARC Monographs[3]).

Table 1: **Agents recommended for evaluation by the IARC Monographs with high priority**


Public Engagement during *Monographs* development
Monograph in-person meeting
Meeting announced (-1 year):
• Preliminary List of Agents
• Call for Data and Experts
• Request for Observer Status
• WHO DoI form
Call for Experts closed (-8 mos)
Request for Observers closed (-4 mos)
List of Participants announced (-2 mos)
Call for Data closed (-1 mo)
The Lancet Oncology publication (+2-4 weeks)
Monograph publication (+9 mos)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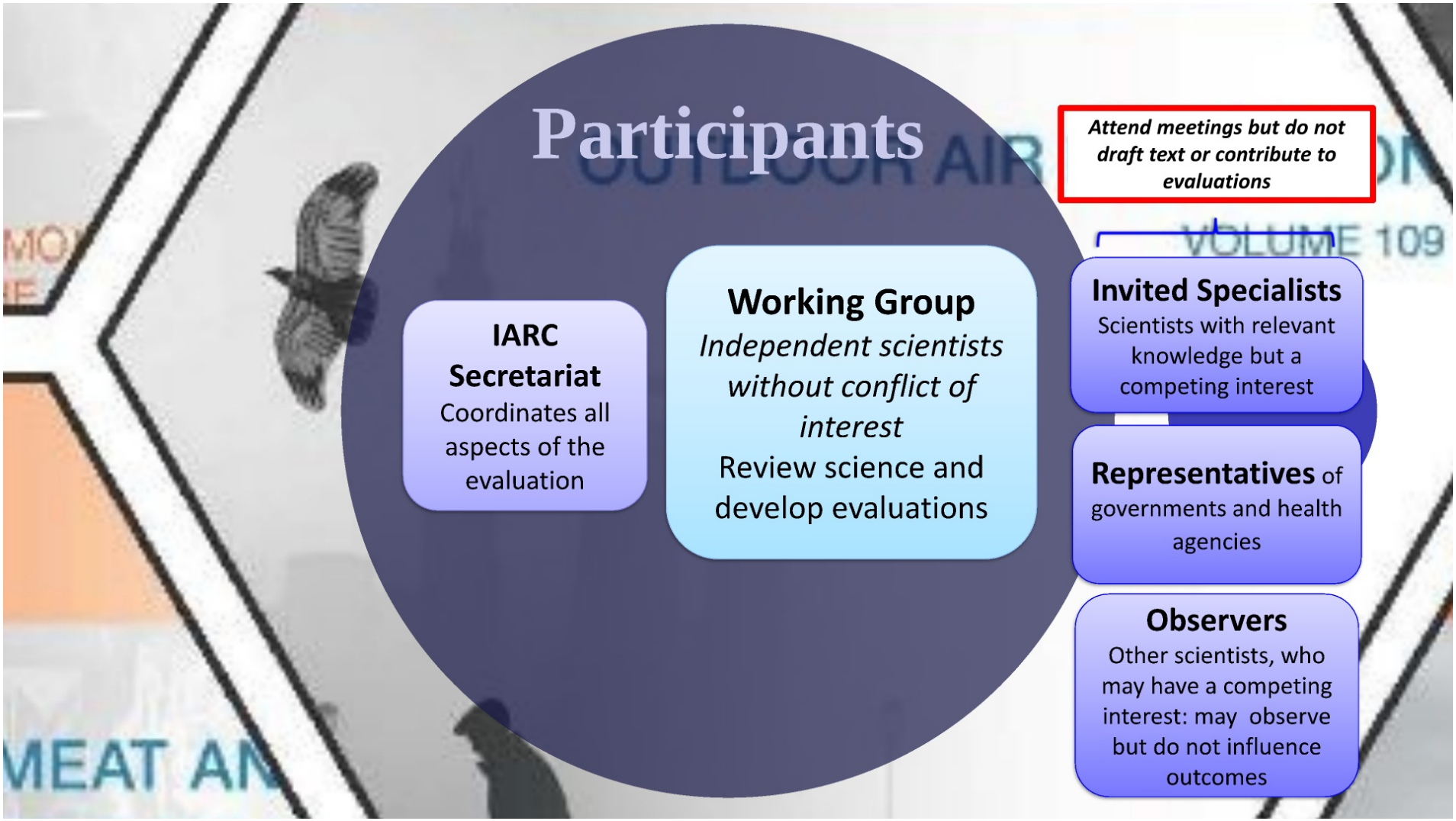

Participants
IARC Secretariat
Coordinates all aspects of the evaluation
Working Group
Independent scientists without conflict of interest
Review science and develop evaluations
Attend meetings but do not draft text or contribute to evaluations
Invited Specialists
Scientists with relevant knowledge but a competing interest
Representatives of governments and health agencies
Observers
Other scientists, who may have a competing interest: may observe but do not influence outcomes

Table 1. Roles of participants at *IARC Monographs* meetings

Category of participant	Role			
	Prepare text, tables, and analyses	Participate in discussions	Participate in evaluations	Eligible to serve as Chair
Working Group members	√	√	√	√
Invited Specialists	√[a]	√		
Representatives of health agencies		√[b]		
Observers		√[b]		
IARC Secretariat	√[c]	√	√[d]	

[a] Only for the section on exposure characterization

[b] Only at times designated by the Meeting Chair and Subgroup Chairs

[c] When needed or requested by the Meeting Chair and Subgroup Chairs

[d] Only for clarifying or interpreting the Preamble

WHO Declaration of Interest for IARC/WHO experts

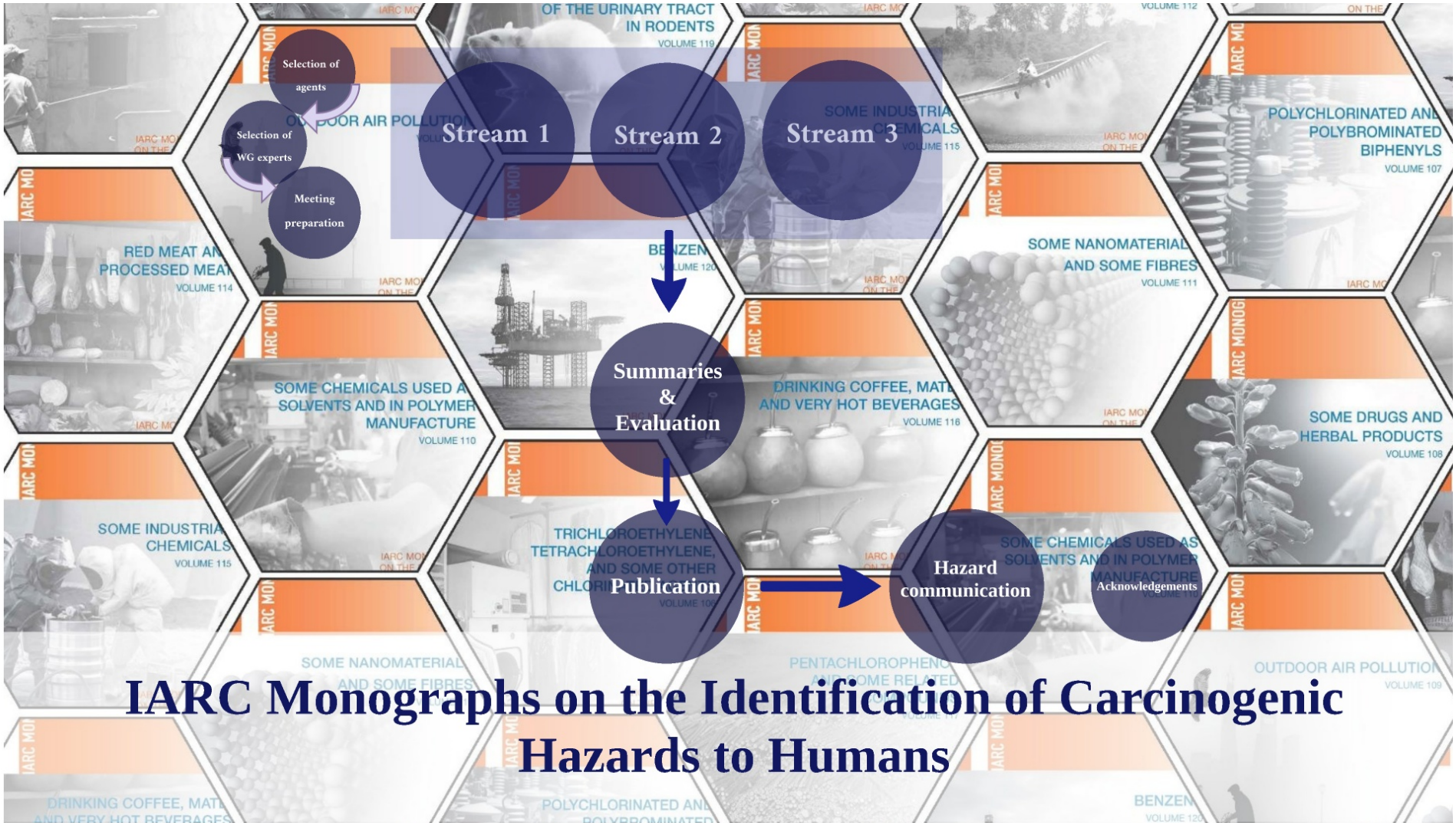
To ensure public confidence that interested parties do not have links to the Working Group, IARC strives to identify and avoid conflicts of interests

- Employment, research, and financial interests are declared before the official invitation, and are updated before the evaluation meeting

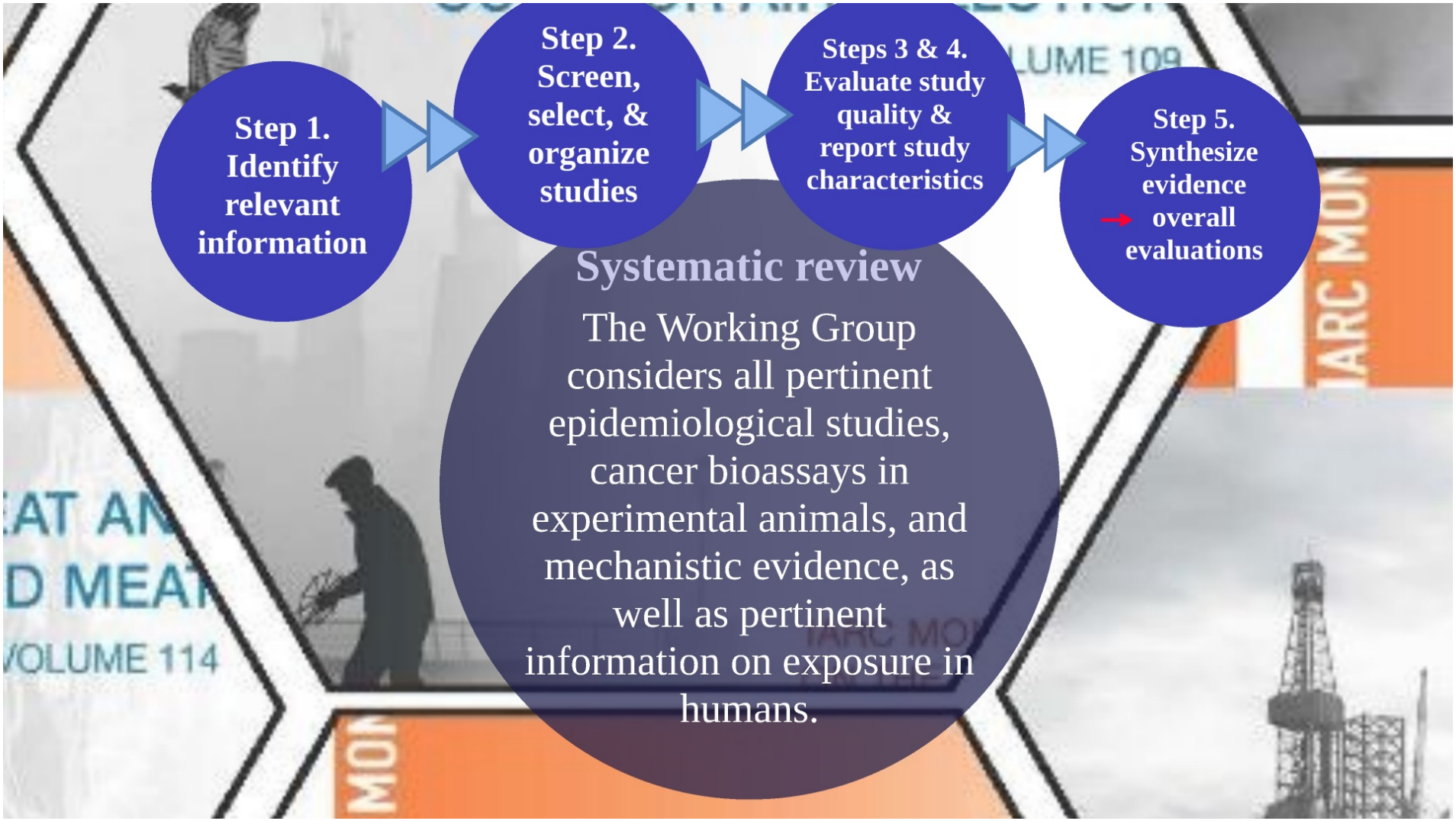
Pertinent interests are disclosed

- To meeting participants
- To the public (http://monographs.iarc.fr/)
- In the published Monograph

Working Group members also complete the conflict-of-interest form required by *The Lancet Oncology*



IARC Monographs on the Identification of Carcinogenic Hazards to Humans


Step 1. Identify relevant information
Step 2. Screen, select, & organize studies
Steps 3 & 4. Evaluate study quality & report study characteristics
Step 5. Synthesize evidence → overall evaluations
Systematic review
The Working Group considers all pertinent epidemiological studies, cancer bioassays in experimental animals, and mechanistic evidence, as well as pertinent information on exposure in humans.

Step 1. Identify relevant information

- Search authoritative databases (PubMed, PubChem)
- Document search terms (developed with libarian, and refined with expert Working Group input)
- Pertinent unpublished studies can be made available through relevant regulatory authorities

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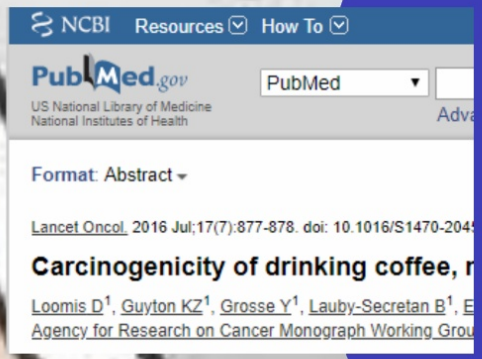

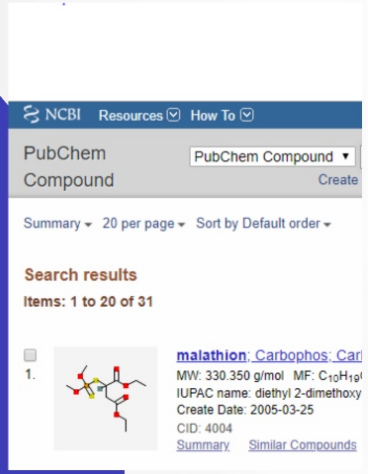

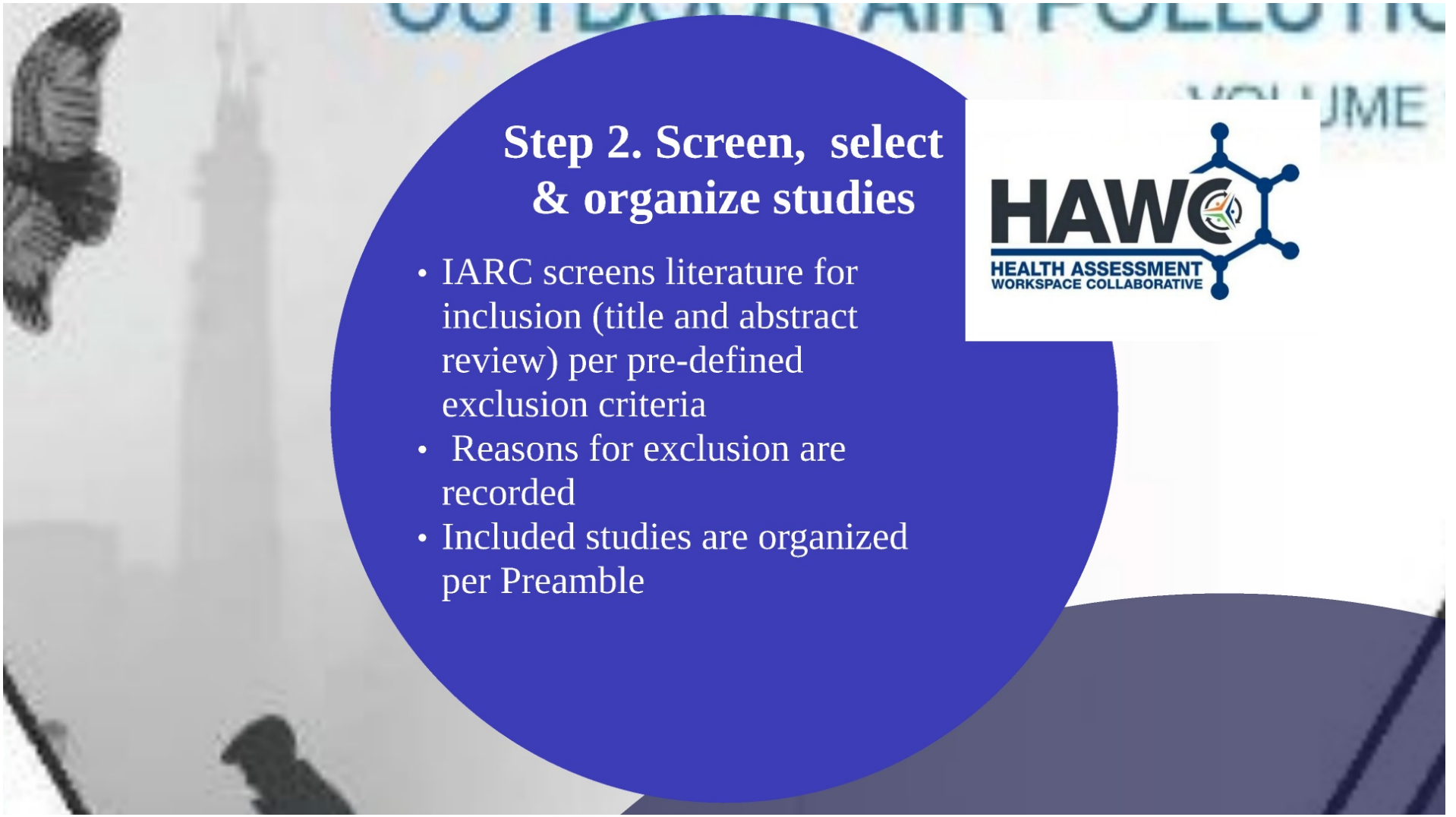

Step 2. Screen, select & organize studies

- IARC screens literature for inclusion (title and abstract review) per pre-defined exclusion criteria
- Reasons for exclusion are recorded
- Included studies are organized per Preamble

HAWC
HEALTH ASSESSMENT WORKSPACE COLLABORATIVE

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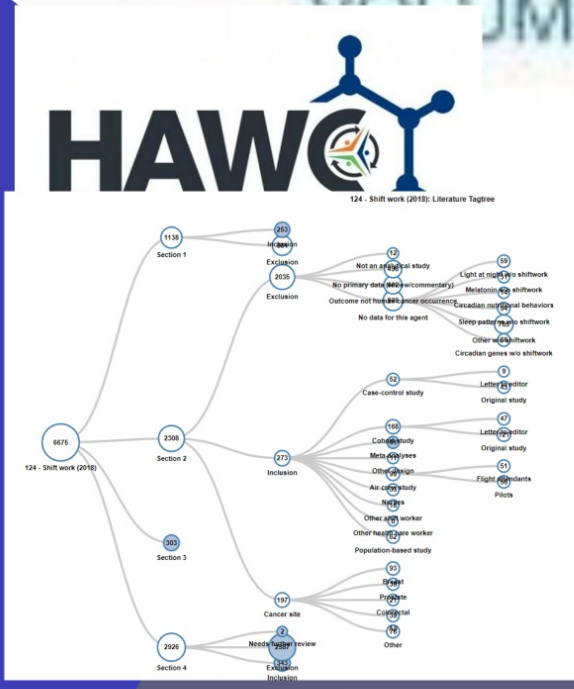

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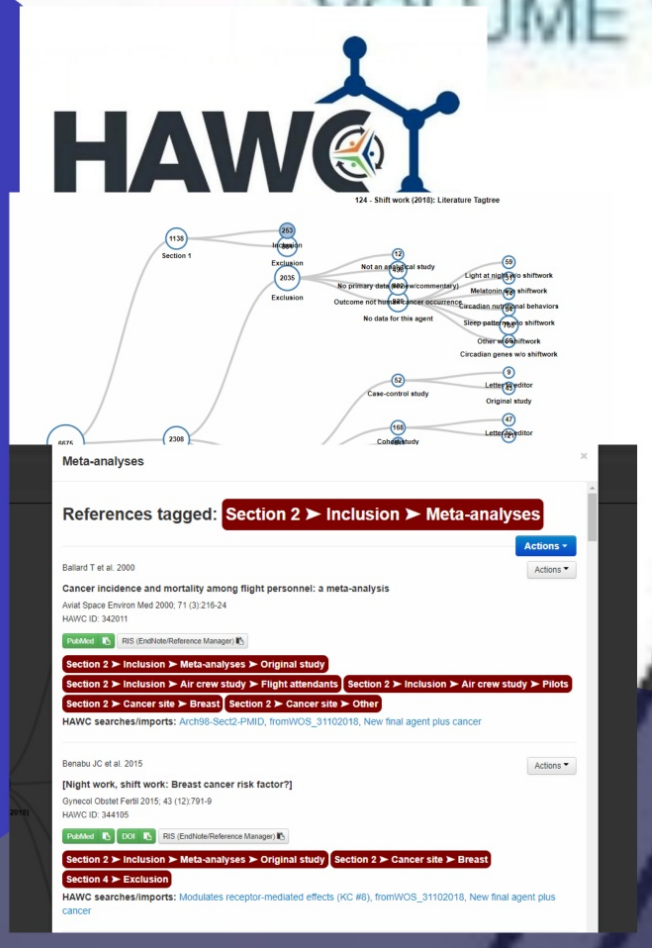

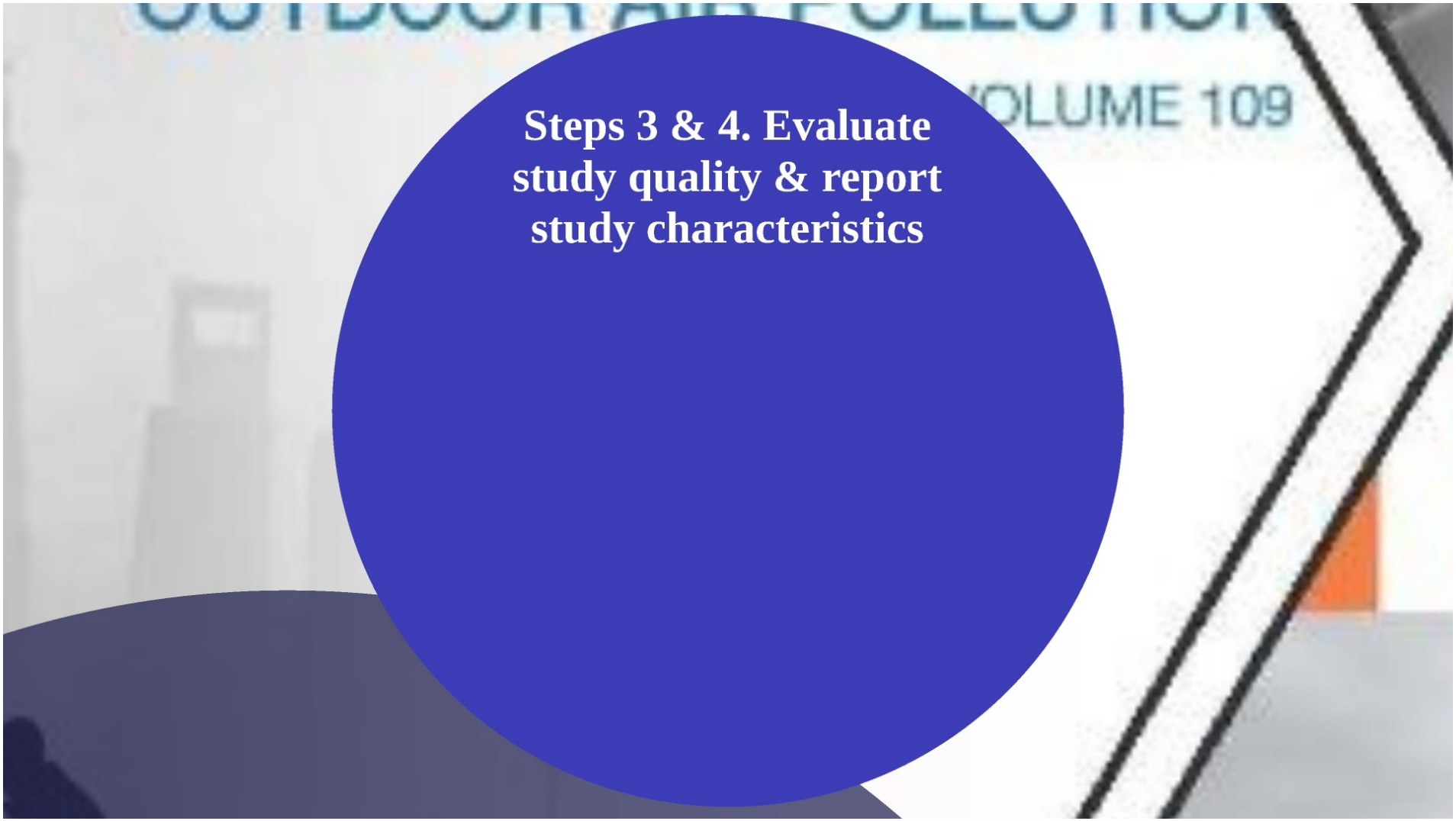
Steps 3 & 4. Evaluate study quality & report study characteristics

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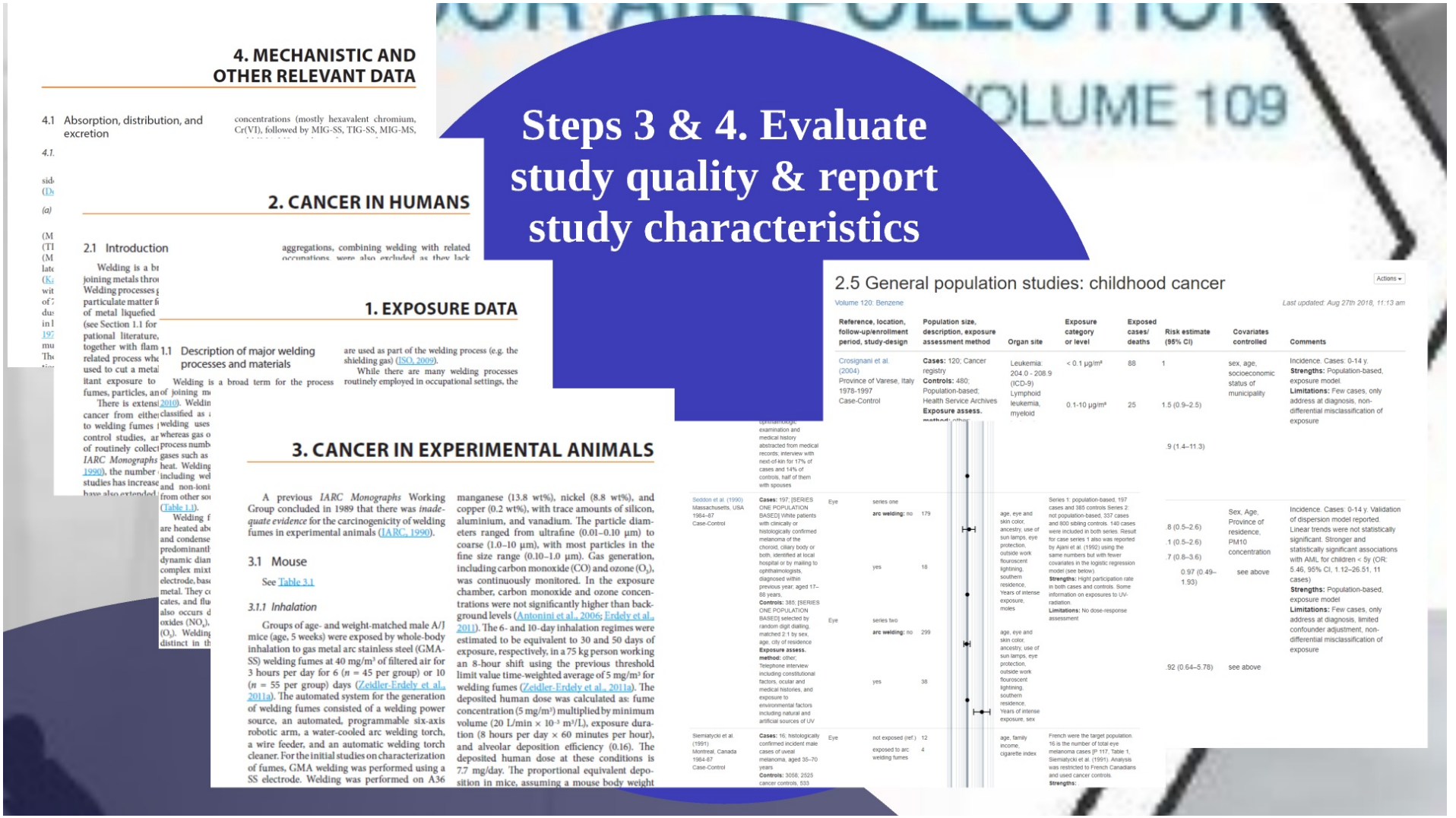
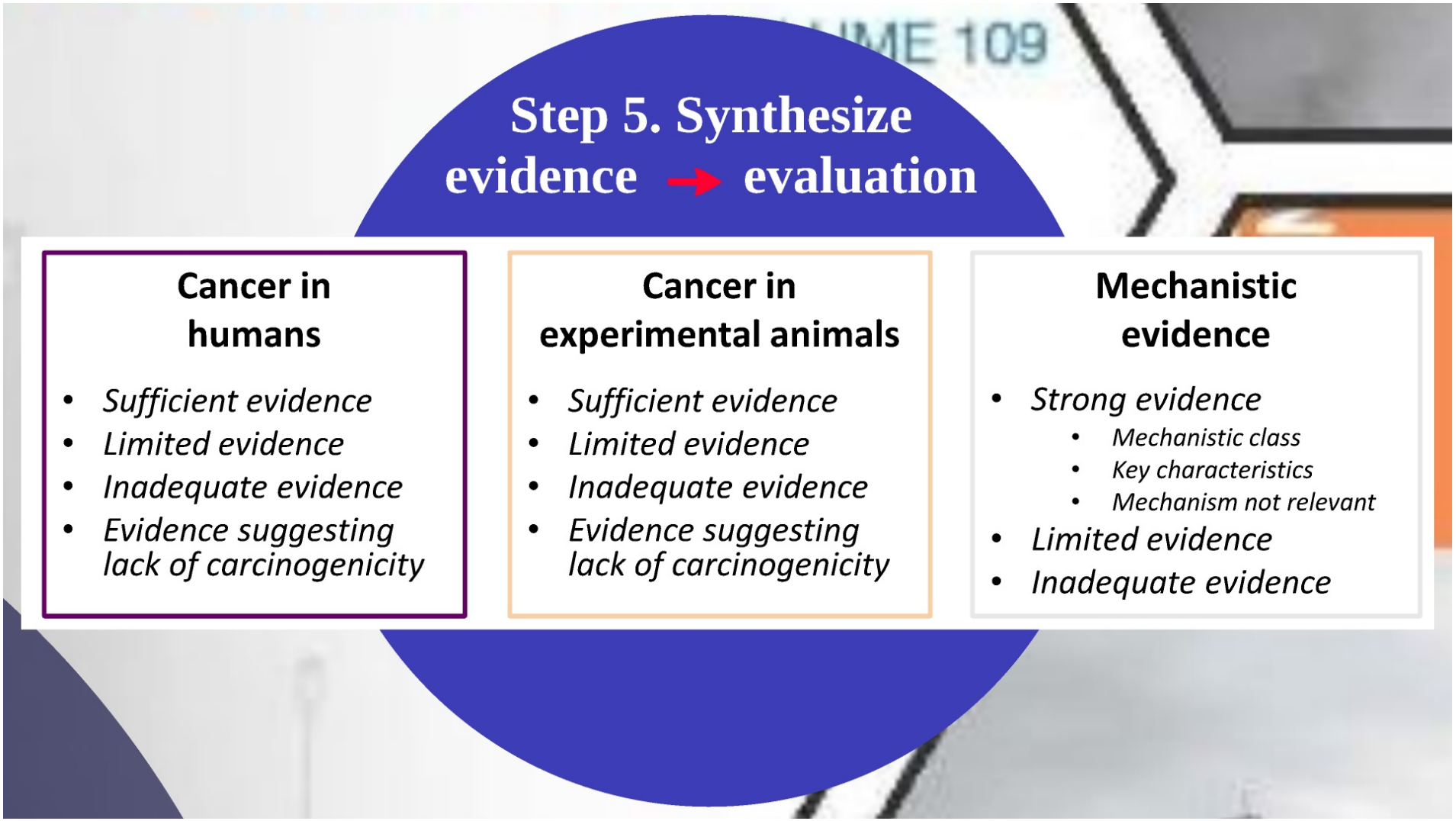
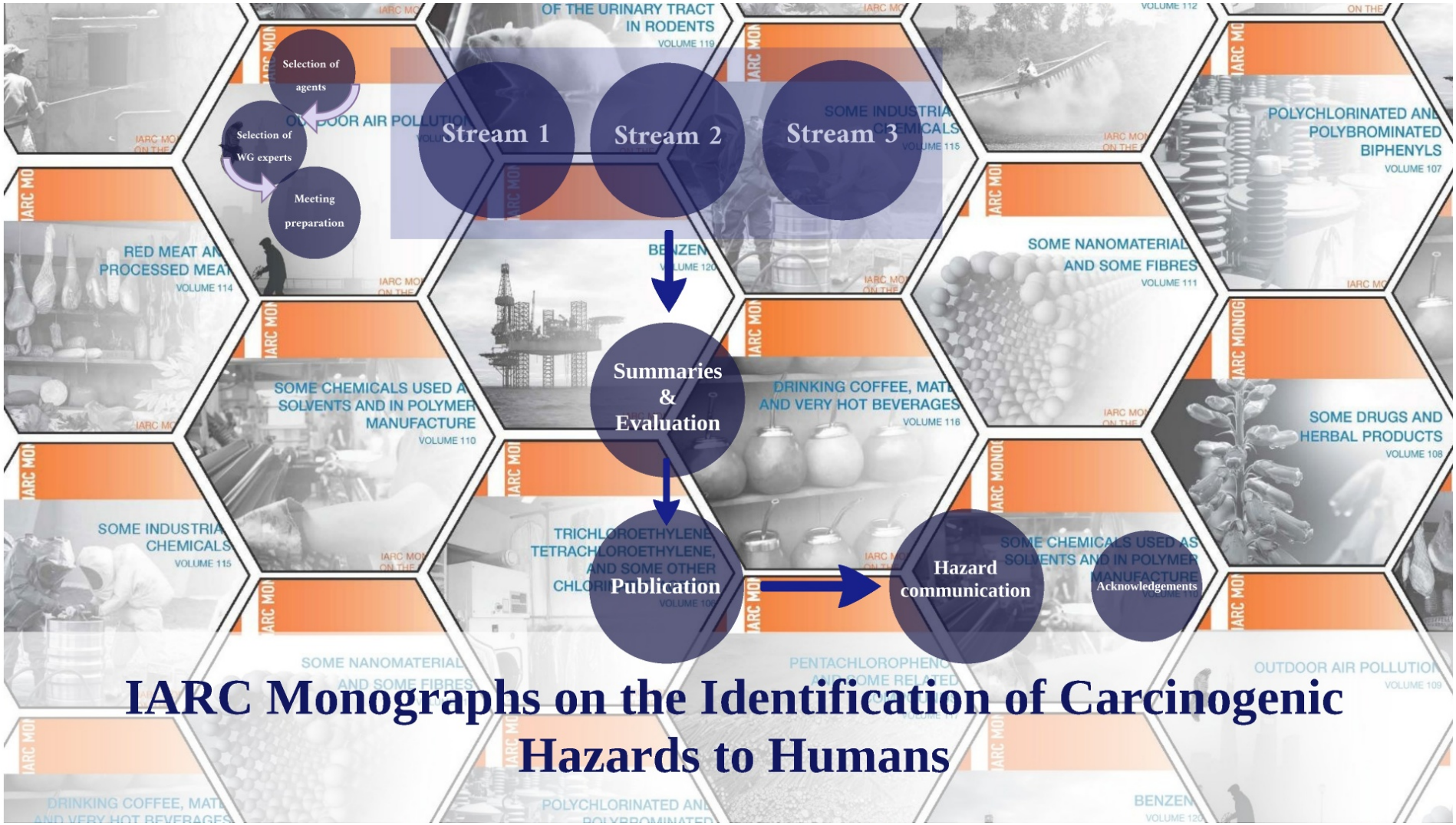
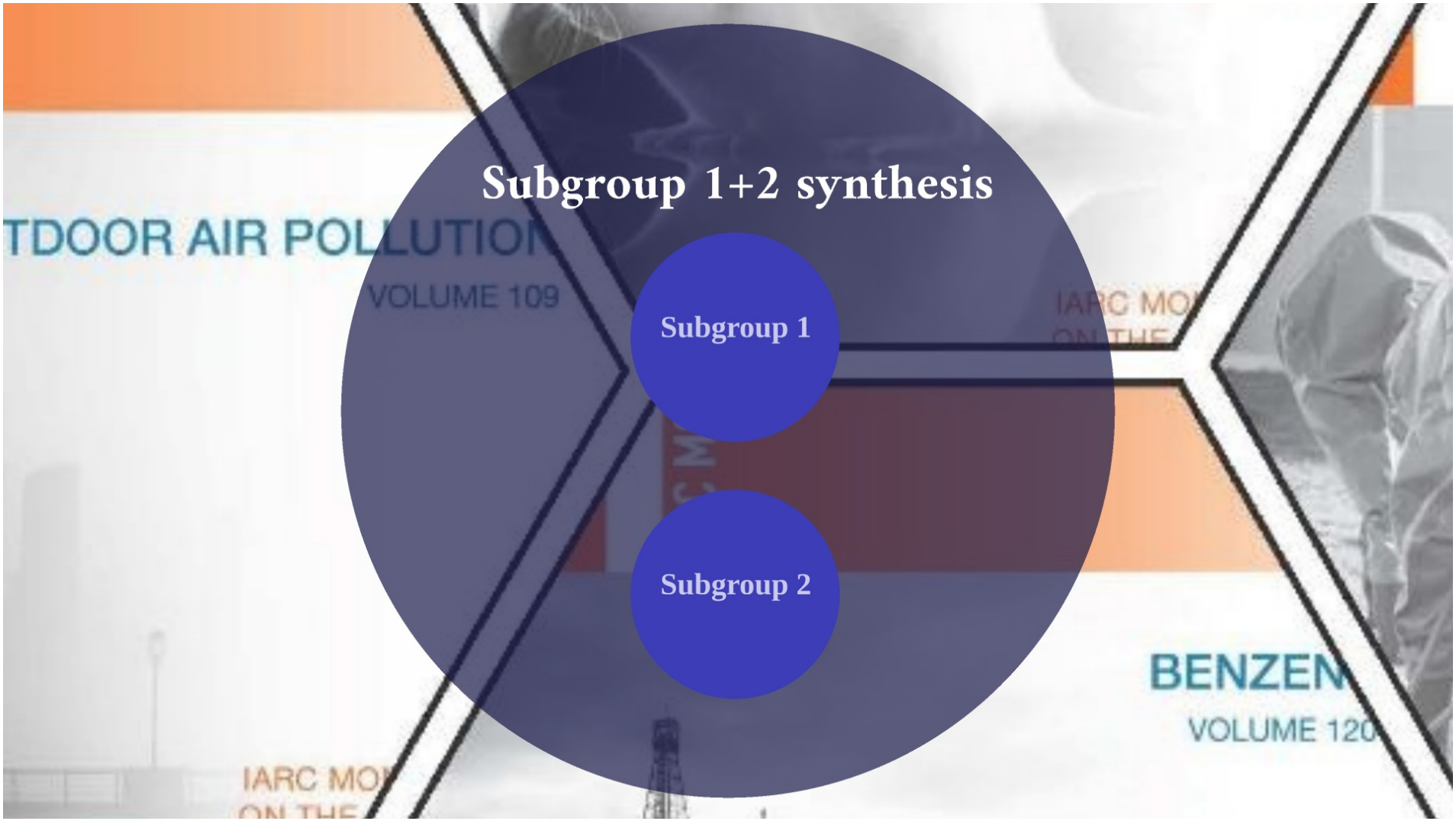
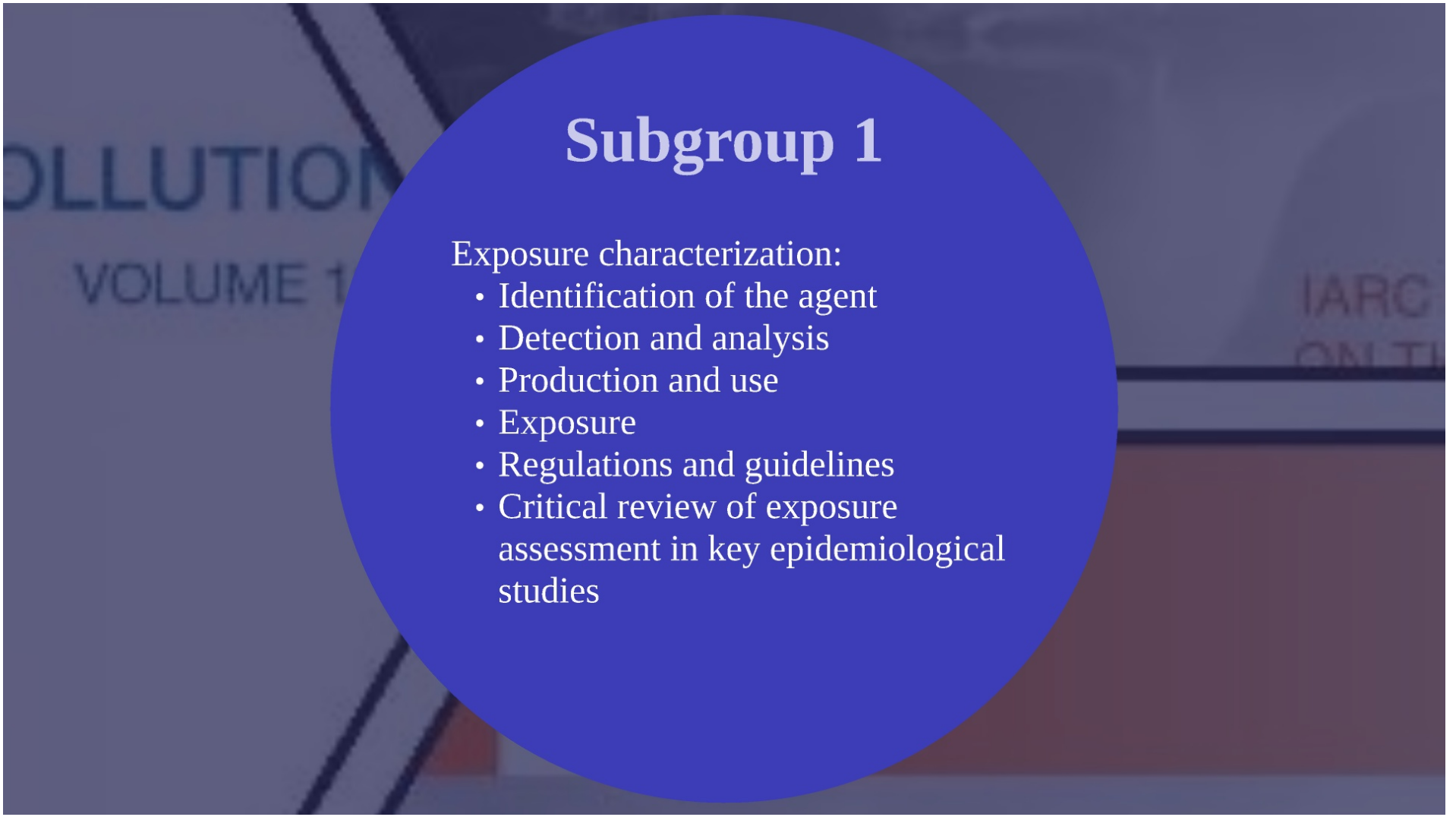



Step 5. Synthesize evidence → evaluation
Cancer in humans
Sufficient evidence
Limited evidence
Inadequate evidence
Evidence suggesting lack of carcinogenicity
Cancer in experimental animals
Sufficient evidence
Limited evidence
Inadequate evidence
Evidence suggesting lack of carcinogenicity
Mechanistic evidence
Strong evidence
Mechanistic class
Key characteristics
Mechanism not relevant
Limited evidence
Inadequate evidence



IARC Monographs on the Identification of Carcinogenic Hazards to Humans


Subgroup 1+2 synthesis
Subgroup 1
Subgroup 2



Subgroup 1

Exposure characterization:

- Identification of the agent
- Detection and analysis
- Production and use
- Exposure
- Regulations and guidelines
- Critical review of exposure assessment in key epidemiological studies

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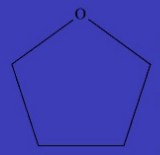
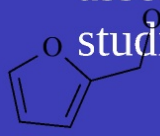
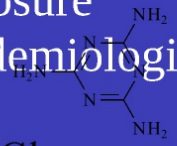
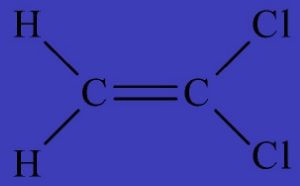


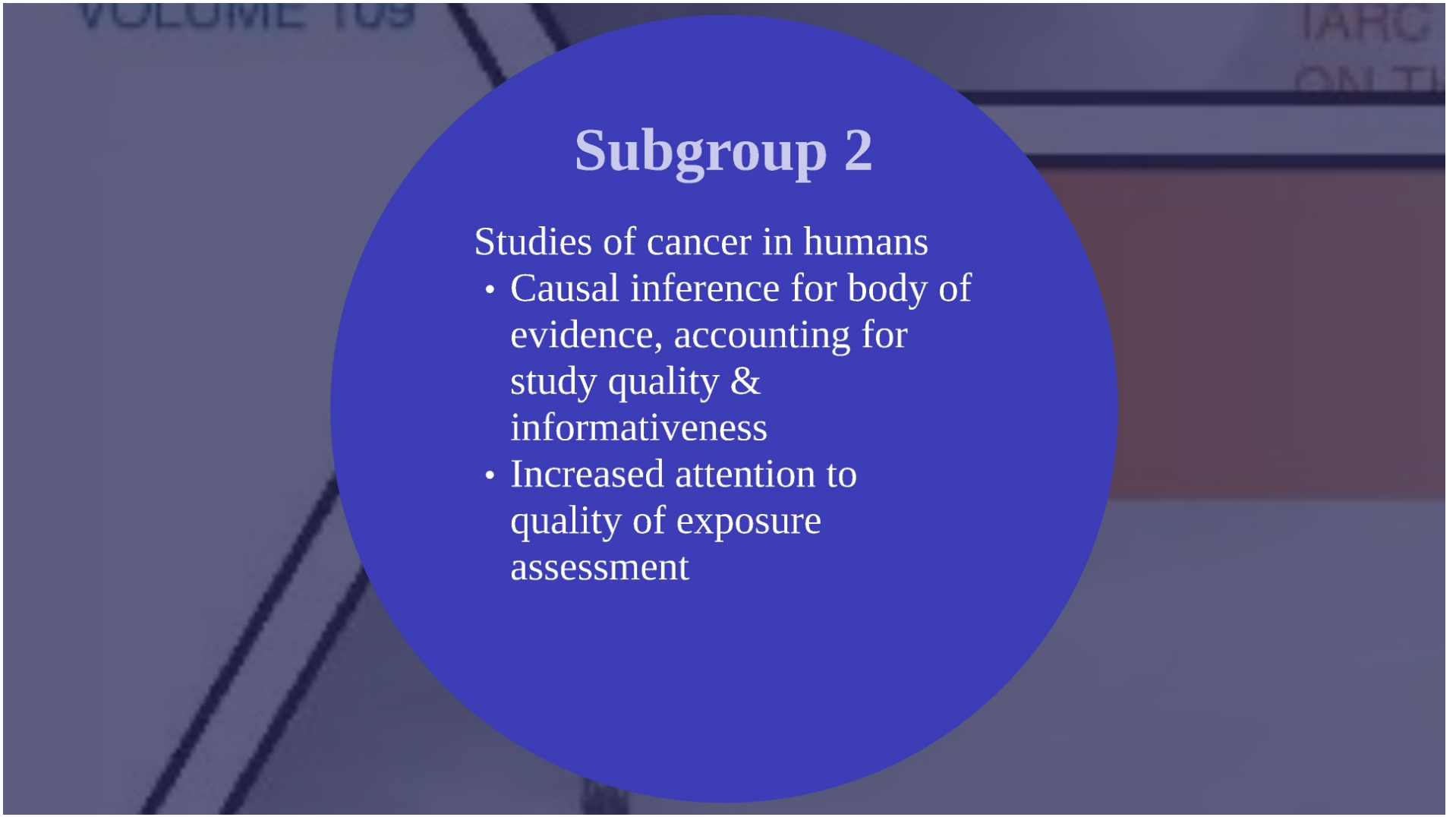






What's new?

- Revised Preamble
  - Reinforces descriptive aims
  - Calls for enhanced LMIC coverage
  - New section on critical review of exposure methods in epidemiologic studies of cancer and mechanisms



Subgroup 2

Studies of cancer in humans

- Causal inference for body of evidence, accounting for study quality & informativeness
- Increased attention to quality of exposure assessment

Subgroup 2

What's new?

- Enhanced use of systematic review tools in evaluating studies
- Explicit consideration of study informativeness as well as quality in weighing evidence
- Emphasis on *impact* of bias and confounding

of cancer in humans
inference for body of
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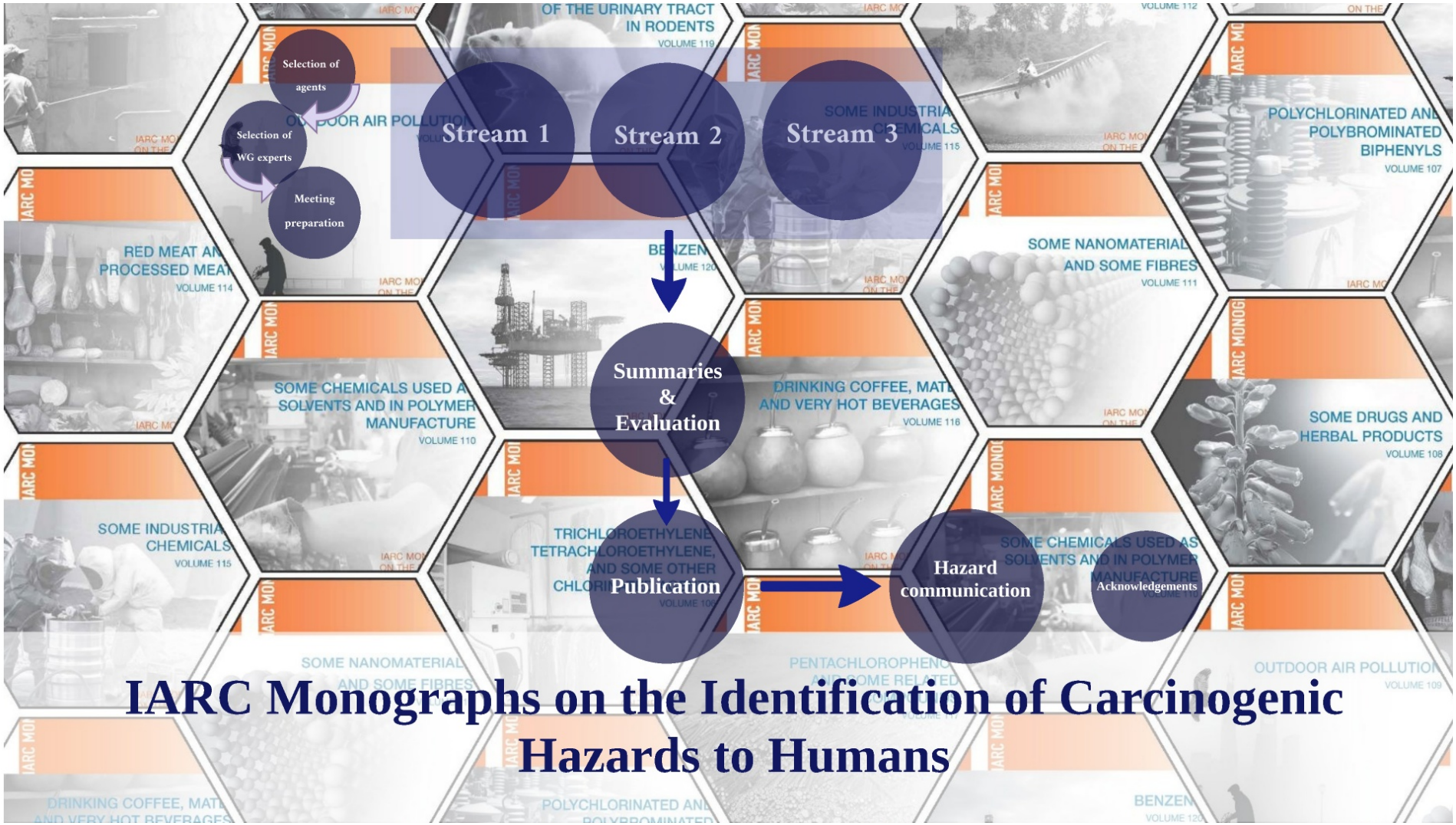
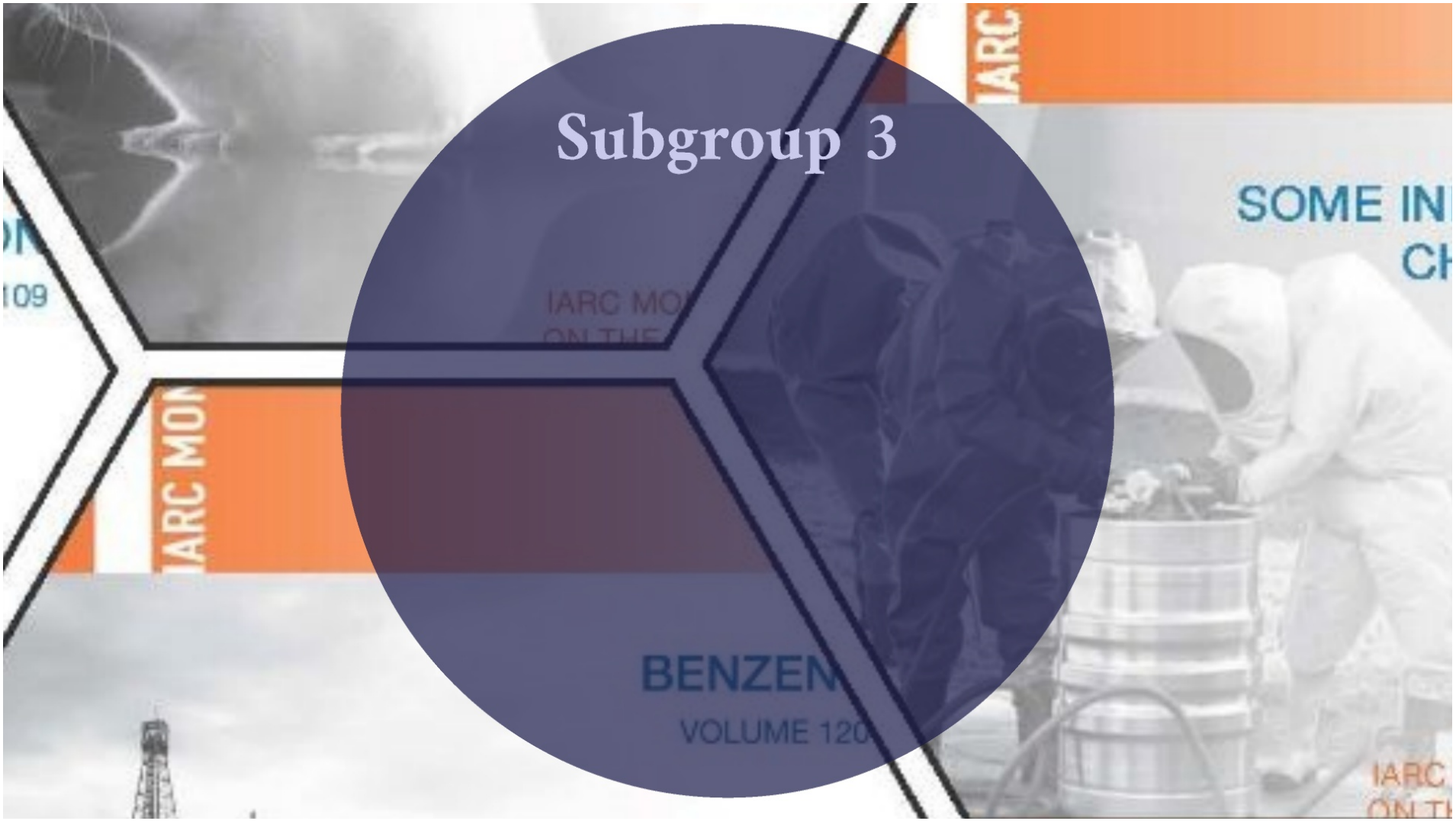

Selection of agents
Selection of WG experts
Meeting preparation
Stream 1
Stream 2
Stream 3
Summaries & Evaluation
Publication
Hazard communication
Acknowledgements
IARC Monographs on the Identification of Carcinogenic Hazards to Humans

Subgroup 3

Cancer in experimental animals

- Evidence of an increased incidence of malignant neoplasms (or of an appropriate combination of benign and malignant neoplasms) in high-quality studies


Subgroup 3
IARC MO
BENZEN
VOLUME 120
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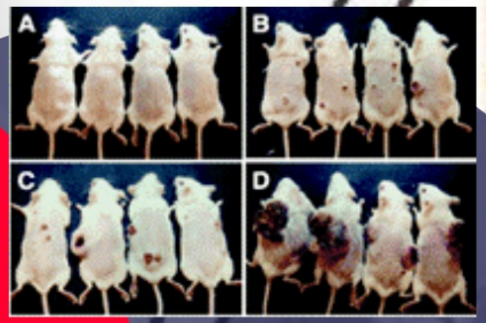
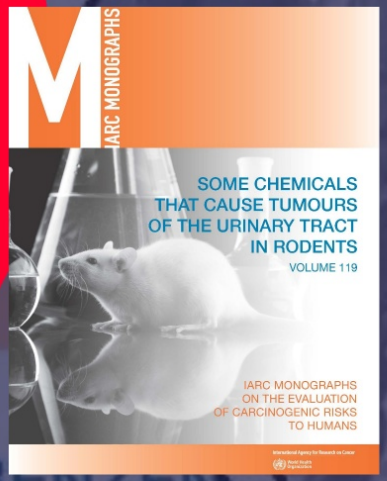
IARC

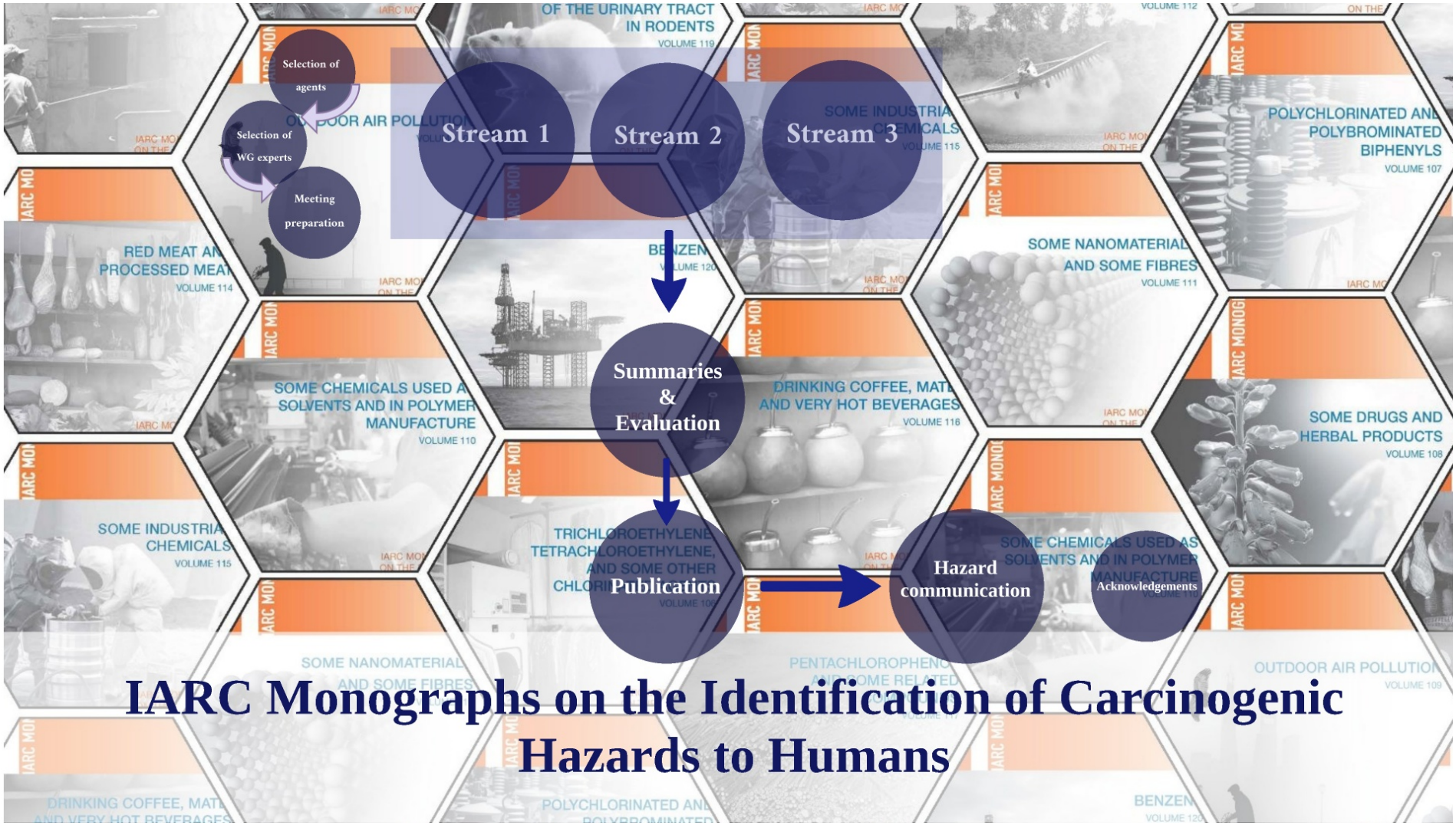
What's new?

Eligibility of genetically modified animals (*Preamble*, 2019):

- Tg.AC (v-Ha-*Ras* oncogene), *Trp53*+/-, or *ras*H2 (human *HRAS* proto-oncogene) mice
- Mice with targeted expression of viral genes (to animal tissue from which human cancer arises)
- Humanized mice implanted with human cells normally infected by the virus



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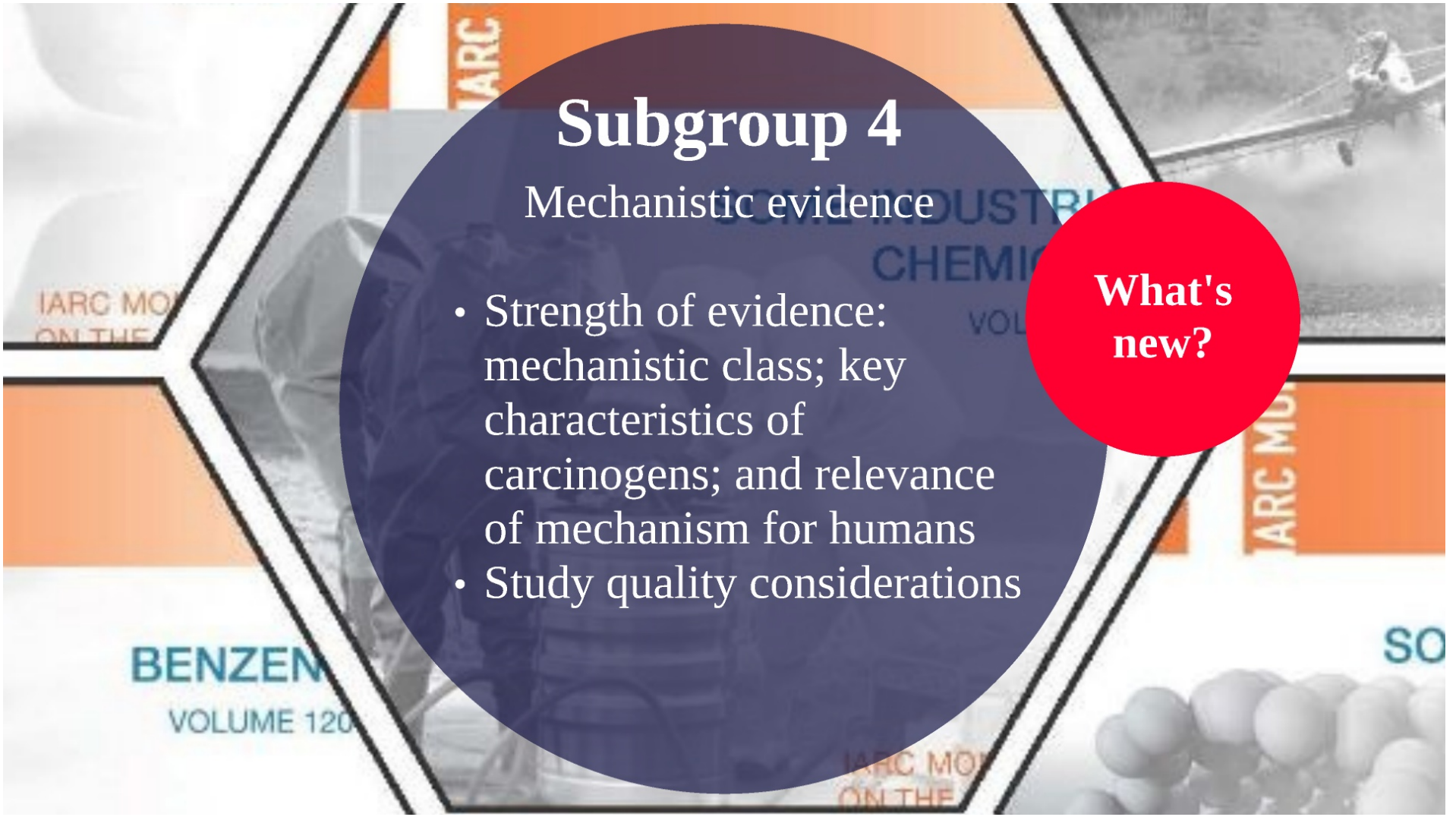
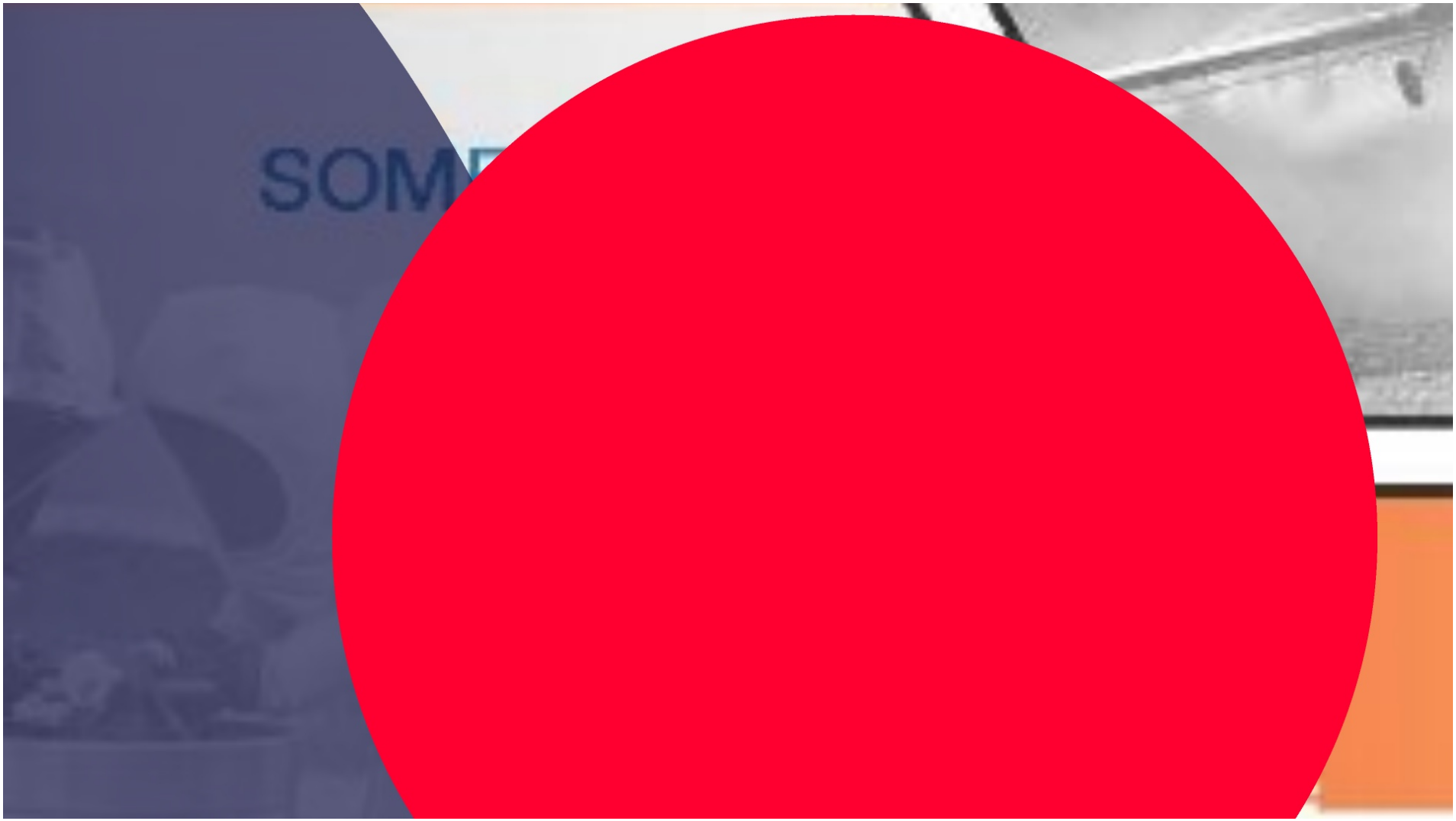

Subgroup 4
Mechanistic evidence
• Strength of evidence: mechanistic class; key characteristics of carcinogens; and relevance of mechanism for humans
• Study quality considerations
What's new?
BENZEN
VOLUME 120

Mechanistic Data: *Challenges*

IARC Monographs
Volume 100

- How to search systematically for relevant mechanisms?
- How to bring uniformity across assessments?
- How to analyze the voluminous mechanistic database efficiently?
- How to avoid bias towards favored mechanisms?



10 Key Characteristics of carcinogens:
1. Is electrophilic or can be metabolically activated
2. Is genotoxic
3. Alters DNA repair or causes genomic instability
4. Induces epigenetic alterations
5. Induces oxidative stress
6. Induces chronic inflammation
7. Is immunosuppressive
8. Modulates receptor-mediated effects
9. Causes immortalization
10. Alters cell proliferation, cell death, or nutrient supply

- Chemical and biological properties of established human carcinogens
- Data on key characteristics can provide evidence of carcinogenicity
- Used to assemble data relevant to mechanisms of carcinogens– without needing an *a priori* hypothesis of the mechanism

- Smith MT, Guyton KZ, Gibbons CF, Fritz JM, Portier CJ, Rusyn I, DeMarini DM, Caldwell JC, Kavlock RJ, Lambert PF, Hecht SS, Bucher JR, Stewart BW, Baan RA, Cogliano VJ, Straif K (2016); Key characteristics of carcinogens as a basis for organizing data on mechanisms of carcinogenesis. *Env Health Persp.*, 124(6):713-21.
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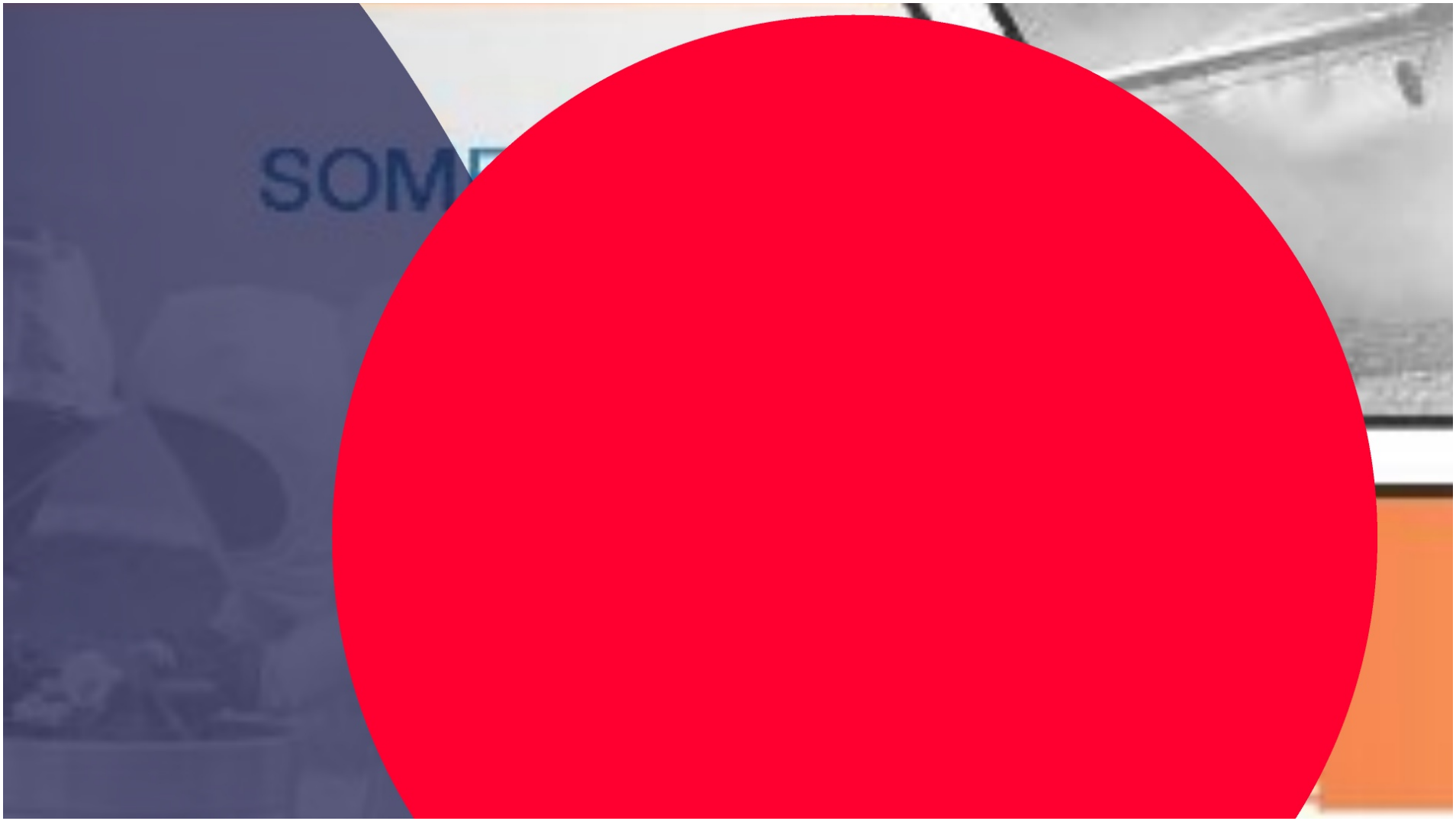
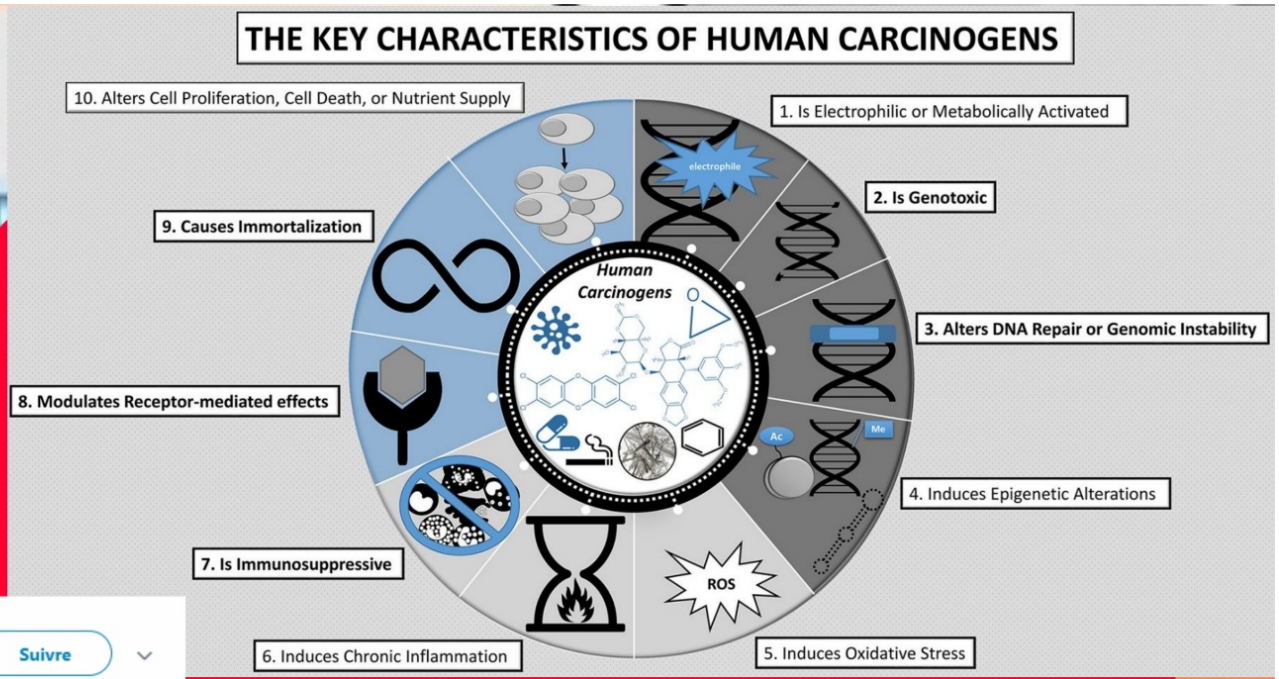
- IARC Scientific Publication No. 165: Tumour Site Concordance and Mechanisms of Carcinogenesis (2019). https://publications.iarc.fr/578.
- Smith MT, Guyton KZ (2020). Identifying carcinogens from 10 key characteristics: a new approach based on mechanisms. In: Wild CP, Weiderpass E, Stewart BW, editors. World Cancer Report: Cancer Research for Cancer Prevention. http://publications.iarc.fr/586.



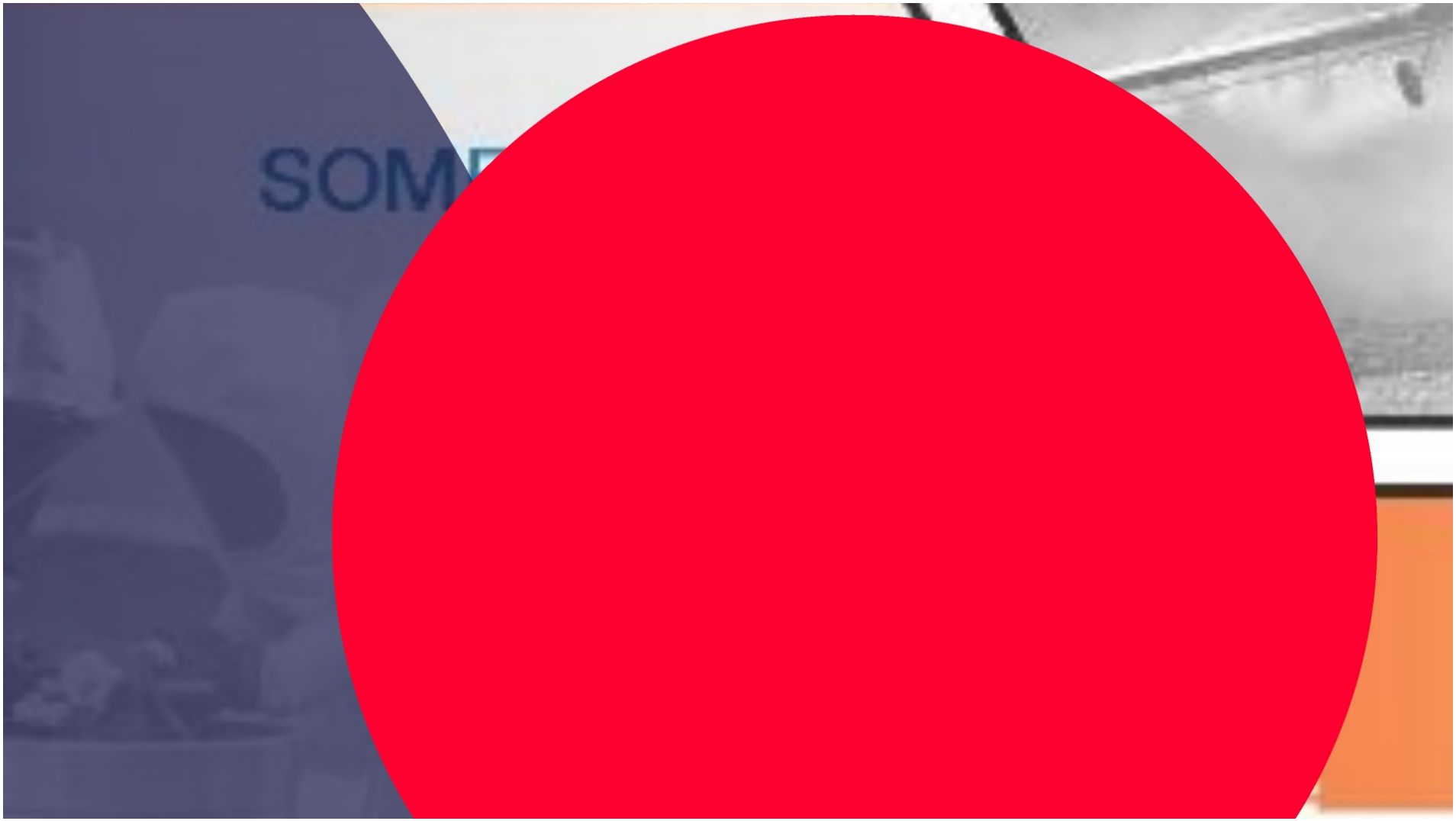


IARC
@IARCWHO

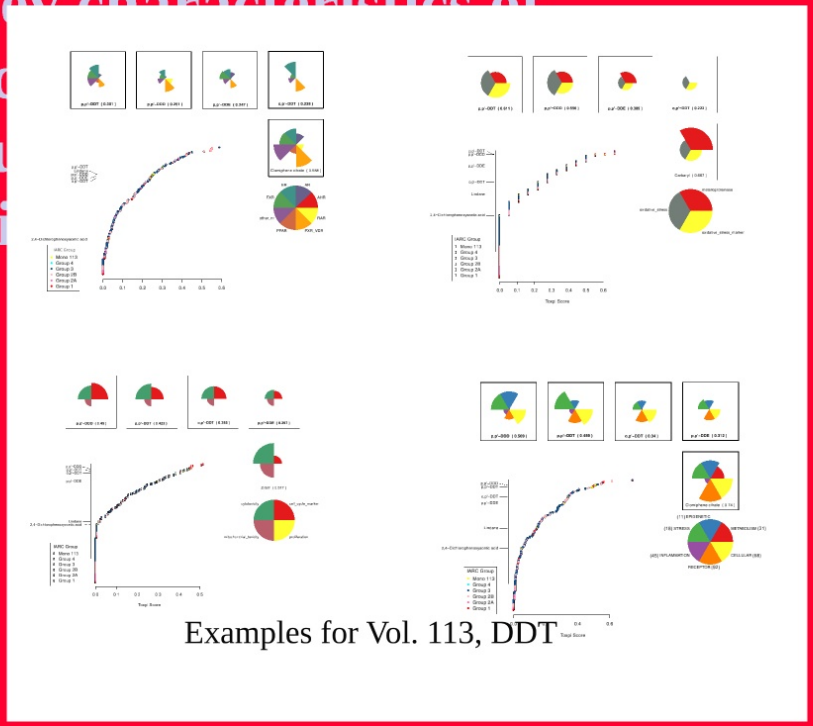
Suivre

What causes #cancer? An IARC collaboration offers a fresh approach to this tough question. The key characteristics of carcinogens help ID new cancer causes & make sense of suspected carcinogens. Read the article in @ChemResTox about progress & next steps

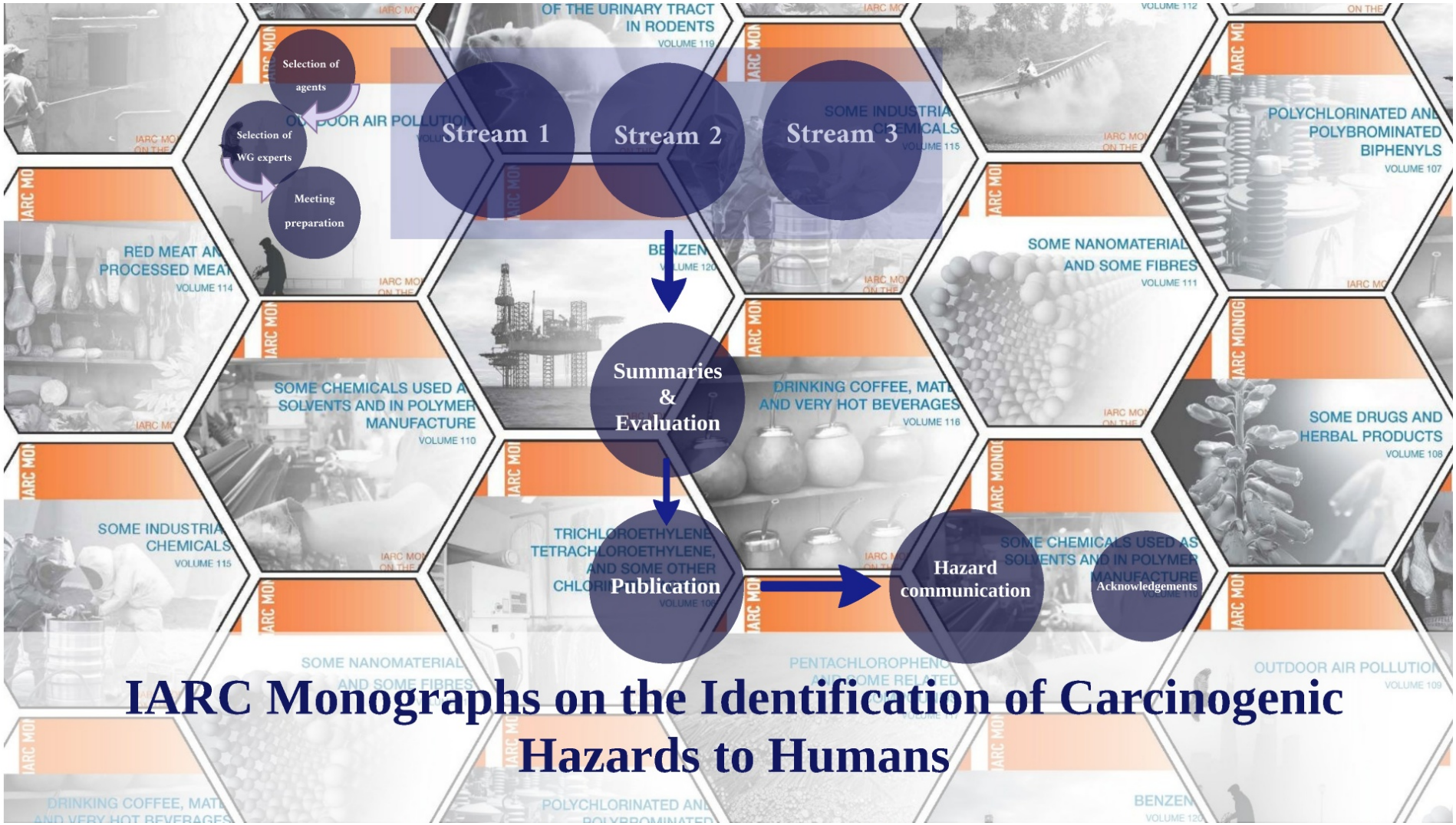
- Guyton KZ, Rieswijk L, Wang A, Chiu WA, Smith MT (2018); Key characteristics approach to carcinogenic hazard identification. *Chemical Research in Toxicology,* 31(12): 1290-1292.
- Smith MT, Guyton KZ, Kleinstreuer N, Borrel A, Cardenas A, Chiu WA, Felsher DW, Gibbons CF, Goodson WH, Houck KA, Kane A, La Merrill MA, Lebrec H, Lowe L, McHale CM, Minocherhomji S, Rieswijk L, Sandy MS, Sone H, Wang A, Zhang L, Zeise L, Fielden M (2020). The key characteristics of carcinogens: relationship to the hallmarks of cancer, relevant biomarkers, and assays to measure them. *Cancer Epidemiol Biomarkers Prev*. 29(10):1887-1903.
- For more on the key characteristics of hazardous exposures, see: https://keycharacteristics.org/




Key characteristics of carcinogens can be used to interrogate high-throughput and high-content databases



Examples for Vol. 113, DDT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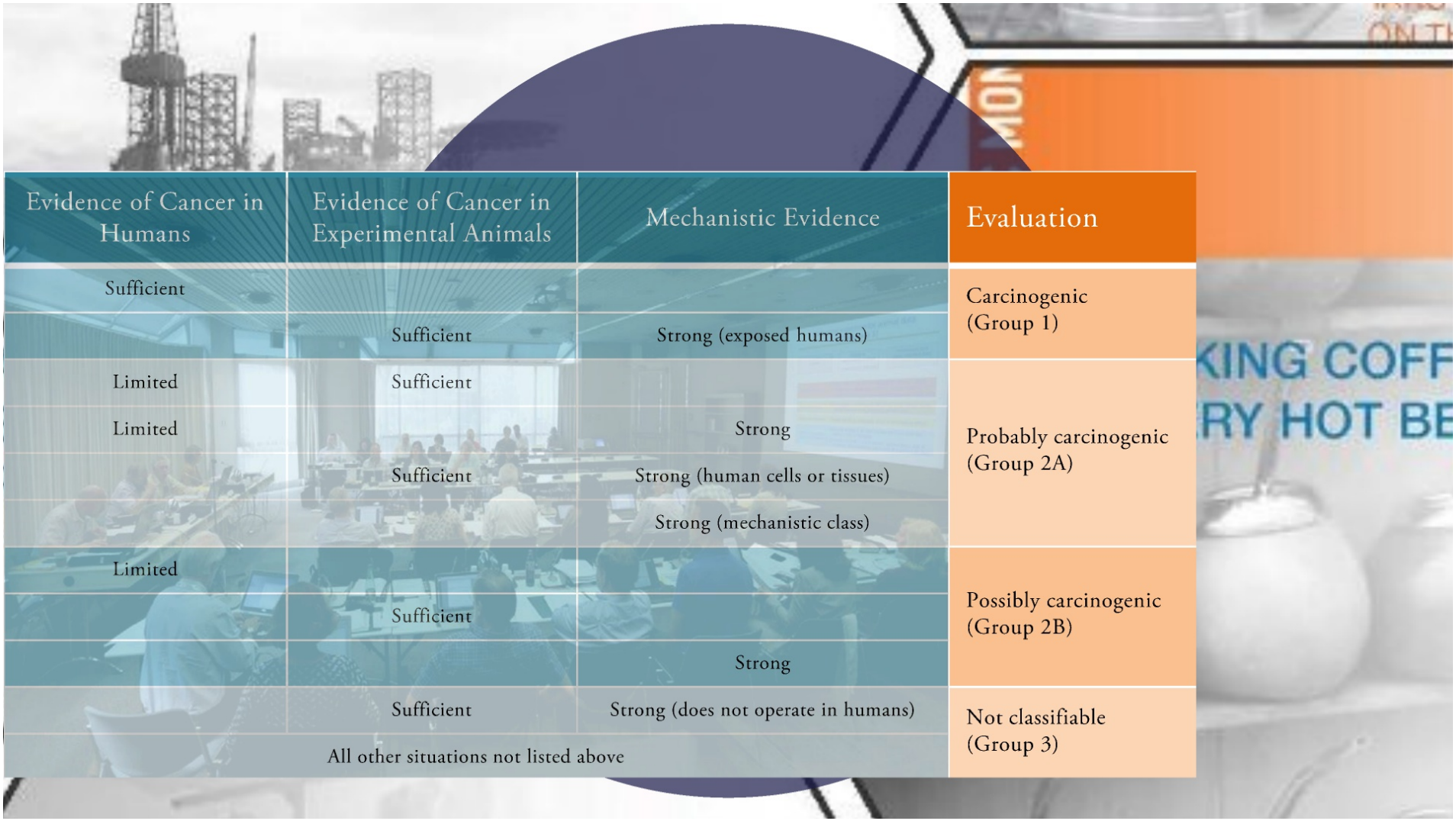

Evidence of Cancer in Humans	Evidence of Cancer in Experimental Animals	Mechanistic Evidence	Evaluation
Sufficient			Carcinogenic (Group 1)
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Limited	Sufficient		Probably carcinogenic (Group 2A)
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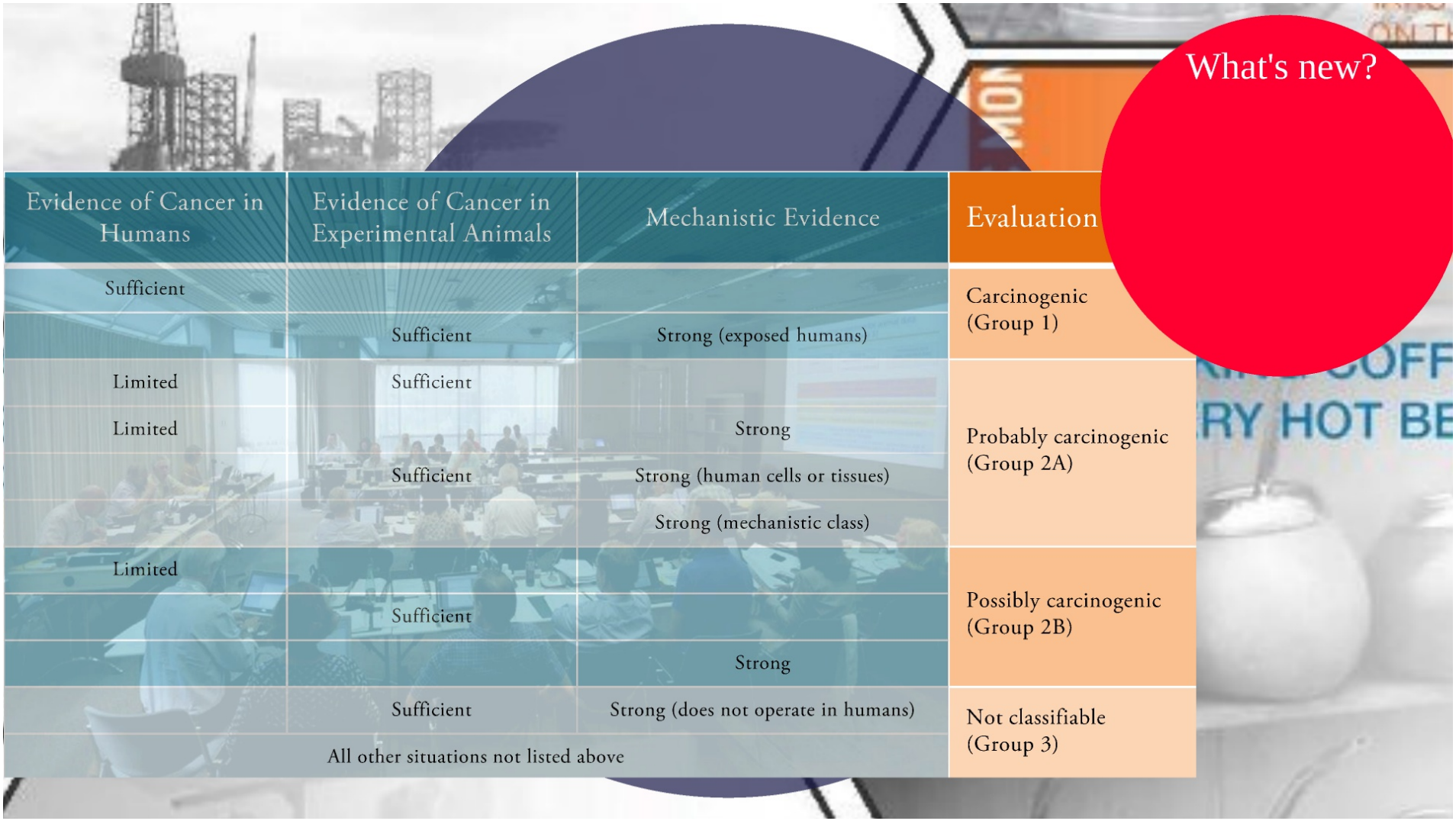
	Sufficient	Strong (human cells or tissues)	
		Strong (mechanistic class)	
Limited			Possibly carcinogenic (Group 2B)
	Sufficient		
		Strong	
	Sufficient	Strong (does not operate in humans)	Not classifiable (Group 3)
All other situations not listed above			



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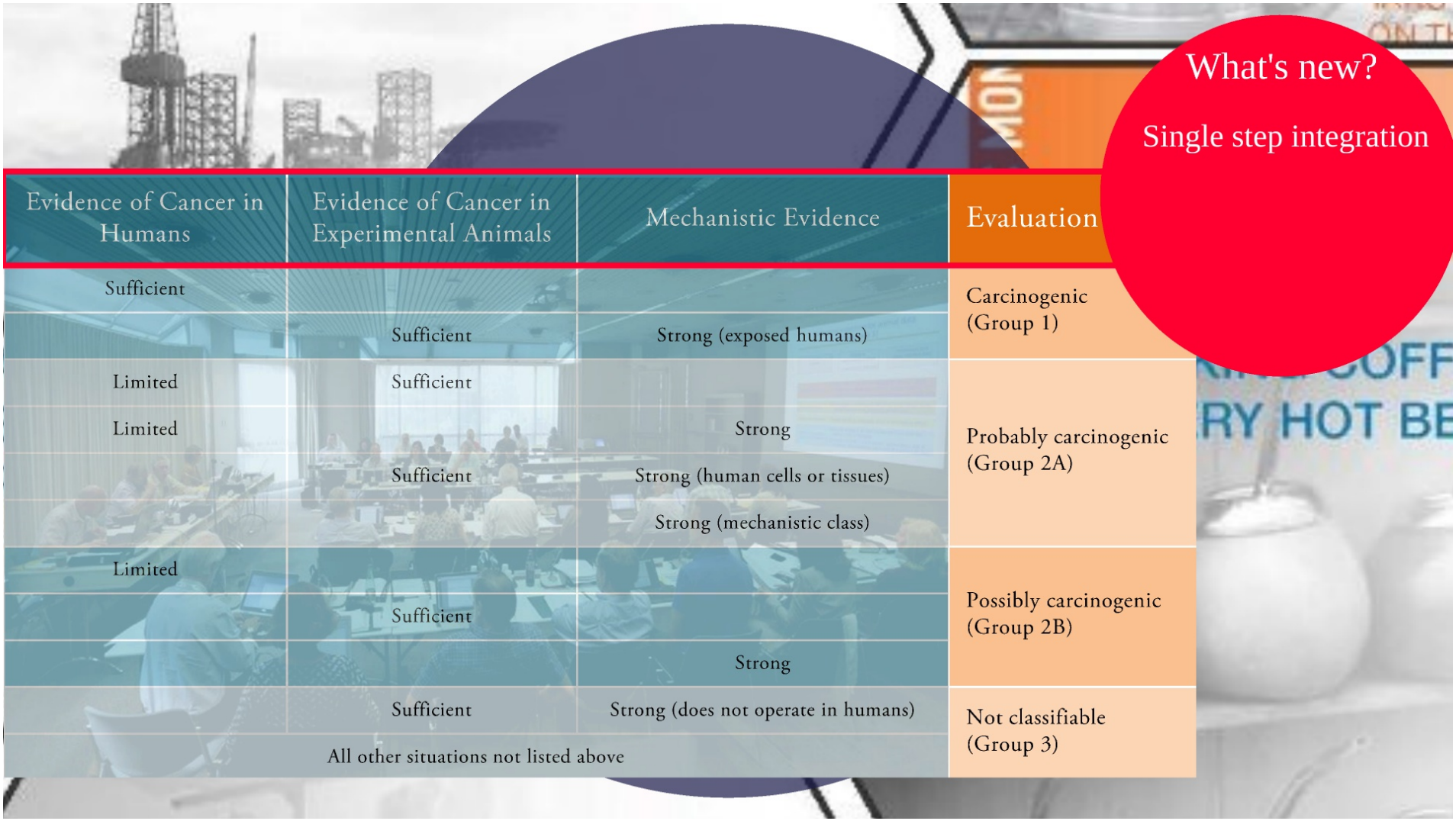

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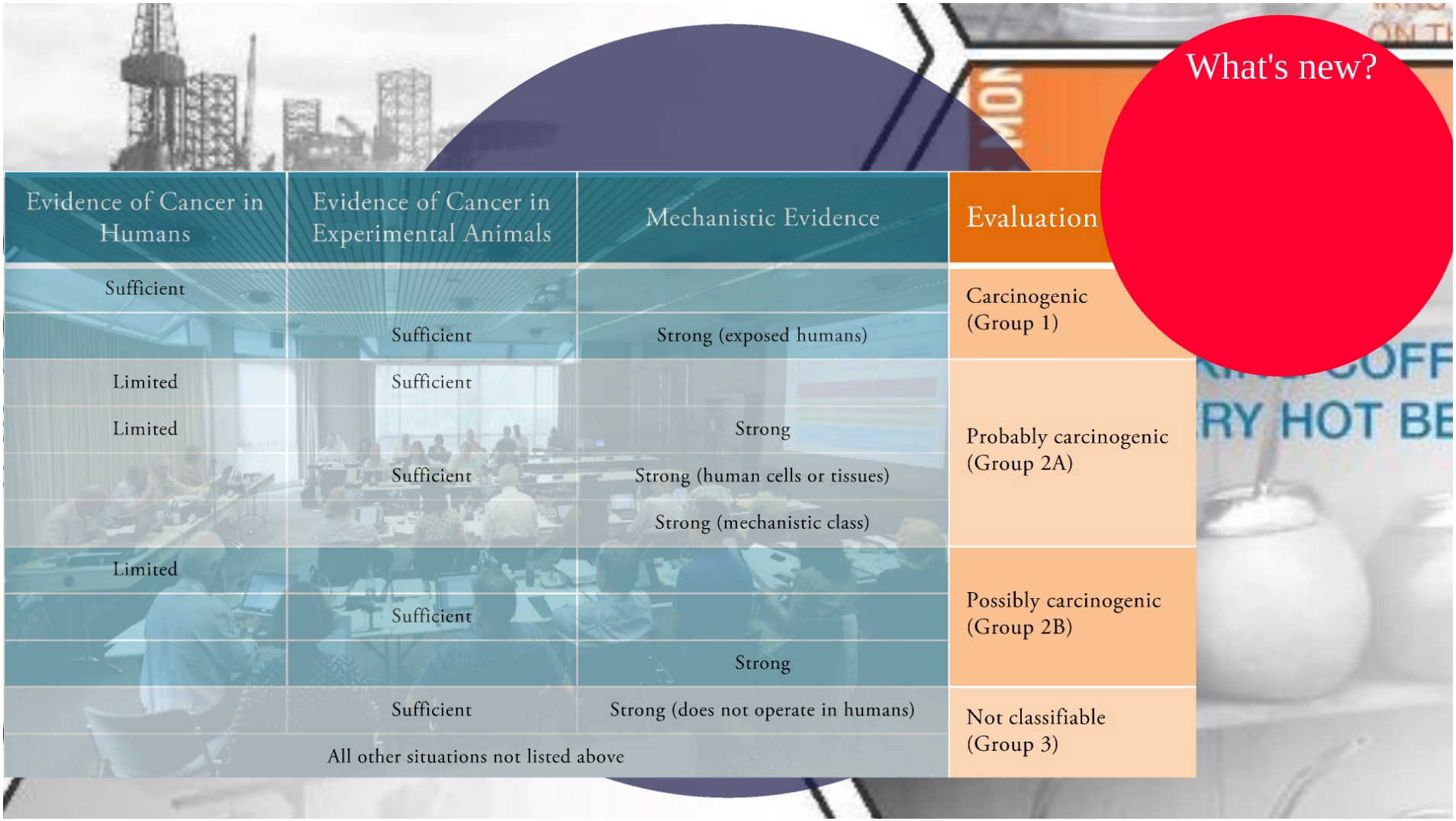

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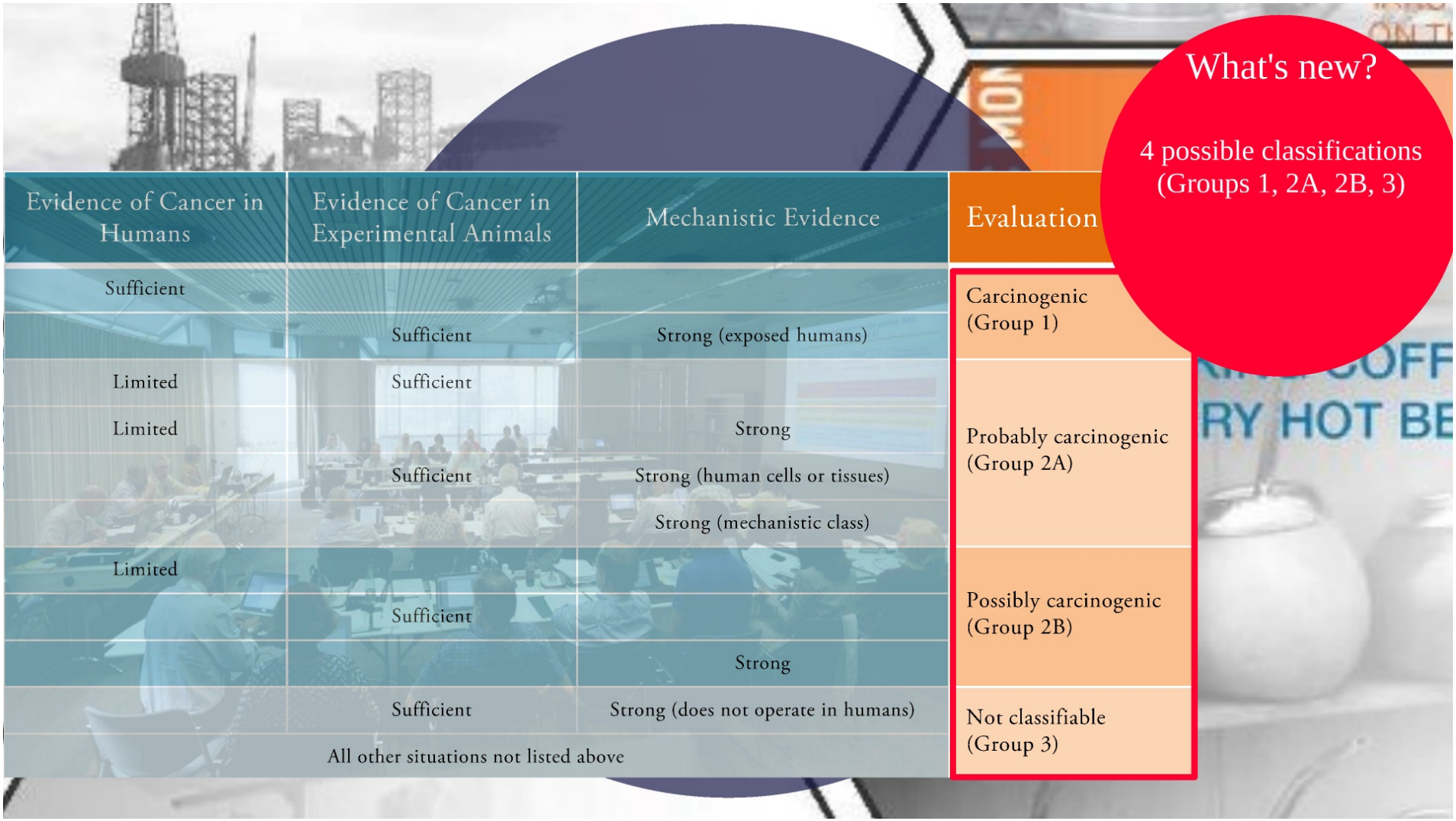

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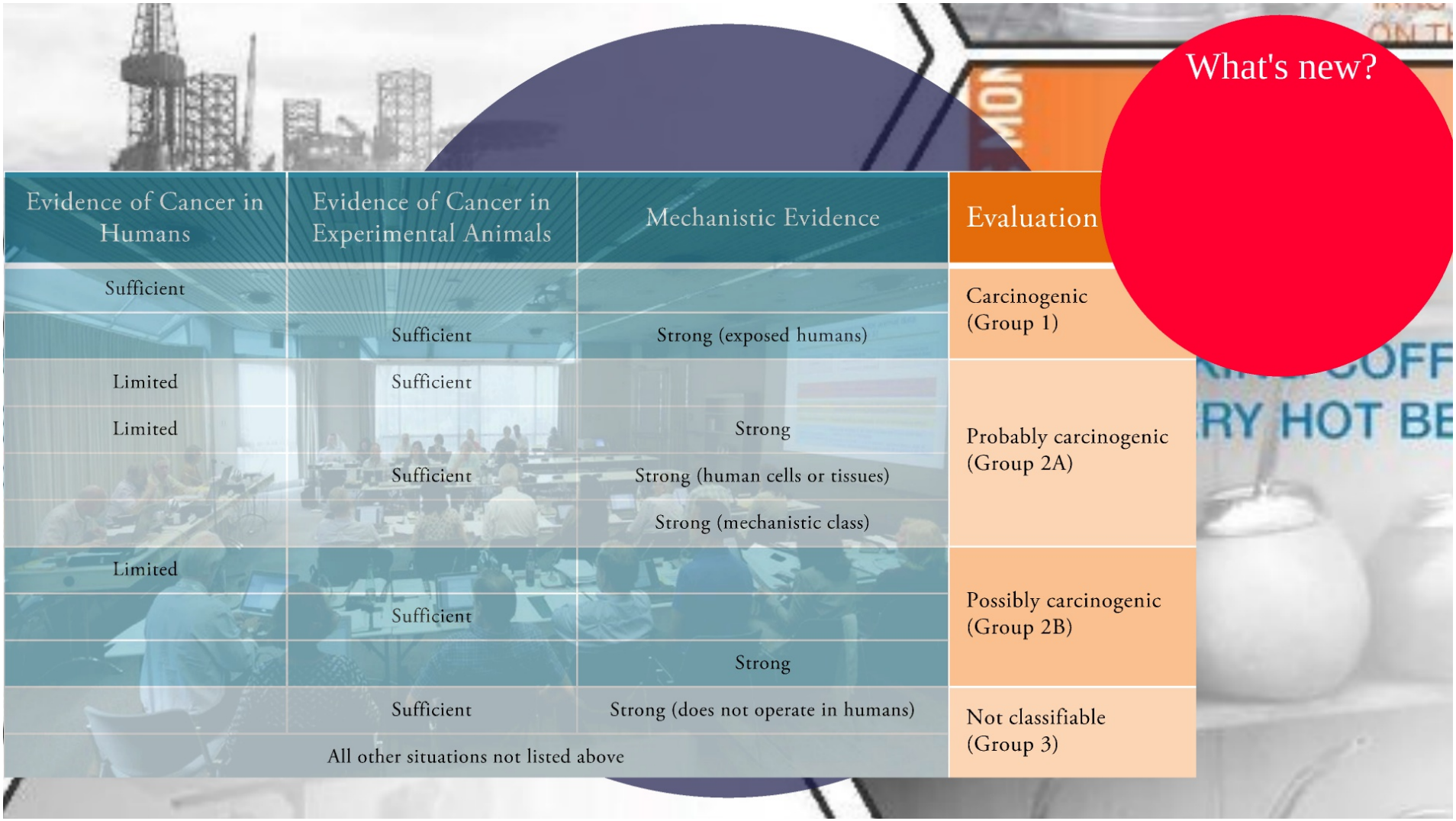

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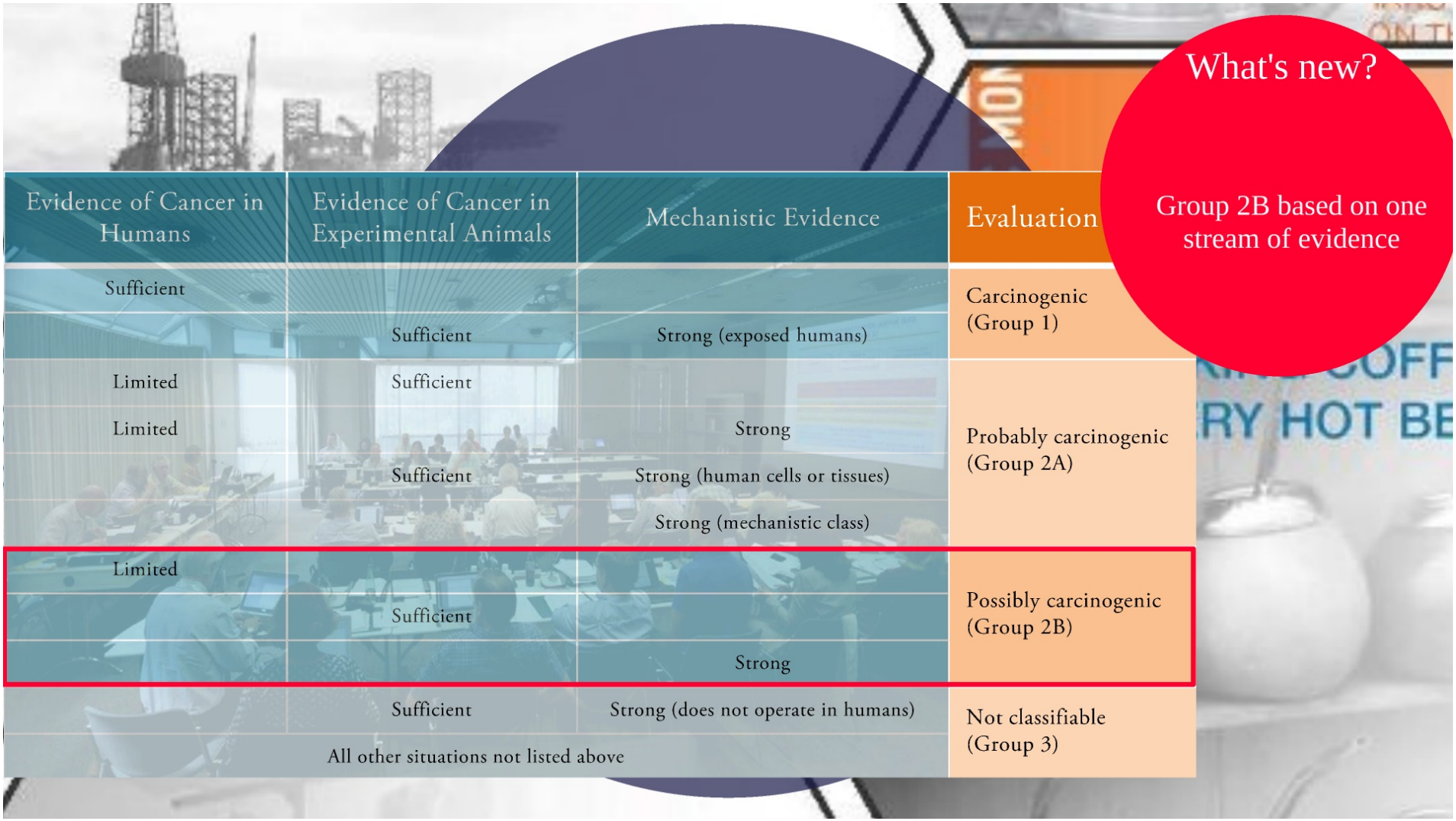

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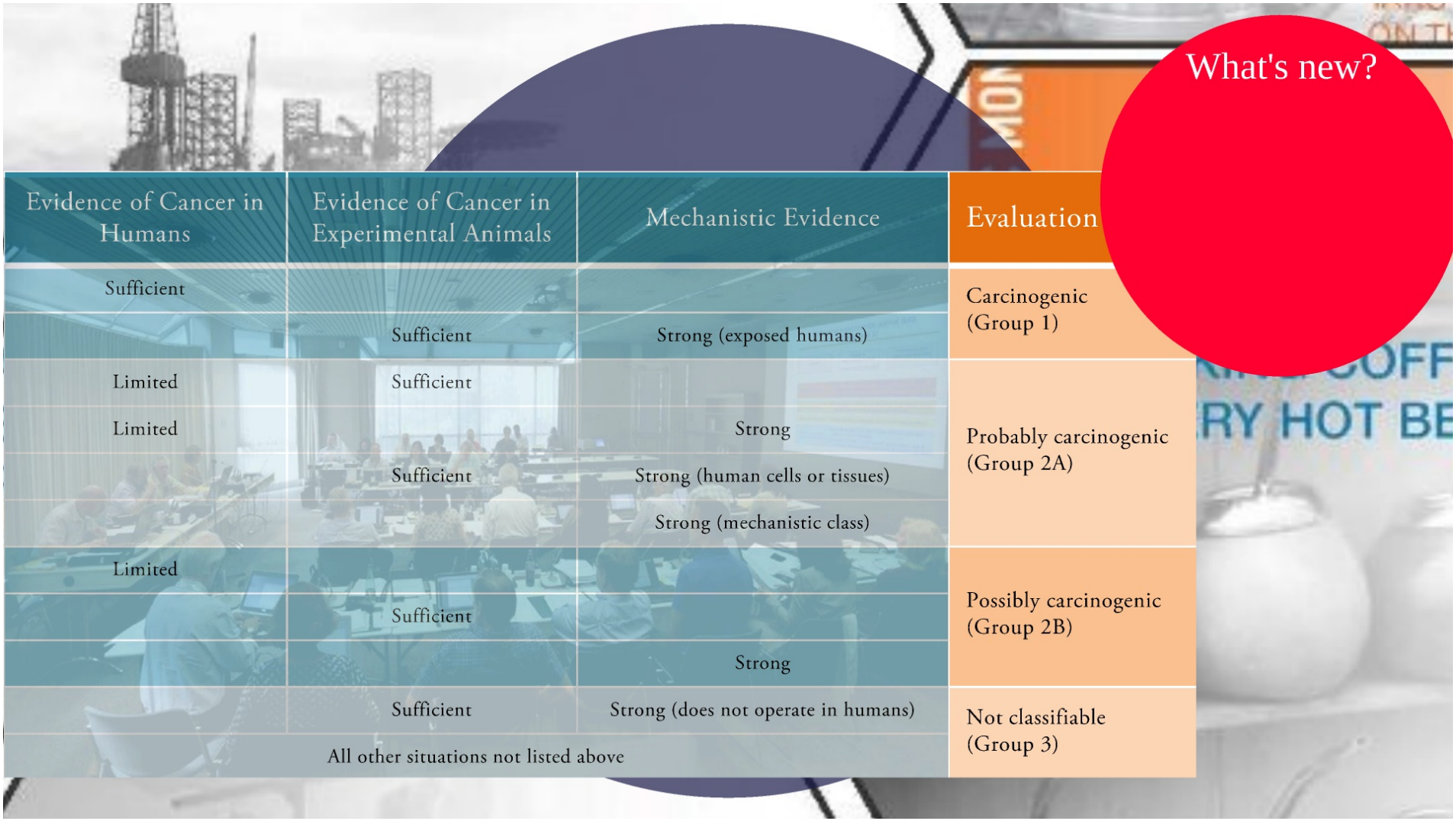

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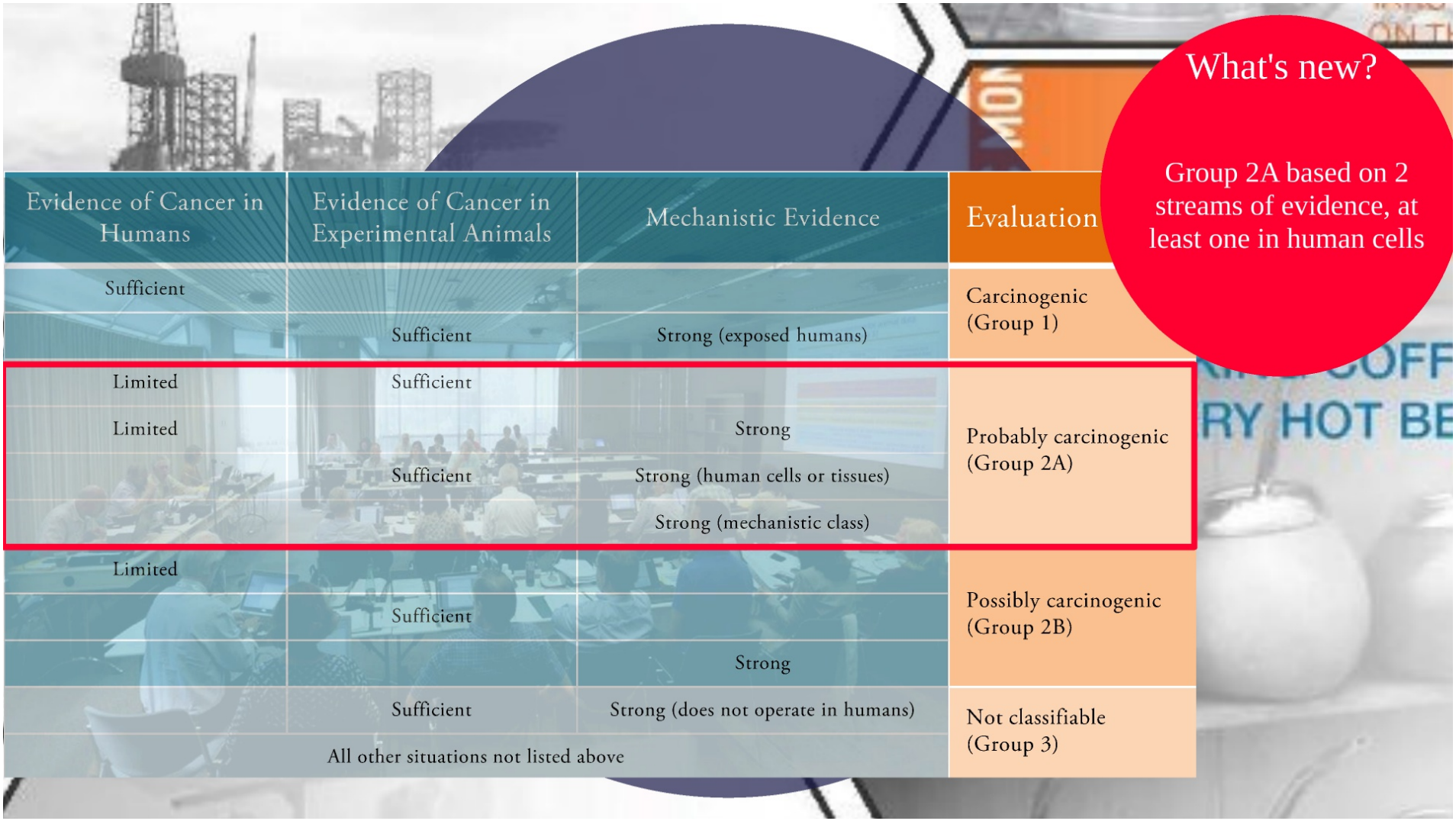

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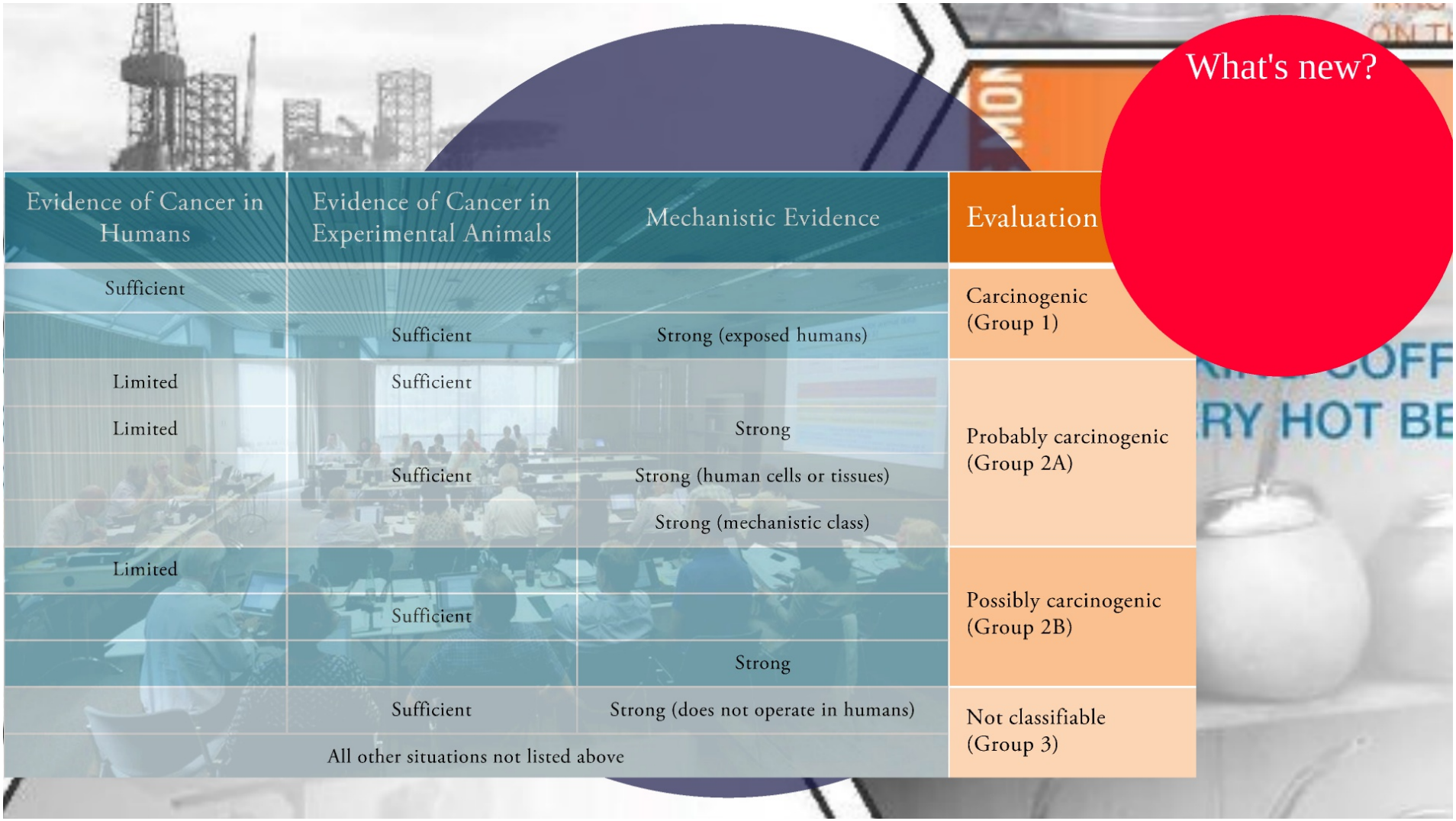

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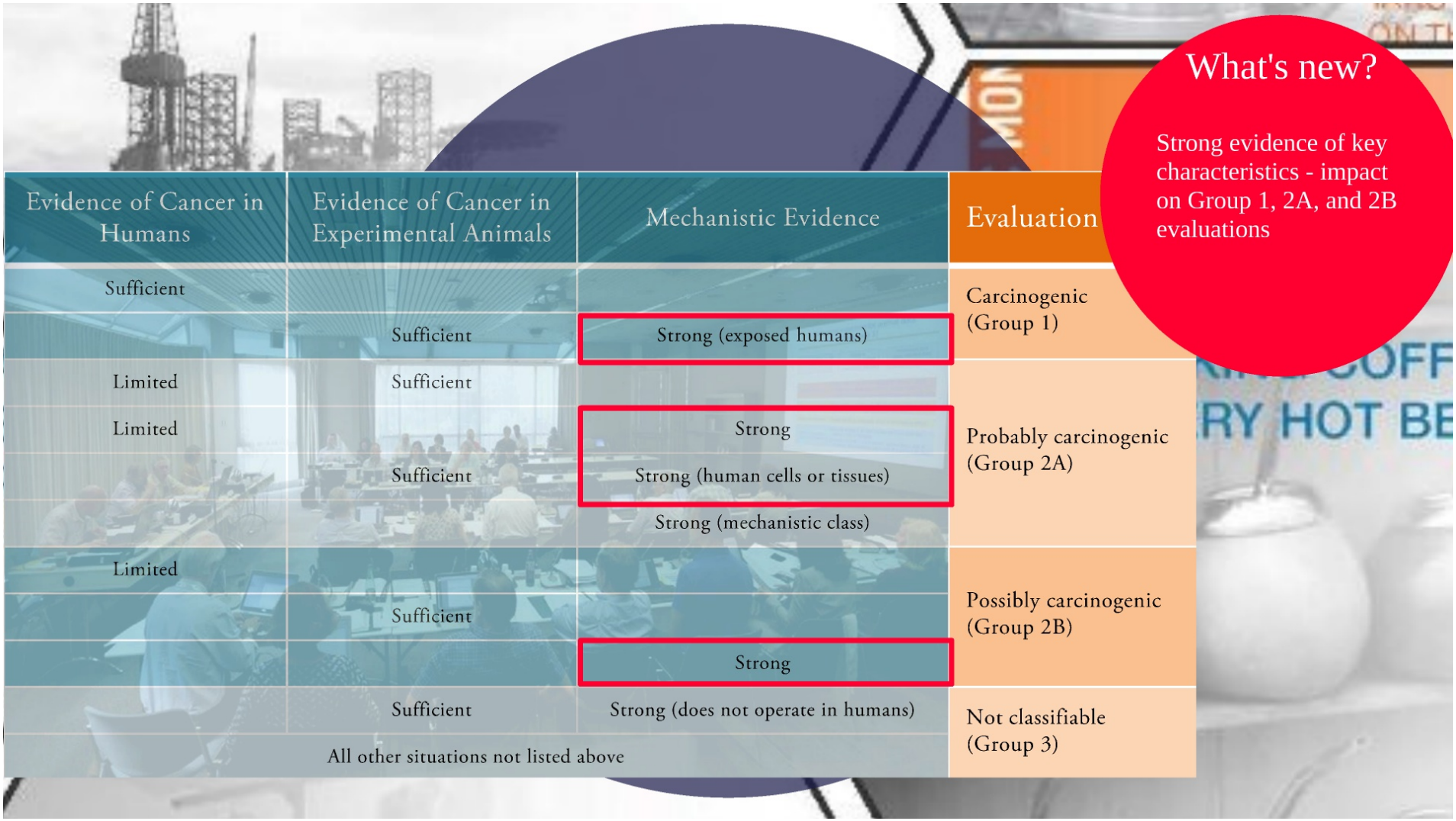
What's new?
Strong evidence of key characteristics - impact on Group 1, 2A, and 2B evaluations
Evidence of Cancer in Humans
Evidence of Cancer in Experimental Animals
Mechanistic Evidence
Evaluation
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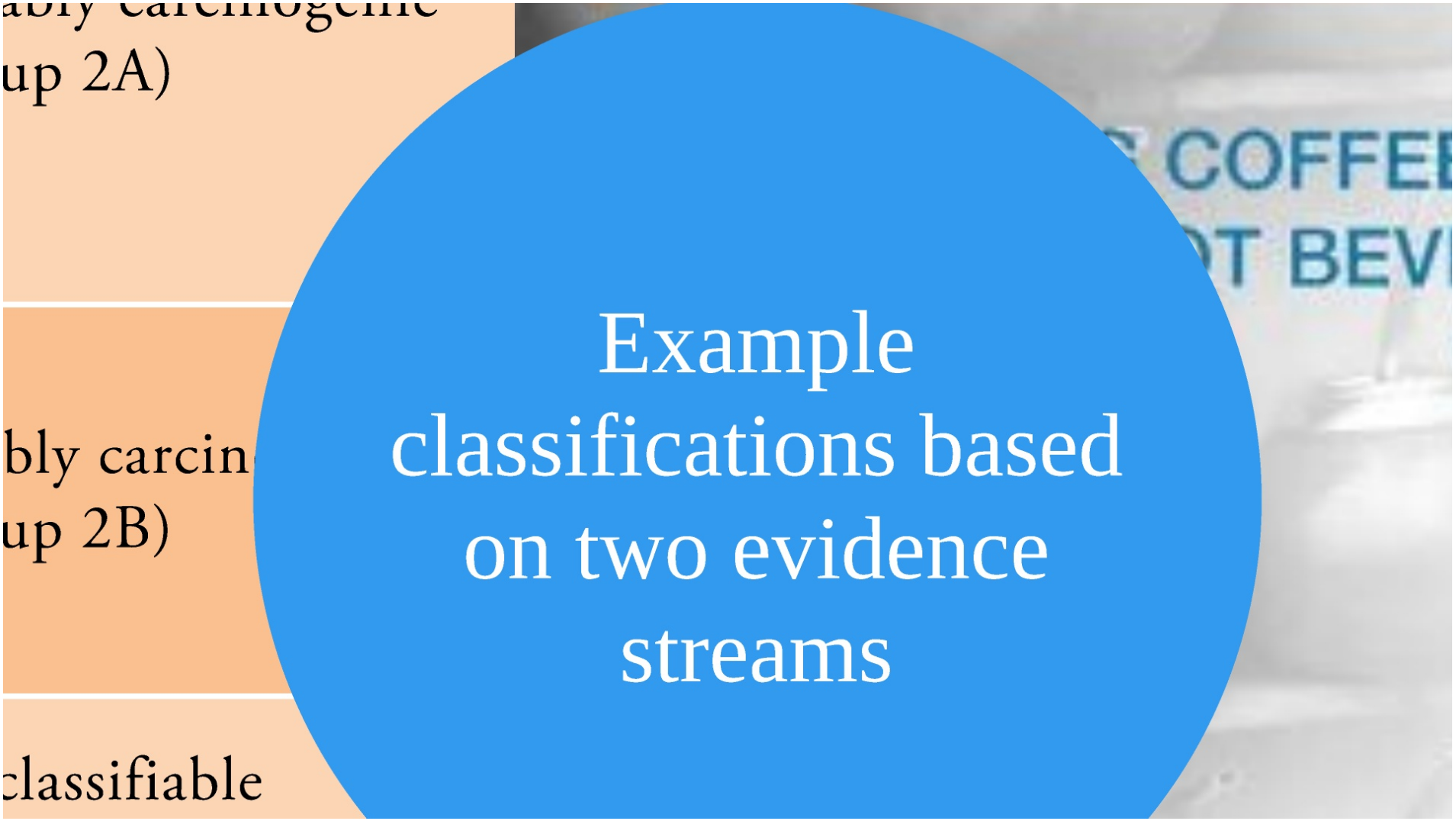
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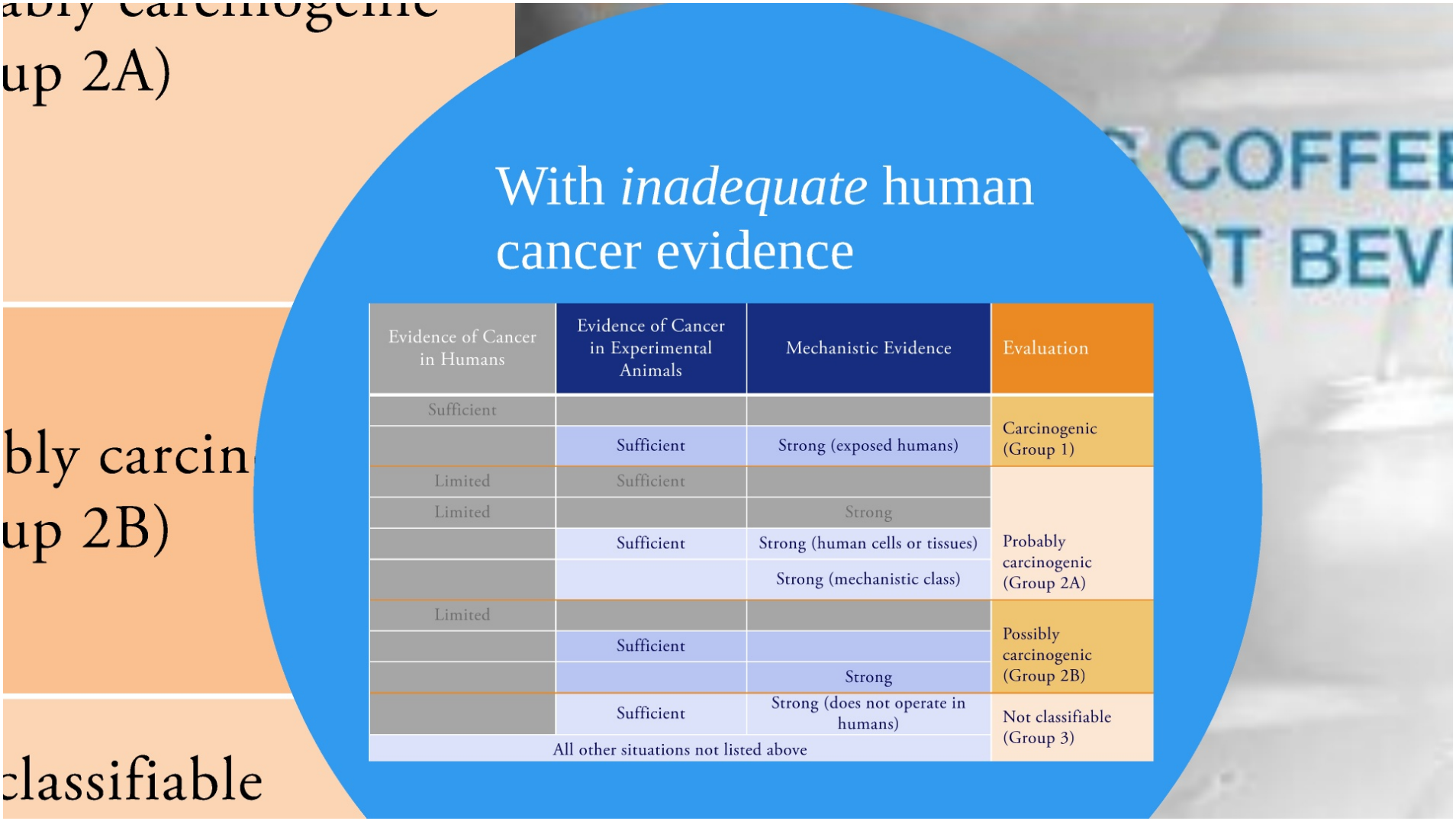
Example classifications based on two evidence streams



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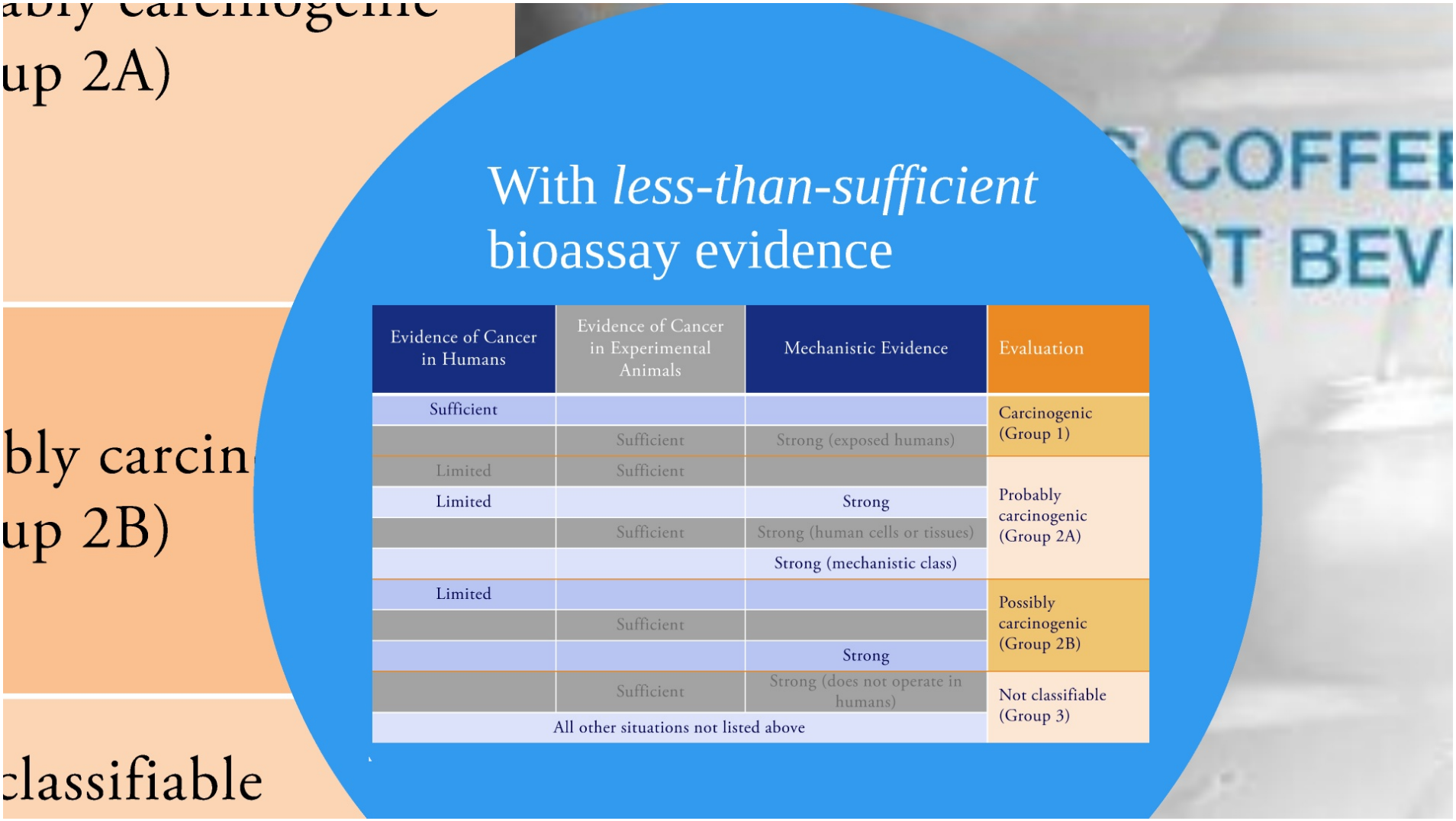

With *less-than-sufficient* bioassay evidence

Evidence of Cancer in Humans	Evidence of Cancer in Experimental Animals	Mechanistic Evidence	Evaluation
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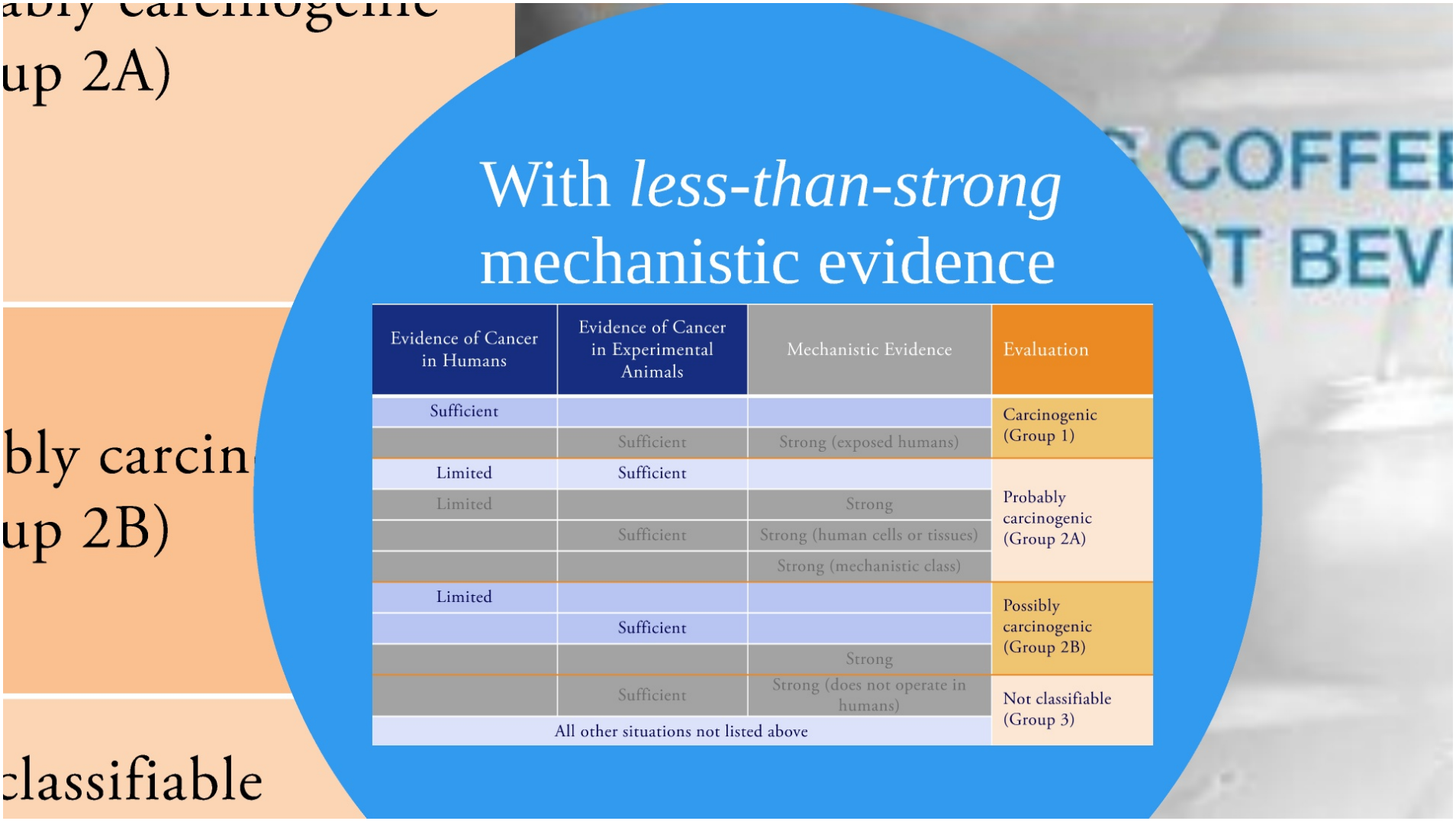

With *less-than-strong* mechanistic evidence

Evidence of Cancer in Humans	Evidence of Cancer in Experimental Animals	Mechanistic Evidence	Evaluation
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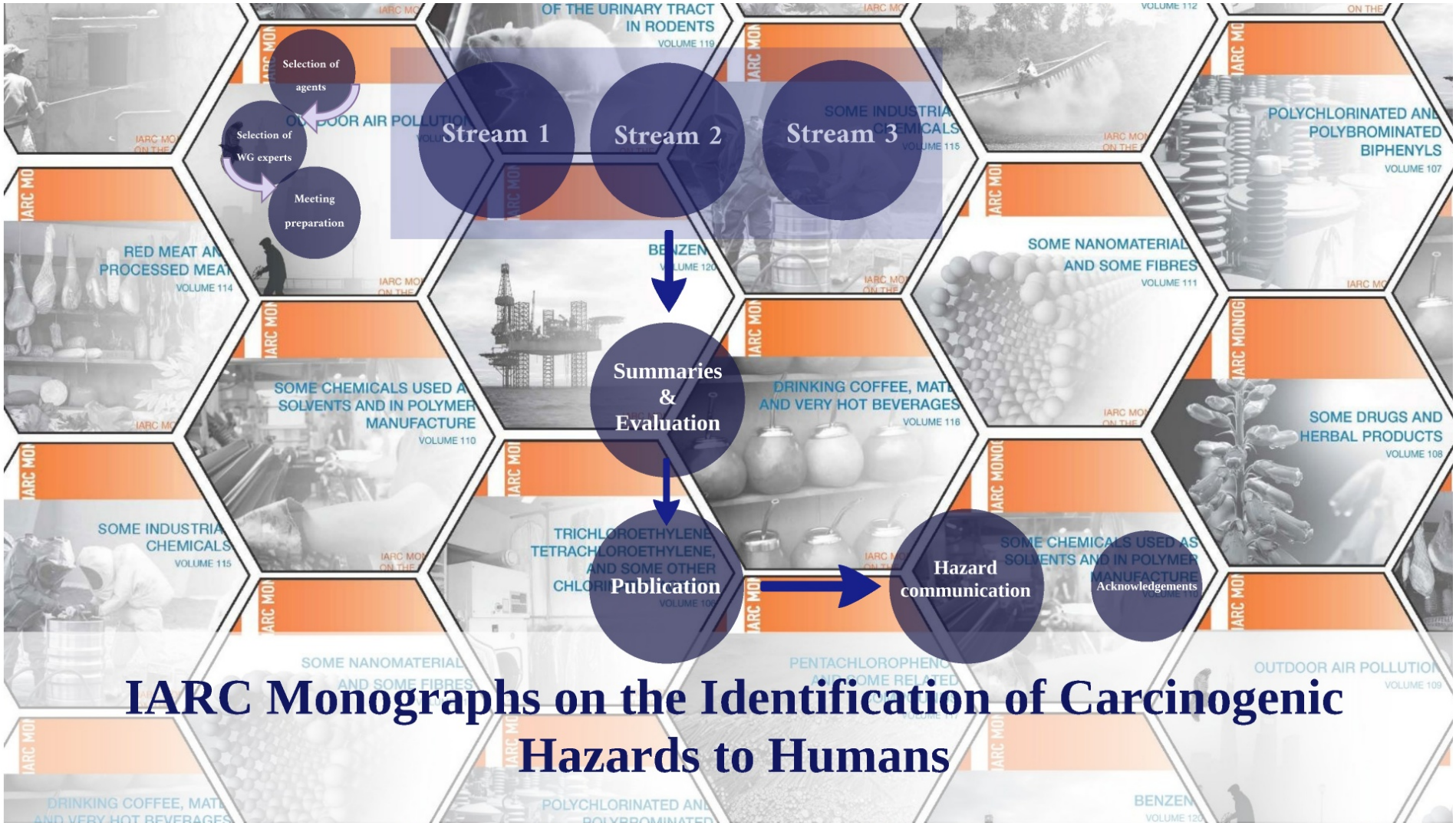
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Results of evidence synthesis and consensus evaluation are published in *The Lancet Oncology* after each meeting
THE LANCET
Oncology
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NEWS | VOLUME 17, ISSUE 12, P1637-1638, DECEMBER 01, 2016
Carcinogenicity of pentachlorophenol and some related compounds
Kathryn Z Guyton • Dana Loomis • Yann Grosse • Fatiha El Ghissassi • Véronique Bouvard • Lamia Benbrahim-Tallaa • et al. Show all authors
Published: October 23, 2016 • DOI: https://doi.org/10.1016/S1470-2045(16)30513-7
References
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NEWS | VOLUME 19, ISSUE 12, PE681-E682, DECEMBER 01, 2018
Carcinogenicity of some nitrobenzenes and other industrial chemicals
IARC Monographs Vol 123 Group † • Show footnotes
Published: November 01, 2018 • DOI: https://doi.org/10.1016/S1470-2045(18)30823-4 •
References
Article Info
In October, 2018, 14 experts from six countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to finalise their evaluation of the carcinogenicity of *ortho*-phenylenediamine and its dihydrochloride salt, 2-chloronitrobenzene, 4-chloronitrobenzene, 1,4-dichloro-2-nitrobenzene, 2,4-dichloro-1-nitrobenzene, 2-amino-4-chlorophenol, *para*-nitroanisole, and *N,N*-dimethylacetamide. These assessments will be published in Volume 123 of the IARC Monographs. [1]


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AND SOME OTHER
CHLORINATED AGENTS
VOLUME 106
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C Monographs on the Identification of Carcinogenic Hazard
Humans
RC Monographs on the Identification of Carcinogenic Hazards to Humans identify environmental factors that can increase the
cancer. Interdisciplinary Working Groups of expert scientists review the published studies and evaluate the weight of the ev
971, more than 1000 agents have been evaluated.
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Lyon (FR): International Agency for Research on Cancer; 1988-.
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The IARC Monographs identify environmental factors that can increase the risk of human cancer. These include chemicals, complex mixtures, occupational exposures, physical agents, biological agents, and lifestyle factors. National health agencies can use this information as scientific support for their actions to prevent exposure to potential carcinogens.
Interdisciplinary working groups of expert scientists review the published studies and evaluate the weight of the evidence that an agent can increase the risk of cancer. The principles, procedures, and scientific criteria that guide the evaluations are described in the Preamble to the IARC Monographs.
Since 1971, more than 900 agents have been evaluated, of which more than 400 have been identified as carcinogenic, probably carcinogenic, or possibly carcinogenic to humans.
Contents
2018
115. Some Industrial Chemicals
IARC Working Group on the Evaluation of Carcinogenic Risk to Humans.
Lyon (FR): International Agency for Research on Cancer; 2018.
114. Red Meat and Processed Meat
IARC Working Group on the Evaluation of Carcinogenic Risk to Humans.
Lyon (FR): International Agency for Research on Cancer; 2018.
113. DDT, Lindane, and 2,4-D
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112. Some Organophosphate Insecticides and Herbicides
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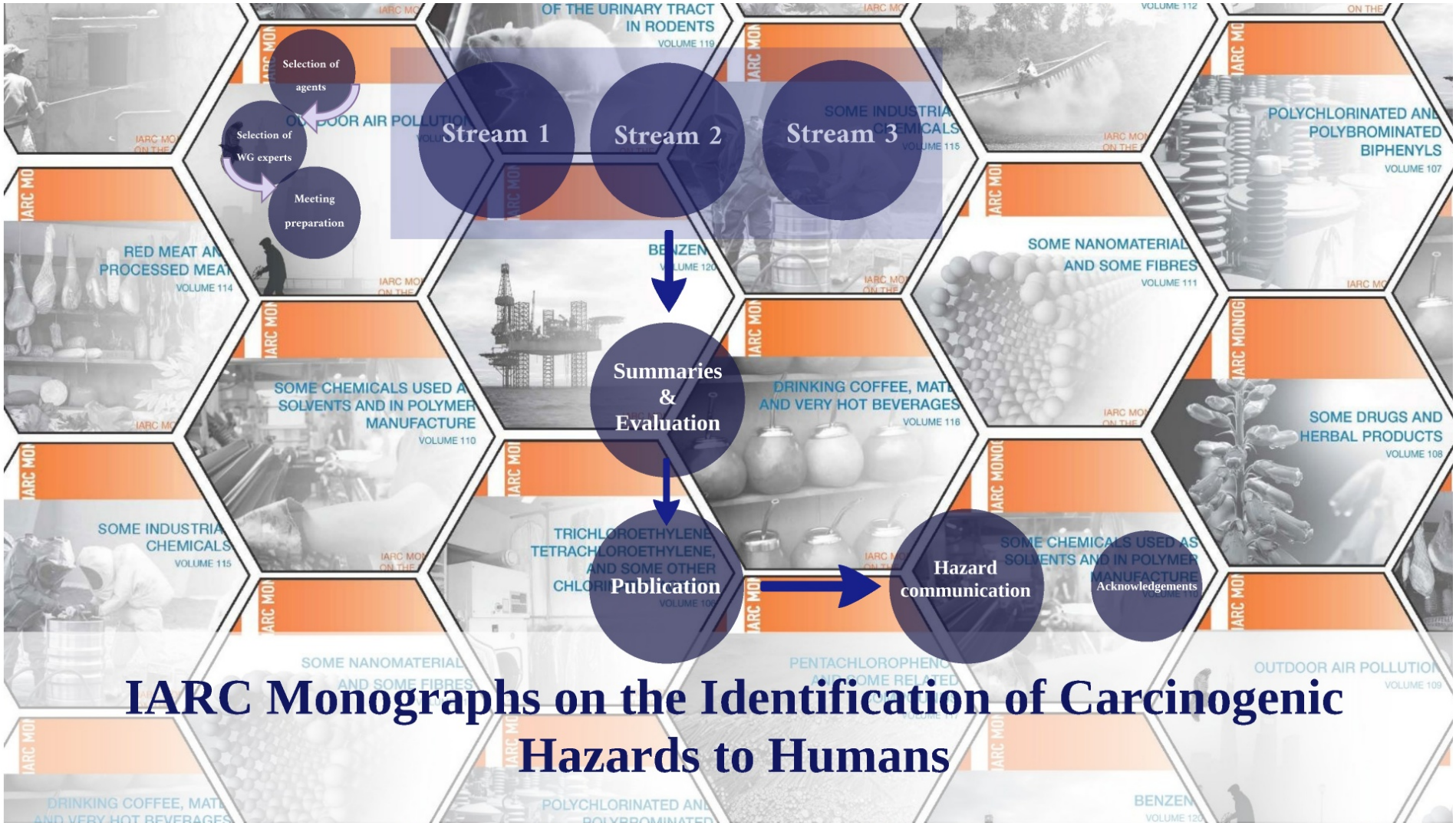
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at all levels
(institutional, major
media outlets, public
conferences, scientific
seminars, etc.)
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AND SOME RELATED


International Agency for Research on Cancer
World Health Organization
IARC MONOGRAPHS CLASSIFICATION OF NIGHT SHIFT WORK
Night shift work is PROBABLY CARCINOGENIC TO HUMANS (Group 2A)
Limited evidence in humans. Sufficient evidence in experimental animals.
GROUP 1
GROUP 2A
GROUP 2B
GROUP 3
The IARC Monographs classification indicates the level of certainty that an agent can cause cancer (hazard identification).
Higher level of certainty
Lower level of certainty
Positive associations have been observed between night shift work and cancers of the:
Breast
Prostate
Colon and rectum
Night shift work includes both working at night and working in a job that involves rapidly crossing many time zones.
Specific types of workers
Nurses
Factory workers
Flight attendants
Airplane pilots
Higher percentages of night shift workers are seen in
Health care
Manufacturing
Retail, service sector
Transport
International Agency for Research on Cancer
World Health Organization
IARC MONOGRAPHS VOL. 131
Cobalt, Antimony Compounds, and Weapons-Grade Tungsten Alloy (WGTA)
(2 – 18 March 2022)
27 Co Cobalt 58.93
51 Sb Antimony 121.76
74 W Tungsten 183.84
Co Cobalt 58.93
Ni Nickel 58.69
GROUP
USES
POTENTIAL EXPOSURE
WHO?
Cobalt metal*
*without tungsten carbide or other metal alloys
Soluble cobalt(II) salts
Cobalt(II) oxide
Cobalt(II,III) oxide
Cobalt(II) sulfide
Other cobalt(II) compounds
Group 2A
Probably carcinogenic to humans
Group 2A
Probably carcinogenic to humans
Group 2B
Possibly carcinogenic to humans
Group 3
Not classifiable as to its carcinogenicity to humans
Used in many industries, including in the manufacture of cutting and grinding tools, in pigments and paints, coloured glass, medical implants, batteries, and electroplating
Production of hard metal
Production of cobalt powder
Use of cobalt-containing pigments and driers, and production and recycling of lithium-ion batteries
General population: exposed via ambient air, drinking-water, tobacco smoke, and food
Trivalent antimony
Pentavalent antimony
Group 2A
Probably carcinogenic to humans
There is limited evidence for cancer in humans (for lung cancer)
Group 3
Not classifiable as to its carcinogenicity to humans
Used in the production of flame retardants, plastics, lead-acid batteries, lead alloys, glass, pigments, and paints
Used in some antileishmanial drugs
Production of flame retardants and electronic waste
Production or use of antileishmanial drugs
General population: by inhalation of fuel and coal combustion products and road traffic dust and through drinking-water and consumer products such as toys and cosmetics
WGTA
Group 2B
Possibly carcinogenic to humans
WGTA (91–93% tungsten, 3–5% nickel, and 2–4% cobalt) is used in armour-penetrating munitions as a replacement for depleted uranium
Production, firing, or impact of the munitions; war-related injuries by alloy fragments


Hazard communication
at all levels
(institutional, major
media outlets, public
conferences, scientific
seminars, etc.)
SOME CHEMICALS US
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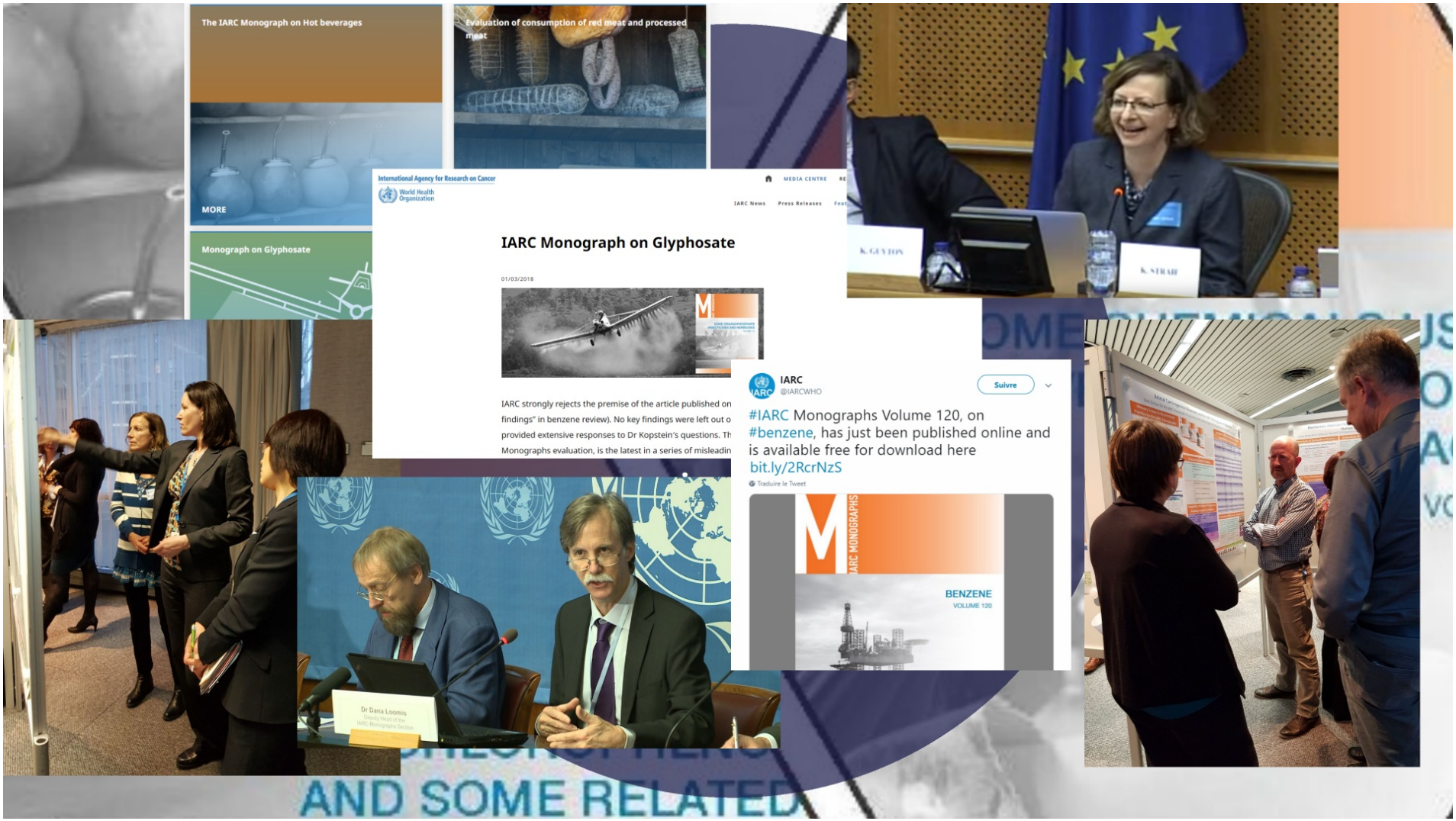
AND SOME RELATED


The IARC Monograph on Hot beverages
MORE
Evaluation of consumption of red meat and processed meat
Monograph on Glyphosate
International Agency for Research on Cancer
World Health Organization
MEDIA CENTRE
IARC News
Press Releases
IARC Monograph on Glyphosate
01/03/2018
IARC strongly rejects the premise of the article published on
findings" in benzene review). No key findings were left out o
provided extensive responses to Dr Kopstein's questions. Th
Monographs evaluation, is the latest in a series of misleadin
IARC
@IARCWHO
Suivre
#IARC Monographs Volume 120, on #benzene, has just been published online and is available free for download here bit.ly/2RcrNzS
Traduire le Tweet
IARC MONOGRAPHS
BENZENE
VOLUME 120
Dr Dana Loomis
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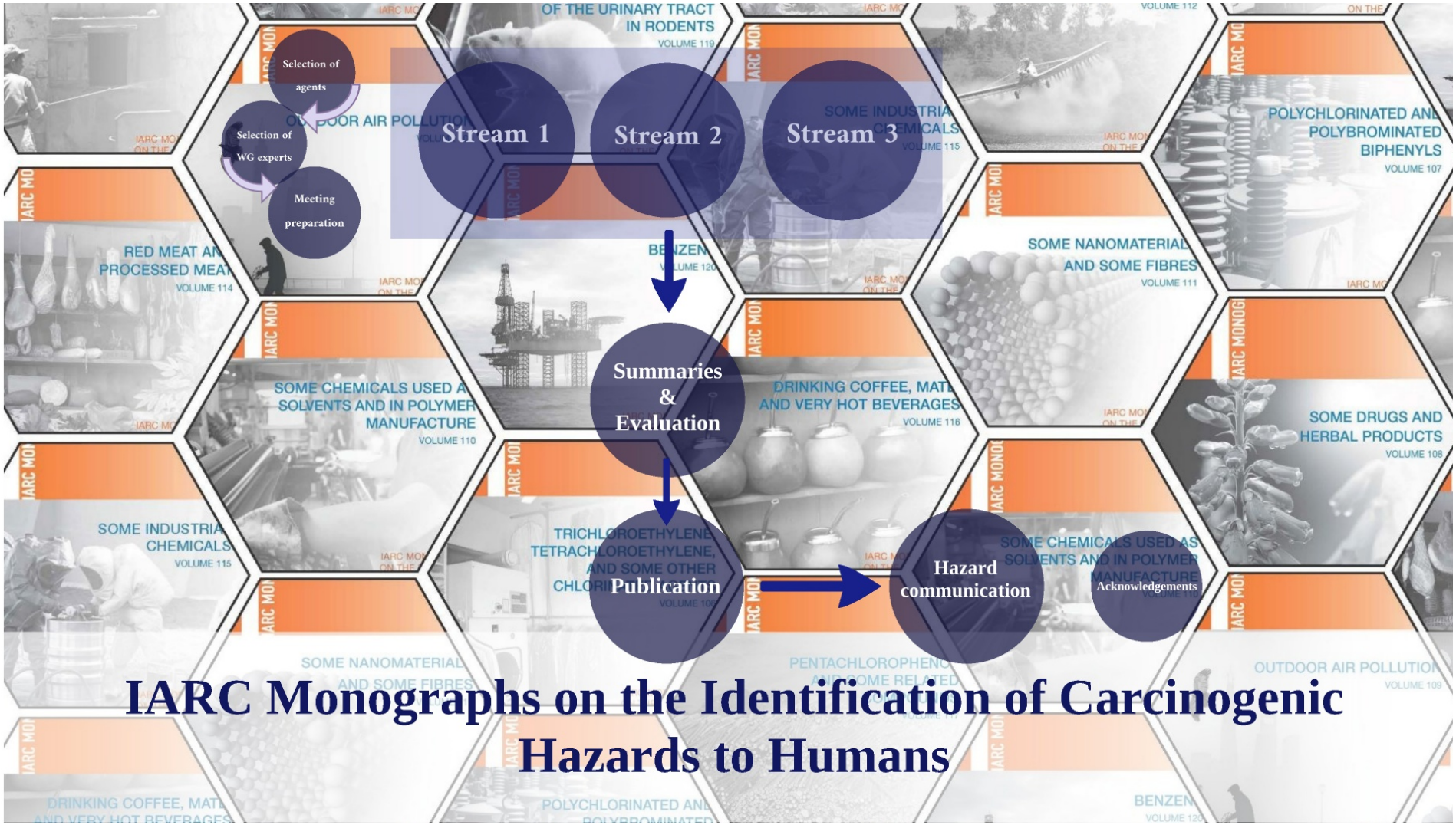
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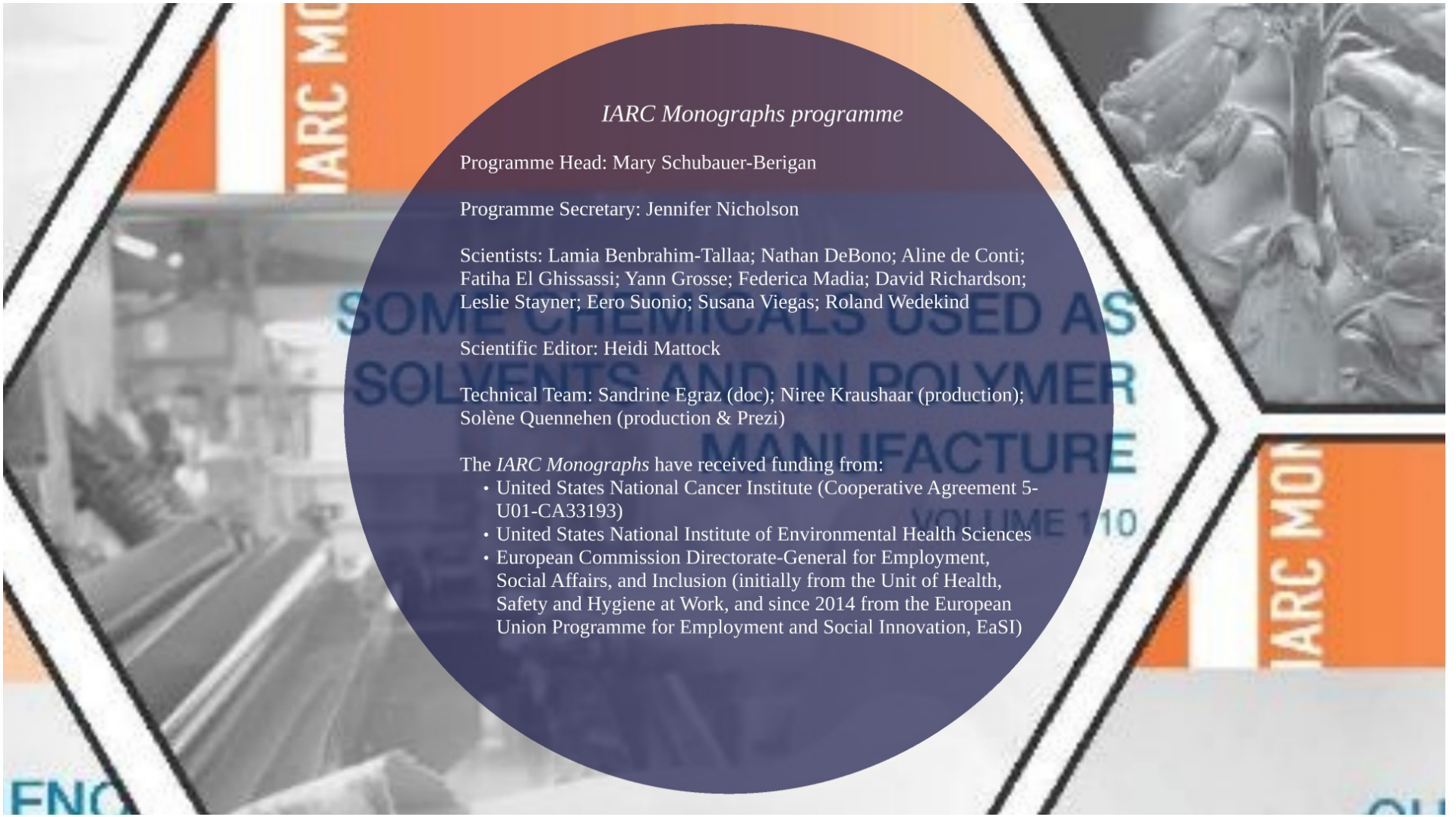
Advisory Group to Recommend an Update to the Preamble
IARC, Lyon, France, 12–14 November 2018



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- European Commission Directorate-General for Employment, Social Affairs, and Inclusion (initially from the Unit of Health, Safety and Hygiene at Work, and since 2014 from the European Union Programme for Employment and Social Innovation, EaSI)

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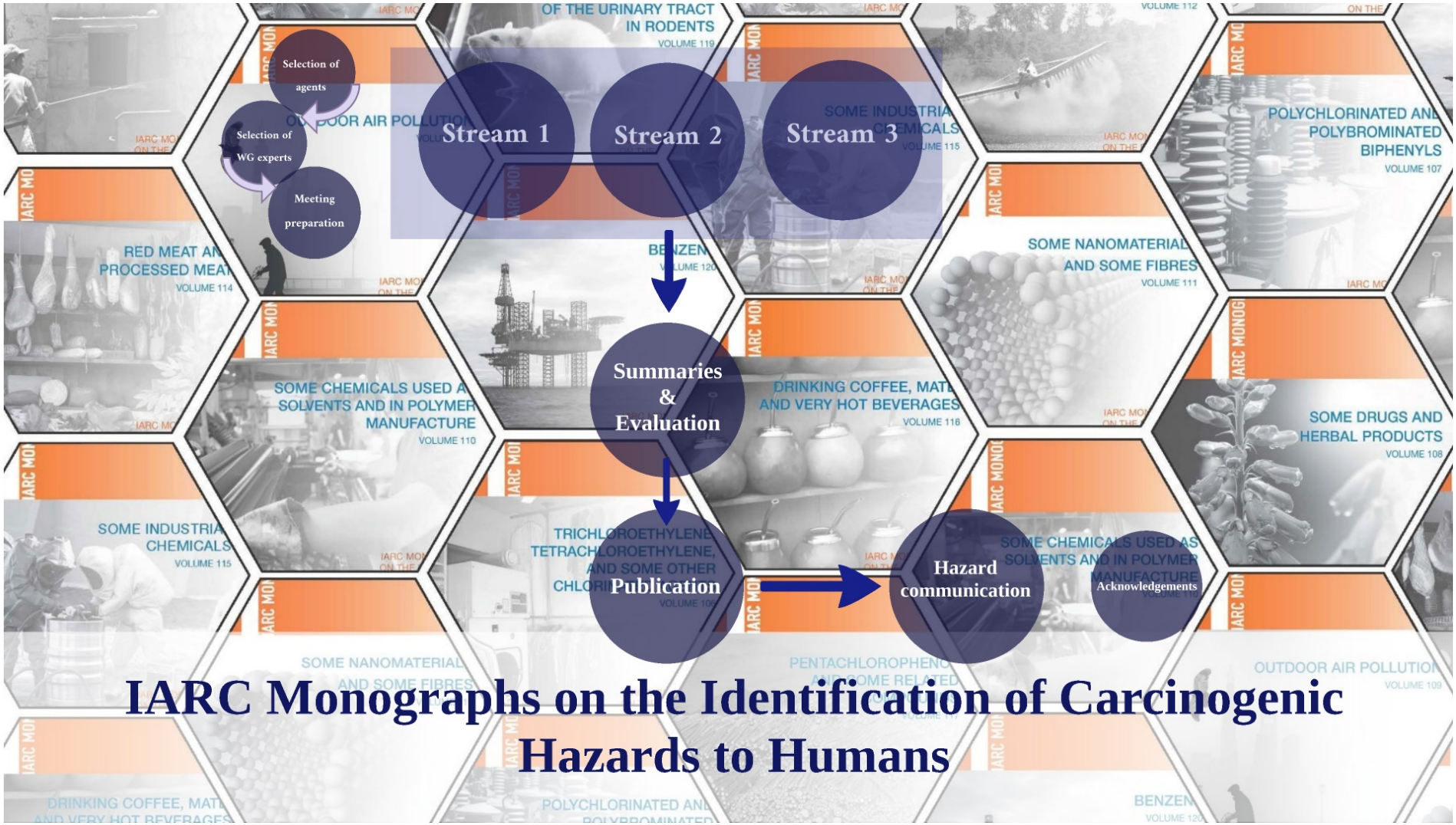
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