



Rendre tangibles les influences de l'environnement sur la santé

Carcinogenicity assessment: technical and political challenges

Forum Environnement et Cancer
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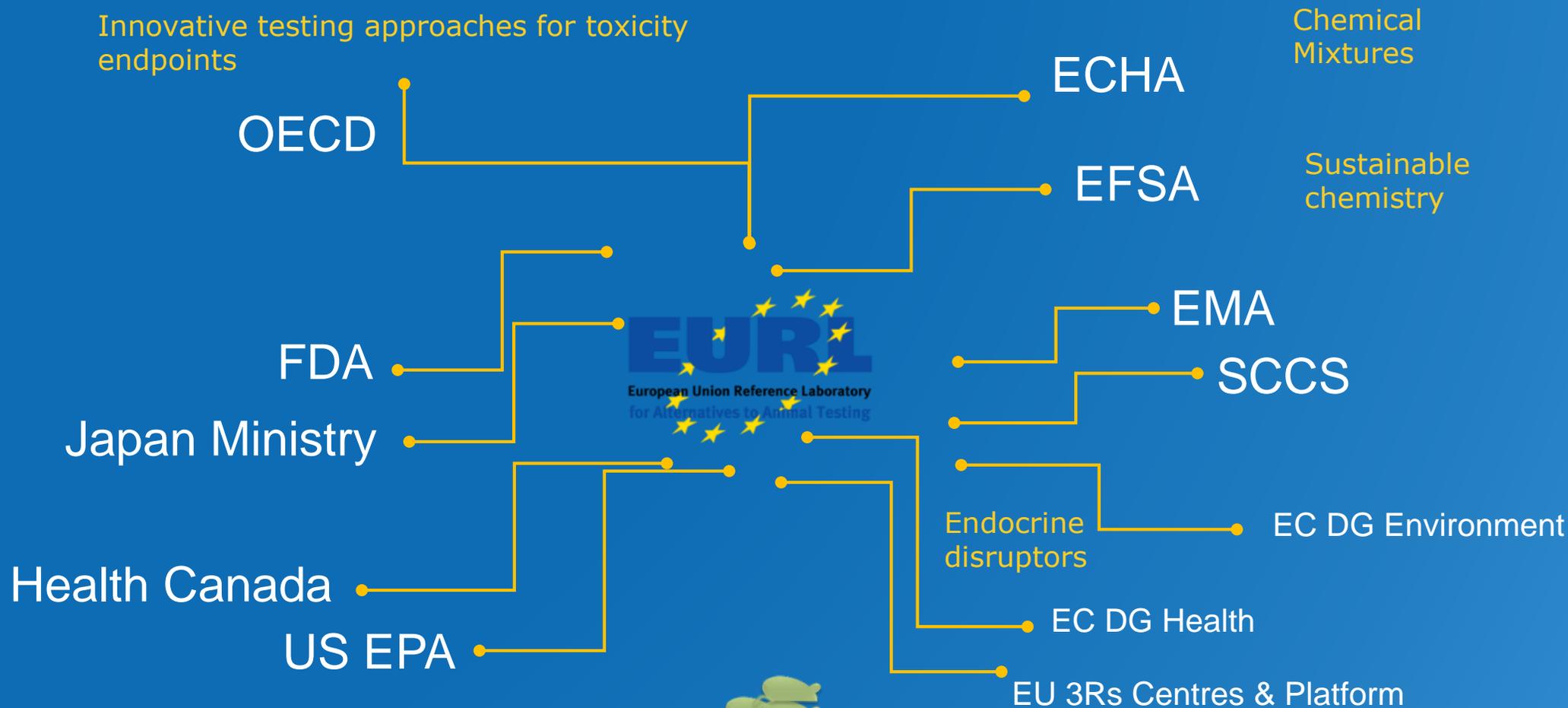
Directorate
Health, Consumers
and Reference
Materials



✓ *As the science and knowledge service of the Commission*

✓ *JRC mission is to support EU policies with independent evidence throughout the whole policy cycle*

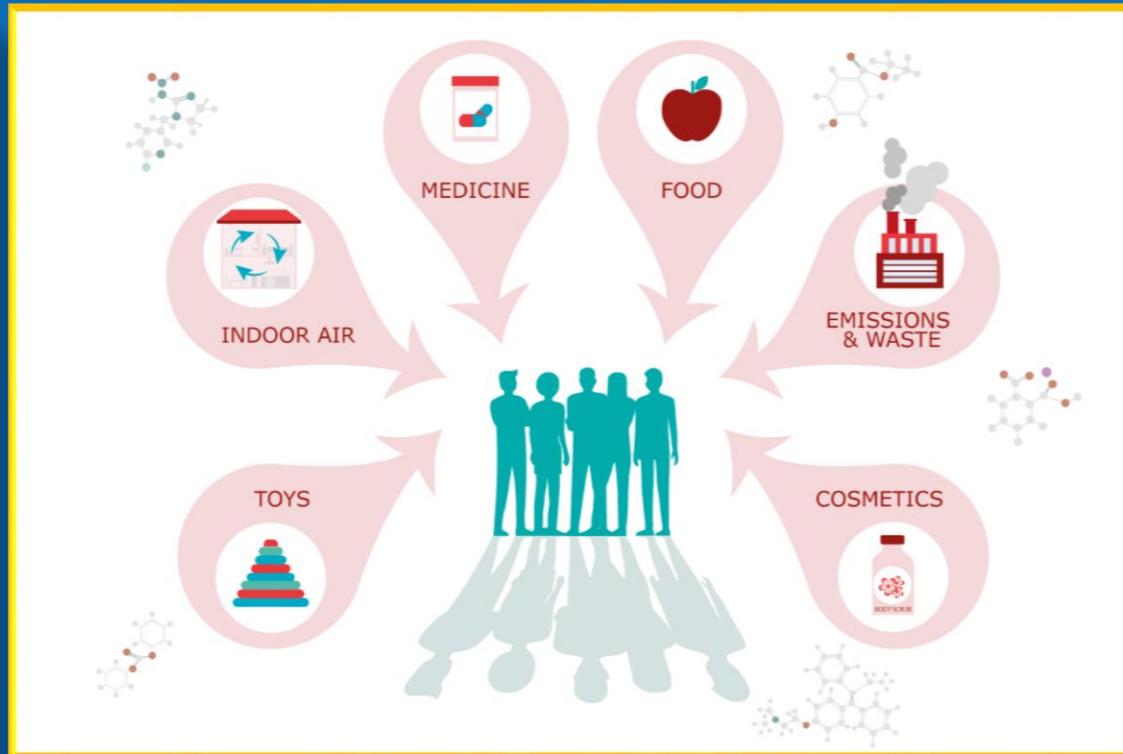
Chemical Safety and Alternative Methods Unit



Hosting EURL ECVAM
Validate alternative methods promote
3Rs as Directive 2010/63/EU



Changing perspective... health & chemical environment



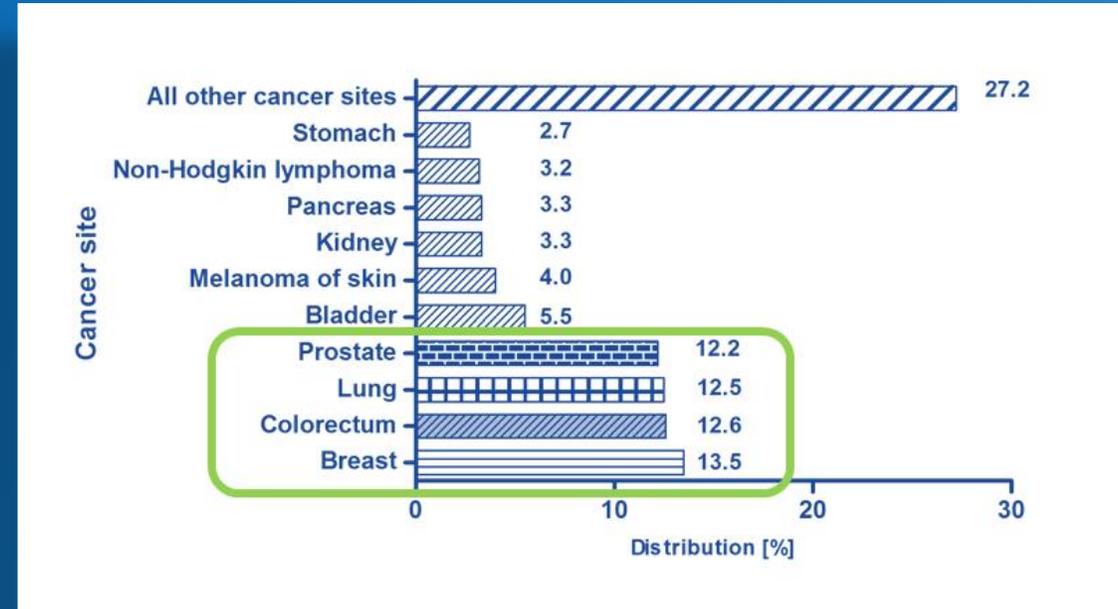
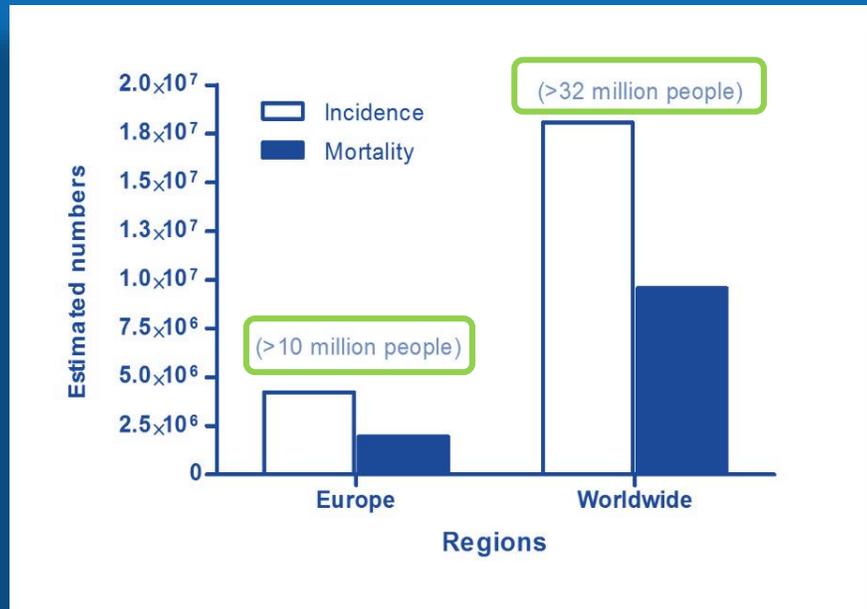
... we get in contact with many different chemicals in combination "cocktail effect"

- ✓ What is the impact on our health?
- ✓ Which role do chemicals play compared to other risk factors?

Cancer disease



Cancer data in 2018



People living with cancer, 5-year survival from first diagnosis

Risk from chemical exposures is preventable

Family history and ageing represent unavoidable risk factors.

For 5-10% of cancer cases, significant correlations with **specific inherited genes** have been identified (e.g. BRCA1-2 in breast cancer)

Preventable risk factors collectively contribute to the development of 70-95% of all cancers,

these **include exposure to chemicals** through occupational or consumer exposure

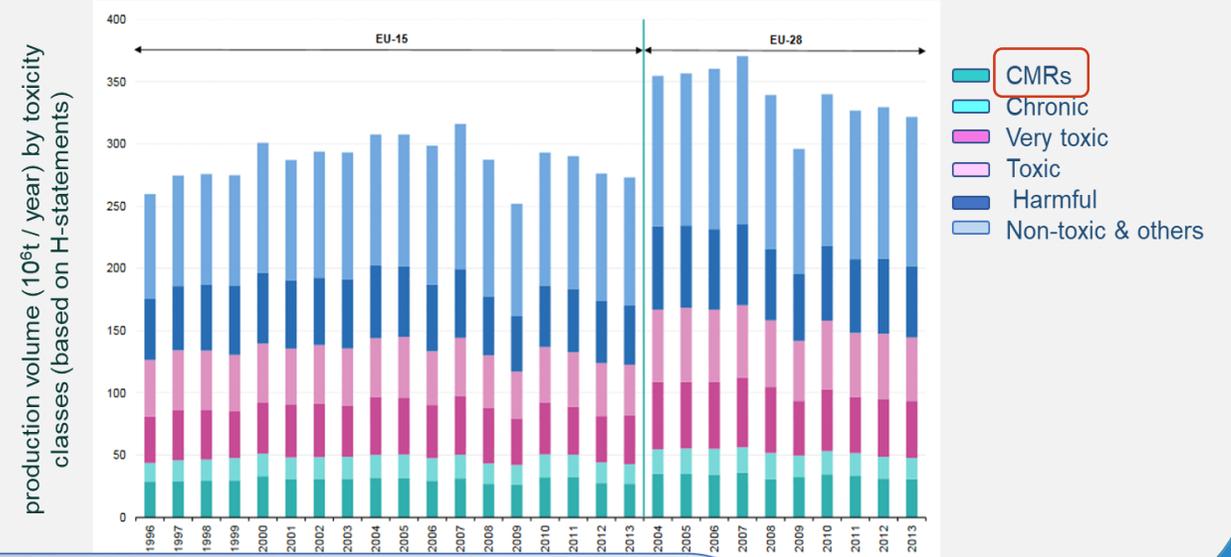
Cancers cannot be completely avoided but, susceptibility to the disease can be reduced significantly by reducing the impact of **several risk factors**



Chemical production in the EU

Cancers cannot be completely avoided but, susceptibility to the disease can be reduced significantly by reducing the impact of **several risk factors including chemical exposure**

- ✓ The EU deals on average with the production of >300 M tons/year
- ✓ 12-15% of the total are classified as CMRs



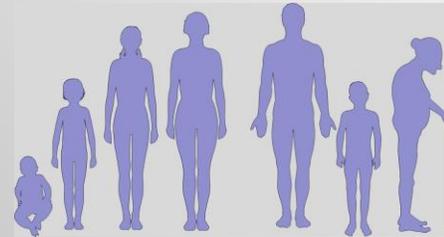
EU REACH Review

10 years of REACH Regulation (EC) No 1907/2006



OCCUPATIONAL EXPOSURE

- 7% Reduced exposure per year
- 1M deaths saved over last 20yrs
- Major control



GENERAL PUBLIC EXPOSURE

Uncertainties

- Mixtures exposure
- Not enough studies
- Indirect links with human diseases
- Window of exposure
- Confounding factors

Advancing carcinogenicity testing... Why???

Chemicals induce 54-75% occupational lung cancer and increasing childhood leukaemia

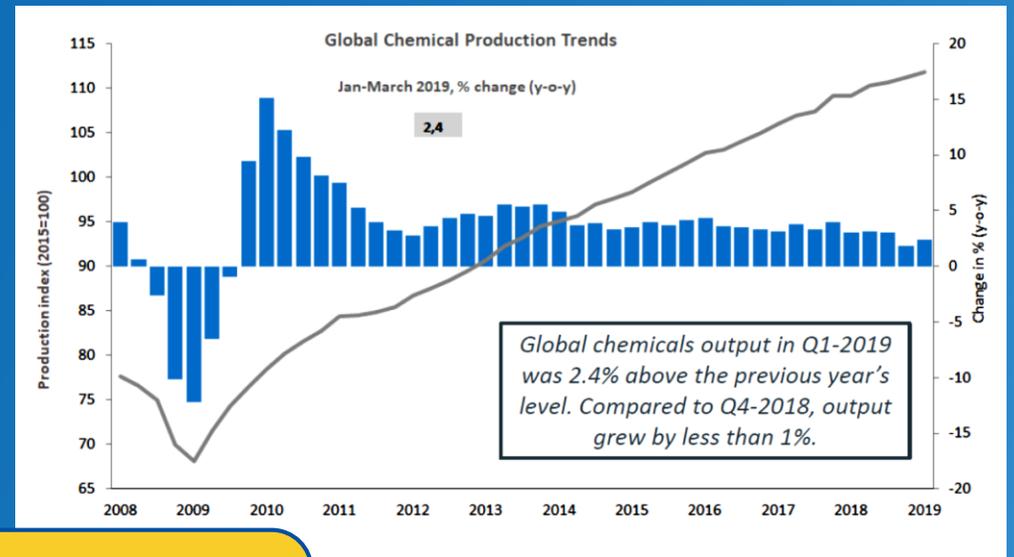
- Cancer facts & statistics
- Increasing incidence

EU ECIS data

Chemicals Trends Report
Monthly Summary: 10th July 2019

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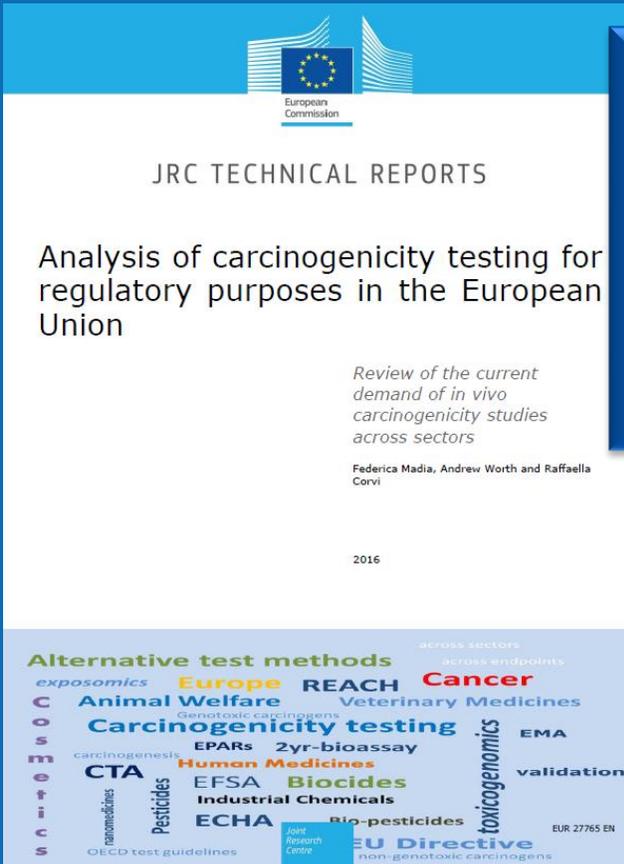
EU chemicals production grows 1.7% in Q1 2019 compared with Q4 2018



Cefic data 2019

Number and diversity of chemicals in use has increased rapidly over past 50 years and still increasing despite various economic crises

Advancing carcinogenicity testing... Why???



JRC Report 2016

- Often relying on old studies in rodents
- Gaps in testing coverage
- Number of animals
- Limited relevance to humans
- Genotoxic vs non-genotoxic carc
- Classification & Labelling
- Differences in regulatory requirements across sectors

Need for adequate and cost effective hazard and risk assessment

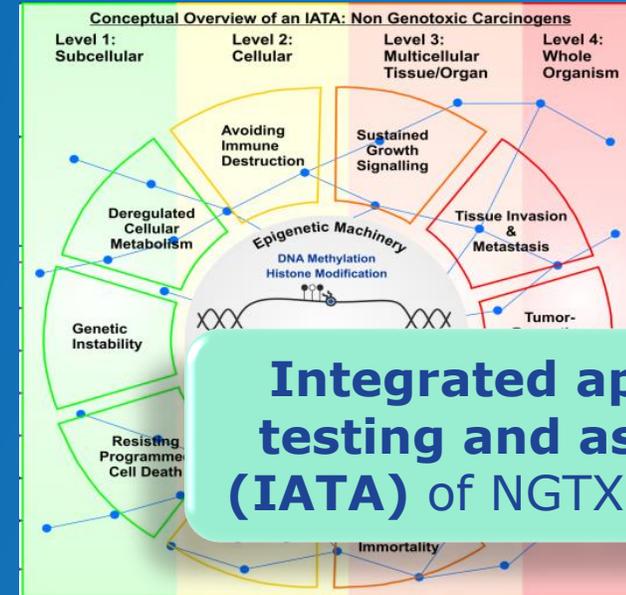
Risk management measures that both sustain market and ensure consumers' health

Ongoing initiatives on carcinogenicity testing

Chemical	CAS No.	Chemical Class	Ames Overall	in vitro overall			in vivo overall			CARC Overall	Other Tests
				in vitro SCA Overall	in vitro MA Overall	in vitro CA Overall	in vitro MA Overall	in vitro CA Overall	in vivo DNA storage Overall		
hexachlor	50-06-6	A	+	+	+	1	1	1	1	+	
hexachlorocyclopentadiene (free base and HCl salt)	58-95-1; 63-82-3	A	+	+	+	1	1	1	1	+	
Phenyl 3,3-dimethylbutane	7227-31-0	A	+	+	+	0	0	0	0	EDNA, IN VIB	
4-Phenylacetamide	106-45-2	A	+	+	+	0	0	0	0	+	
4-Phenylacetamide (free base and HCl salt)	85-54-5; 675-26-1	A	+	+	+	2	2	2	2	+	
4-Phenylacetamide (COLIPA, A7) (free base)	106-58-5; 624-16-0	A	+	+	+	0	0	0	0	COND. SHE 1-4	
4,4'-Diphenylmethane	13024-49-2	A	+	+	+	0	0	0	0	+	
hexylthiothiazole sulphate	156-51-4	A	+	+	+	0	0	0	0	+	
hexylthiothiazole	152-50-1	A	+	+	+	0	0	0	0	+	
hexylthiothiazole (free base and HCl salt)	100-63-0; 98-86-1	A	+	+	+	0	0	0	0	+	
hexylthiothiazole (free base and HCl salt)	90-43-7	A	+	+	+	0	0	0	0	negative in	
hexylthiothiazole	752-11-6	A	+	+	+	0	0	0	0	+	
hexylthiothiazole	13171-21-6	A	+	+	+	0	0	0	0	+	
hexylthiothiazole	13368-73-8	A	+	+	+	0	0	0	0	+	

EURL ECVAM DB of genotoxicity and carcinogenicity data

Madia F et al. 2020, Mutat Res
Corvi R et al 2017, in vitro Tox



Integrated approach to testing and assessment (IATA) of NGTX carcinogens

Jacobs MN et al. 2020, Arch Toxicol



Predicting carcinogenic potential of agrochemicals with info from repeated dose toxicity studies & MoA

JRC co-lead

Luijten M et al. 2020, RTP



EC-JRC project Cross-endpoint evaluation

investigating ways to exploiting existing data to perform a comparative analysis of several toxicological effects measured in different species and using different models.

- ✓ Moving towards mechanistic understanding
Key events and networks
- ✓ Introduce novel methods (*in vitro*, *in silico*, etc.)
- ✓ Moving away from apical toxicity endpoints
- ✓ Design sustainable testing strategies



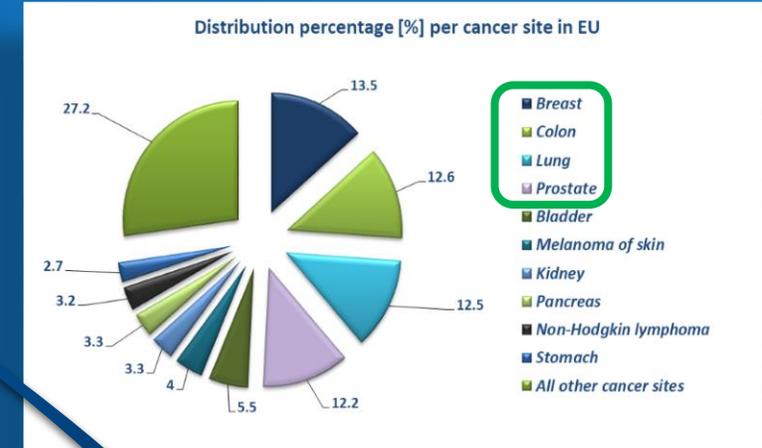
EC-JRC Recommendations to move forward in carcinogenicity assessment

1. Addressing the most prevalent cancers

- Analysis of biomarkers specific to most relevant types of cancers
- Cancer models in vitro, breast, lung, CRC
- Exploit cancer research knowledge and clinical tools

2. Better use of human data and *ad hoc* studies

- Consider intermediate effects leading to cancer
- Design *ad hoc* studies
- Consider human disease aetiology and links to cancer-predisposing conditions or other NCDs to understand



EU ECIS data

3. Use of biomarkers of exposure and human biomonitoring

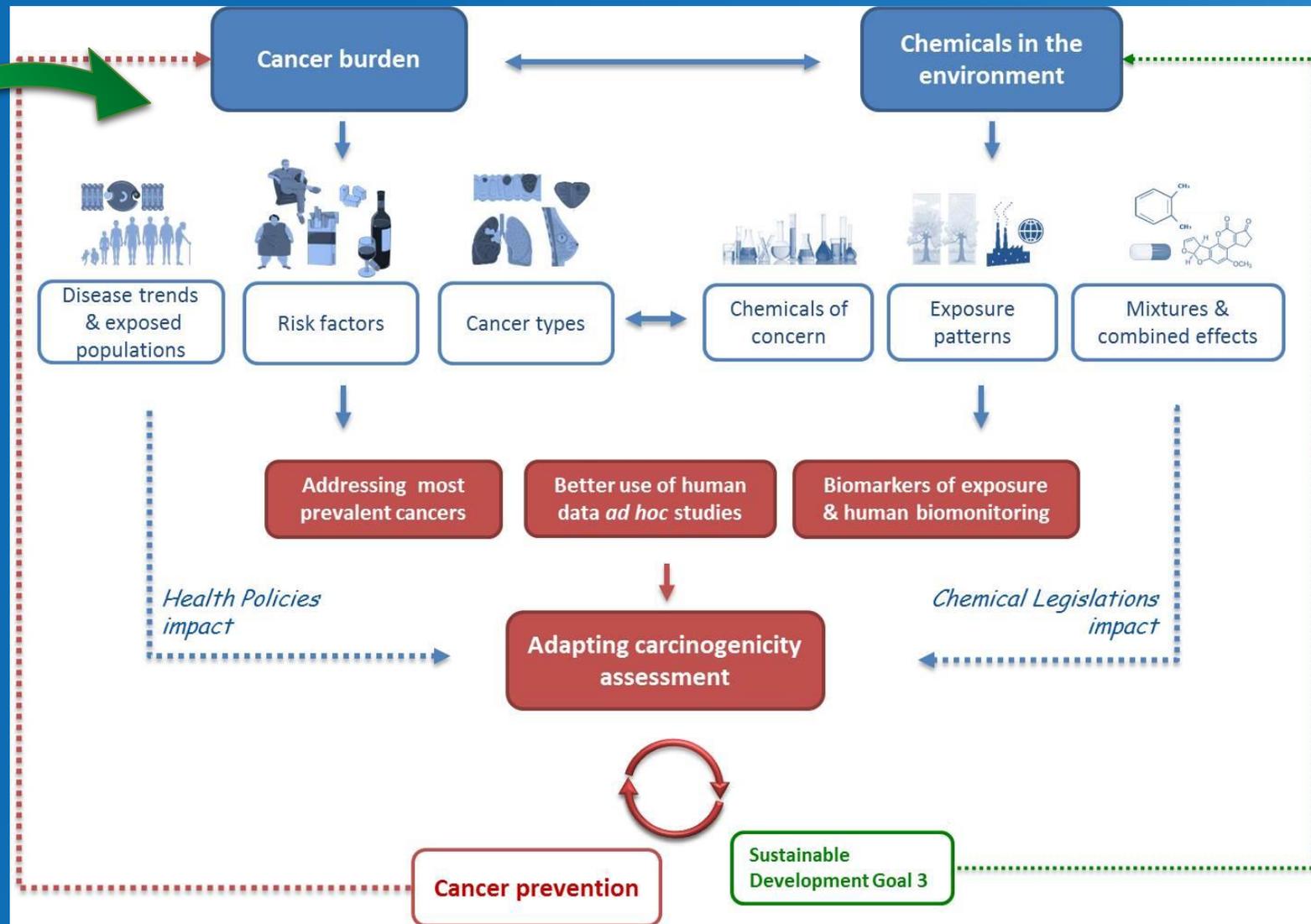
- Tracking exposure levels in general population
- Identify more susceptible populations
- Identify biomarkers of effects

Breaking down silos

HB4EU
Human
biomonitoring
project

IPCHEM
The Information
Platform for
Chemical Monitoring

JRC KCC
Knowledge Centre
on Cancer



Madia F et al. 2019, Environment International

Thank you for your Attention!

Merci pour votre attention!

Any questions?

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