

Green Metrics: Real-Life Tools & Case Study from Fragrance Industry

Goal of the course

Provide a comprehensive perspective of the green metrics developed, used in the chemical industries. The pros/cons and the limitations of all these metrics will be shown as well as the different need between industries. The case of Perfumery industry will be specially emphasized.

Course Syllabus

- Green Chemistry & Sustainability
- Presentation of the different metrics
- Pros/Cons & Limitations
- What is the purpose of these metrics?
- Presentation of different methodologies
- Difference between the pharma industry and Perfumery industry
- Example in the Perfumery industry: Ecoscent Compass, Green Motion or Estée Lauder Companies

fabrice.robvieux@firmenich.com

Senior Scientist, dsm-firmenich

www.dsm-firmenich.com

Green Metrics: Real-Life Tools

Green Chemistry, Sustainable Chemistry? Why ?

Boundaries? Limits? System Thinking?

Metric(s)?

How many?

What kind?

Data Availability? Accuracy?

Why are they needed?

What's next?

Sustainable Development Goal (2015-2030)? After 2030?

What are the Potential Pitfalls?

Planetary Boundaries – Holocene – Anthropocene?

Where do we stand?

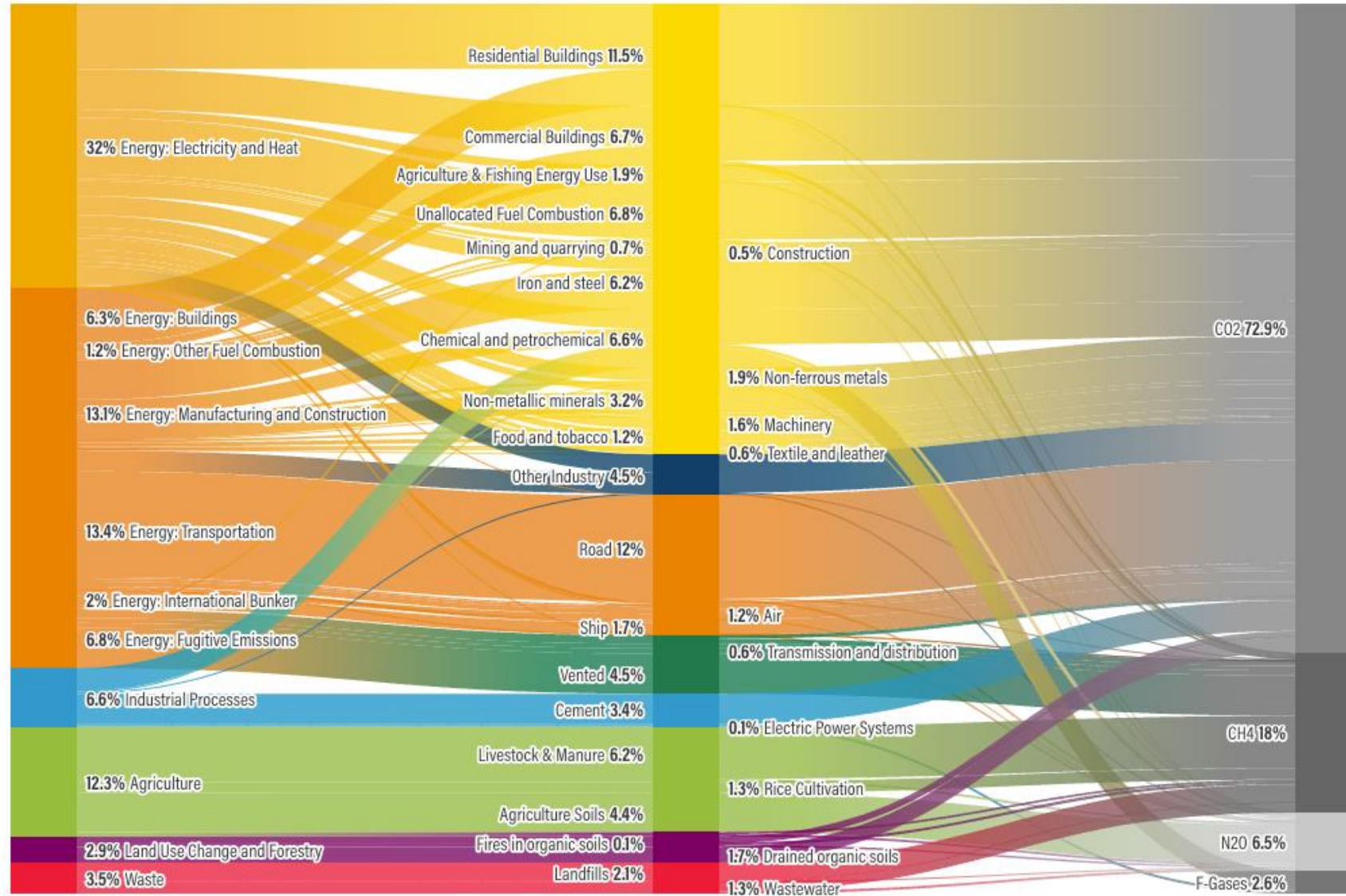
Do Limits exist?

Have they been reached?

Greenhouse Emissions

World Greenhouse Gas Emissions in 2020 (Sector | End Use | Gas)

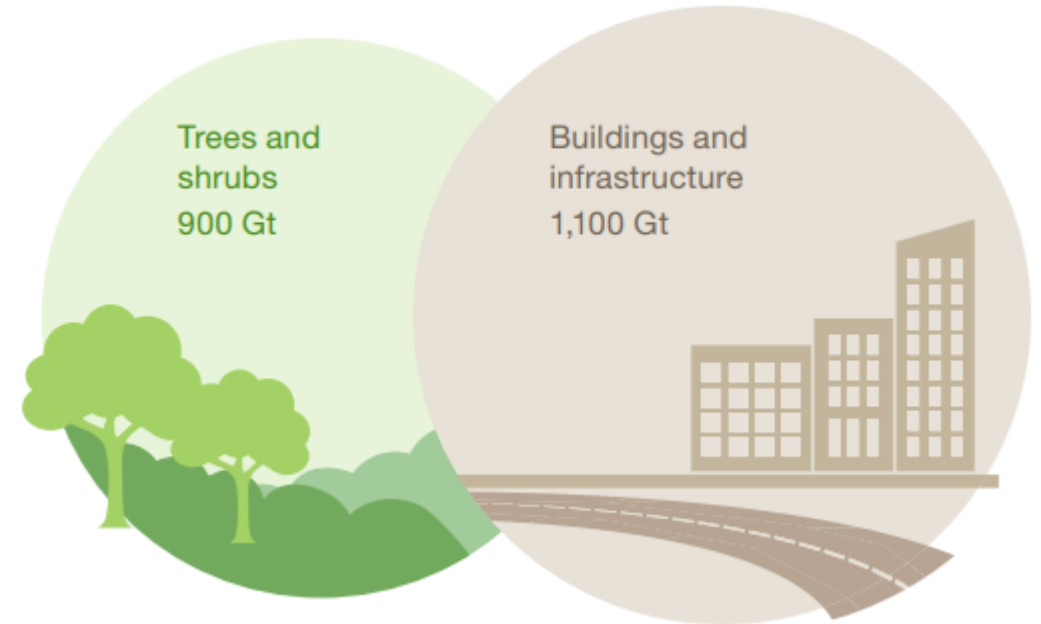
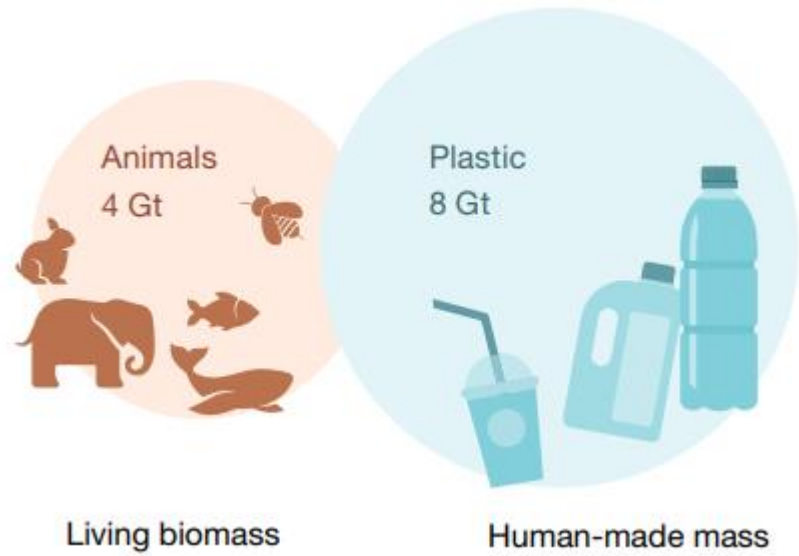
Total: 47.5 GtCO₂e



Past estimation: 49,8 GtCO₂e
(2019)

Holocene -Anthropocene

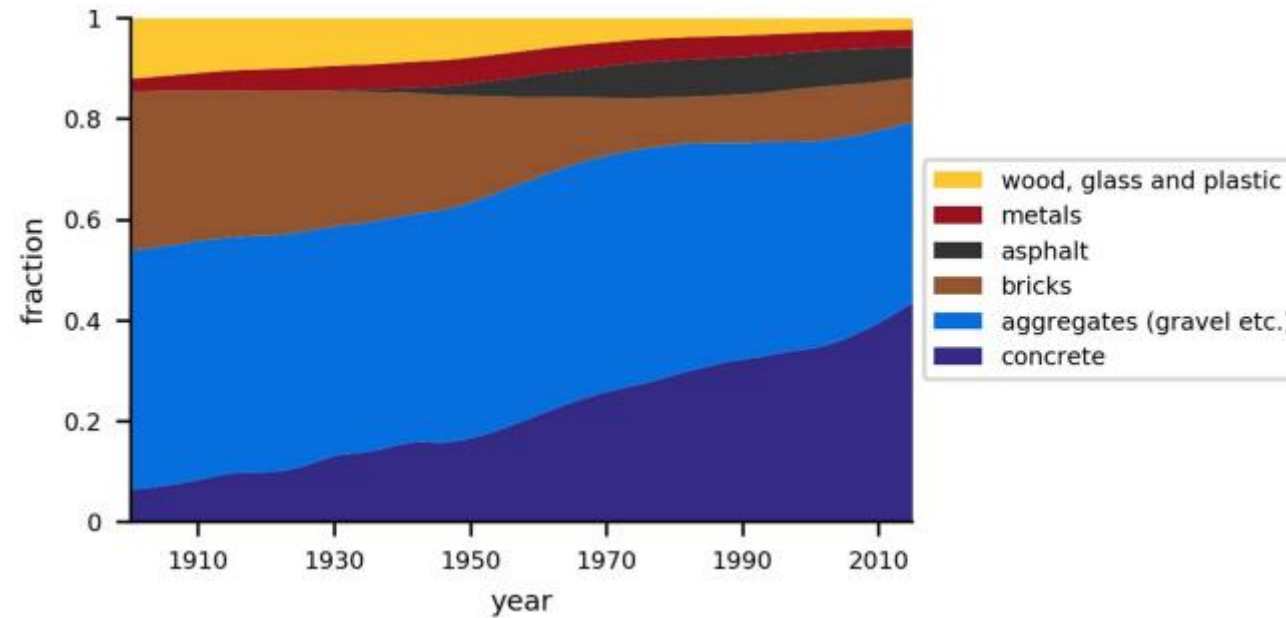
Biomass vs Human-made mass?



Nature **2020**, 588, 442.

<https://doi.org/10.1038/s41586-020-3010-5>

Holocene -Anthropocene



Anthropogenic mass composition since the year 1900, divided into material groups

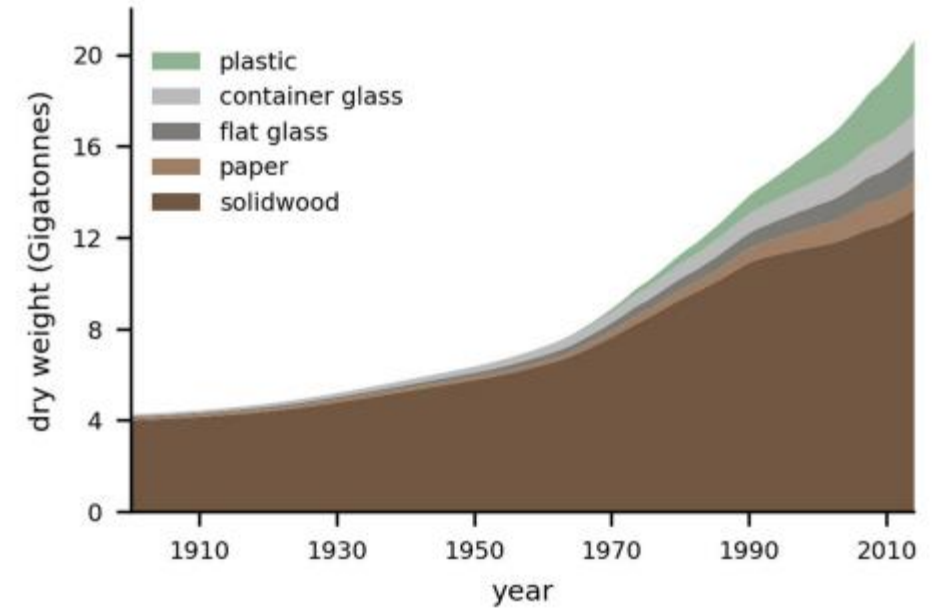
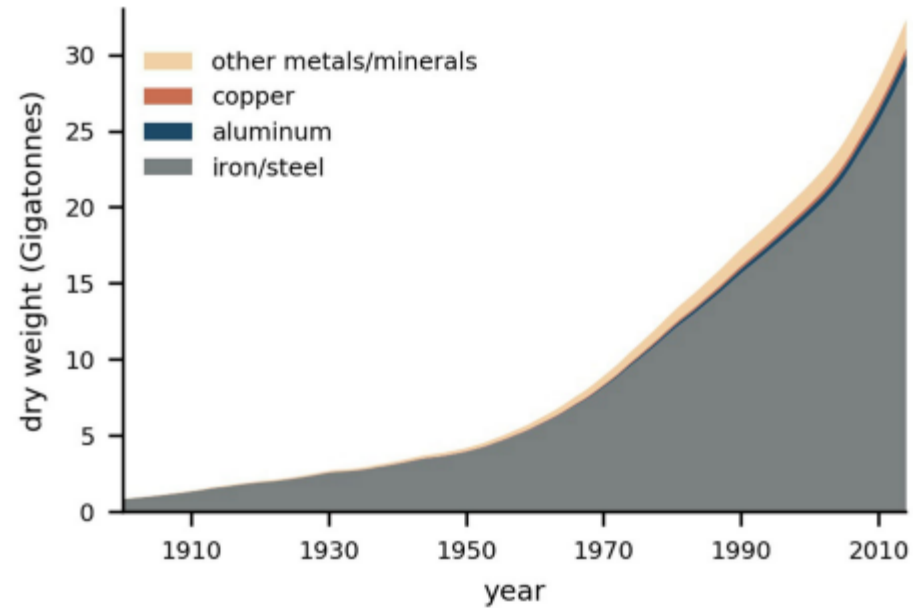
Nature **2020**, 588, 442.

<https://doi.org/10.1038/s41586-020-3010-5>

Krausmann, F., Lauk, C., Haas, W. & Wiedenhofer, D. From resource extraction to outflows of wastes and emissions: the socioeconomic metabolism of the global economy, 1900–2015.

Glob. Environ. Change **2018**, 52, 131–140.

Holocene -Anthropocene

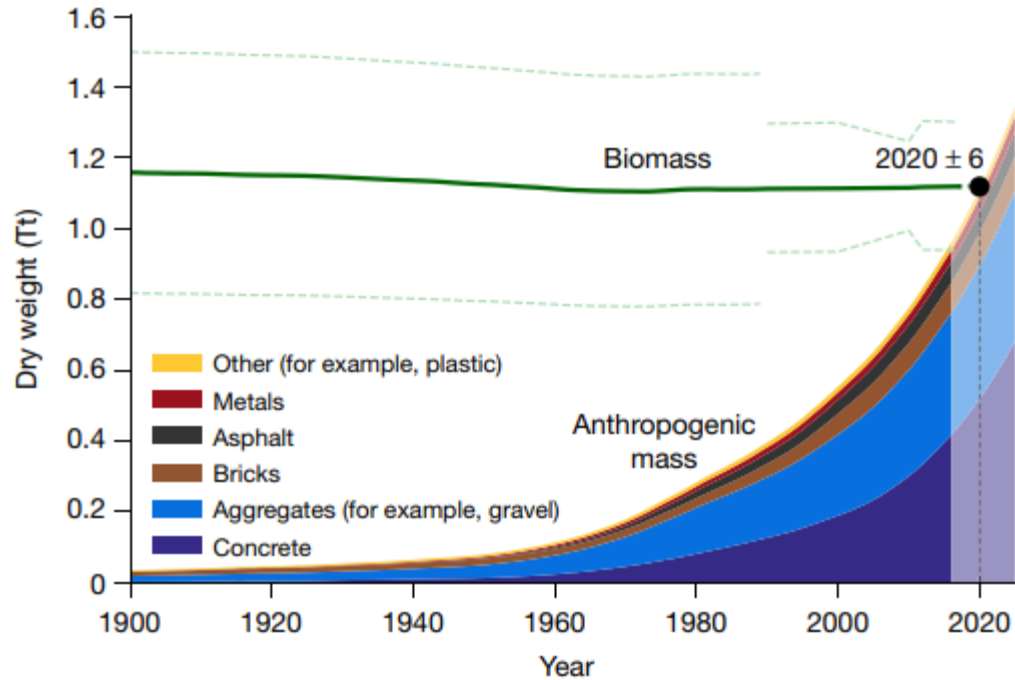


Nature **2020**, 588, 442.

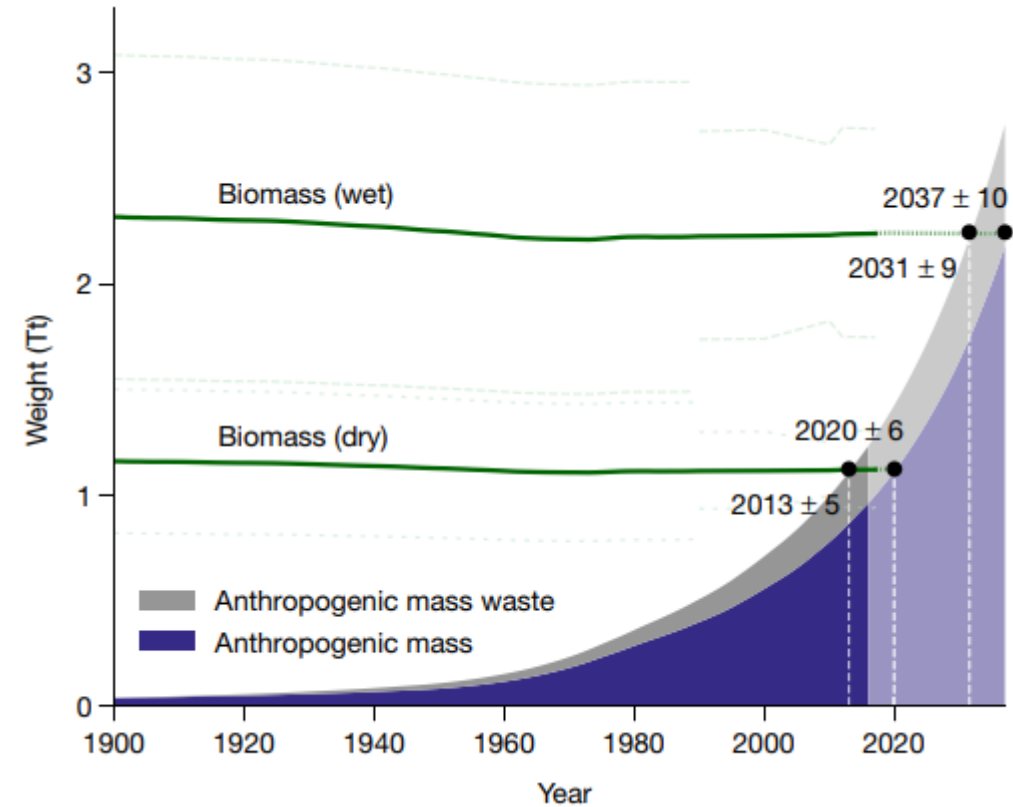
<https://doi.org/10.1038/s41586-020-3010-5>

Holocene -Anthropocene

Biomass dry



Dashed green lines: ± 1 s.d.

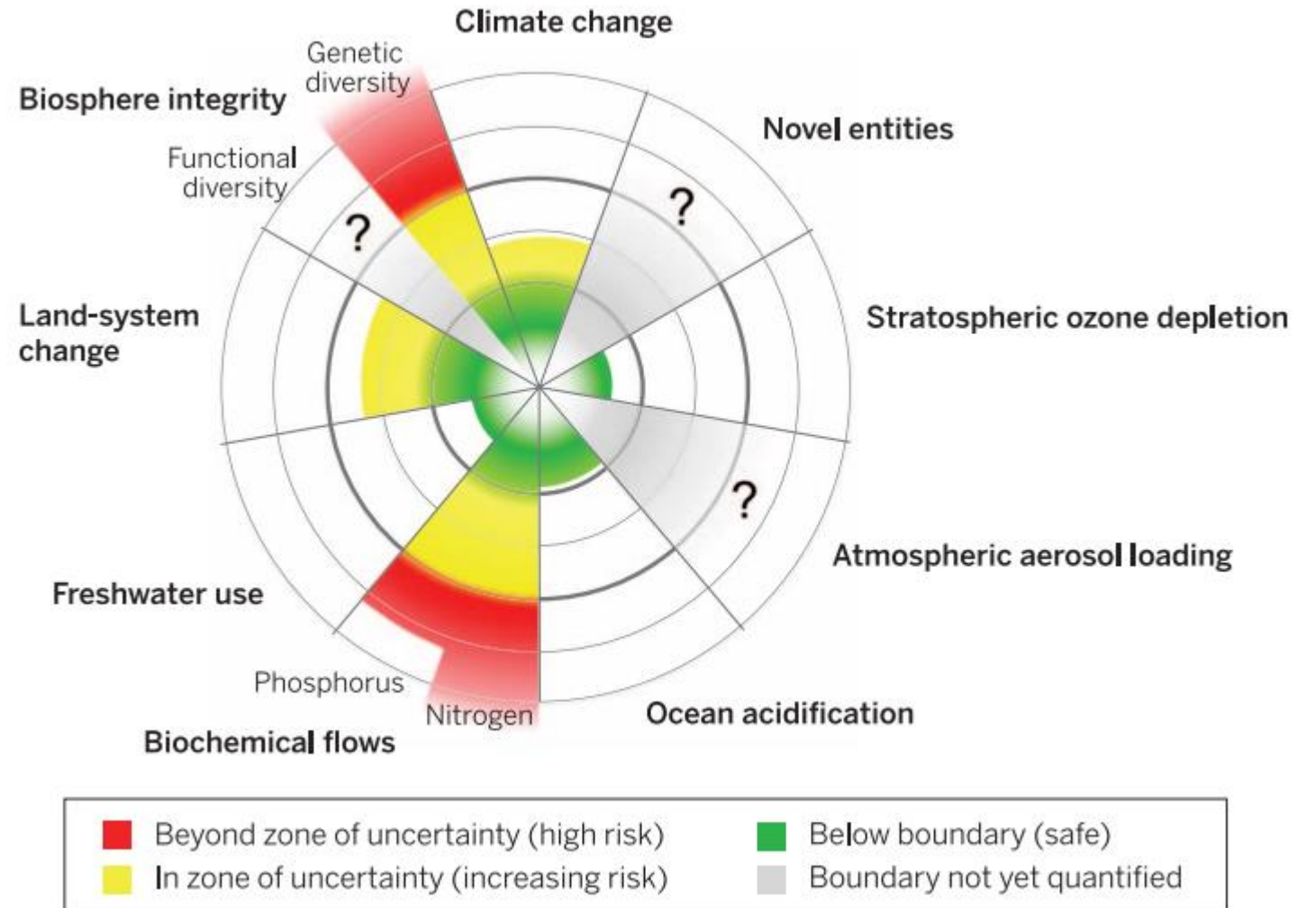


Nature **2020**, 588, 442.

<https://doi.org/10.1038/s41586-020-3010-5>

Planetary Boundaries

What does that means?



Science **2015**, 347, 1259855.
DOI: 10.1126/science.1259855

<https://planetaryboundaries.kcvs.ca/>

Planetary Boundaries

PLANETARY BOUNDARIES				
Earth-system process	Parameters	Proposed boundary	Current status	Pre-industrial value
Climate change	(i) Atmospheric carbon dioxide concentration (parts per million by volume)	350	387	280
	(ii) Change in radiative forcing (watts per metre squared)	1	1.5	0
Rate of biodiversity loss	Extinction rate (number of species per million species per year)	10	>100	0.1-1
Nitrogen cycle (part of a boundary with the phosphorus cycle)	Amount of N ₂ removed from the atmosphere for human use (millions of tonnes per year)	35	121	0
Phosphorus cycle (part of a boundary with the nitrogen cycle)	Quantity of P flowing into the oceans (millions of tonnes per year)	11	8.5-9.5	-1
Stratospheric ozone depletion	Concentration of ozone (Dobson unit)	276	283	290
Ocean acidification	Global mean saturation state of aragonite in surface sea water	2.75	2.90	3.44
Global freshwater use	Consumption of freshwater by humans (km ³ per year)	4,000	2,600	415
Change in land use	Percentage of global land cover converted to cropland	15	11.7	Low
Atmospheric aerosol loading	Overall particulate concentration in the atmosphere, on a regional basis	To be determined		
Chemical pollution	For example, amount emitted to, or concentration of persistent organic pollutants, plastics, endocrine disruptors, heavy metals and nuclear waste in, the global environment, or the effects on ecosystem and functioning of Earth system thereof	To be determined		

Rockström, J. *et al.*,
Planetary boundaries: Exploring the safe operating space for humanity.
Ecol. Soc. **2009**, 14, 32.

<http://www.ecologyandsociety.org/vol14/iss2/art32/>

Rockström, J. *et al.*, A safe operating space for humanity. *Nature* **2009**, 461, 472.

<http://dx.doi.org/10.1038/461472a>

Planetary Boundaries

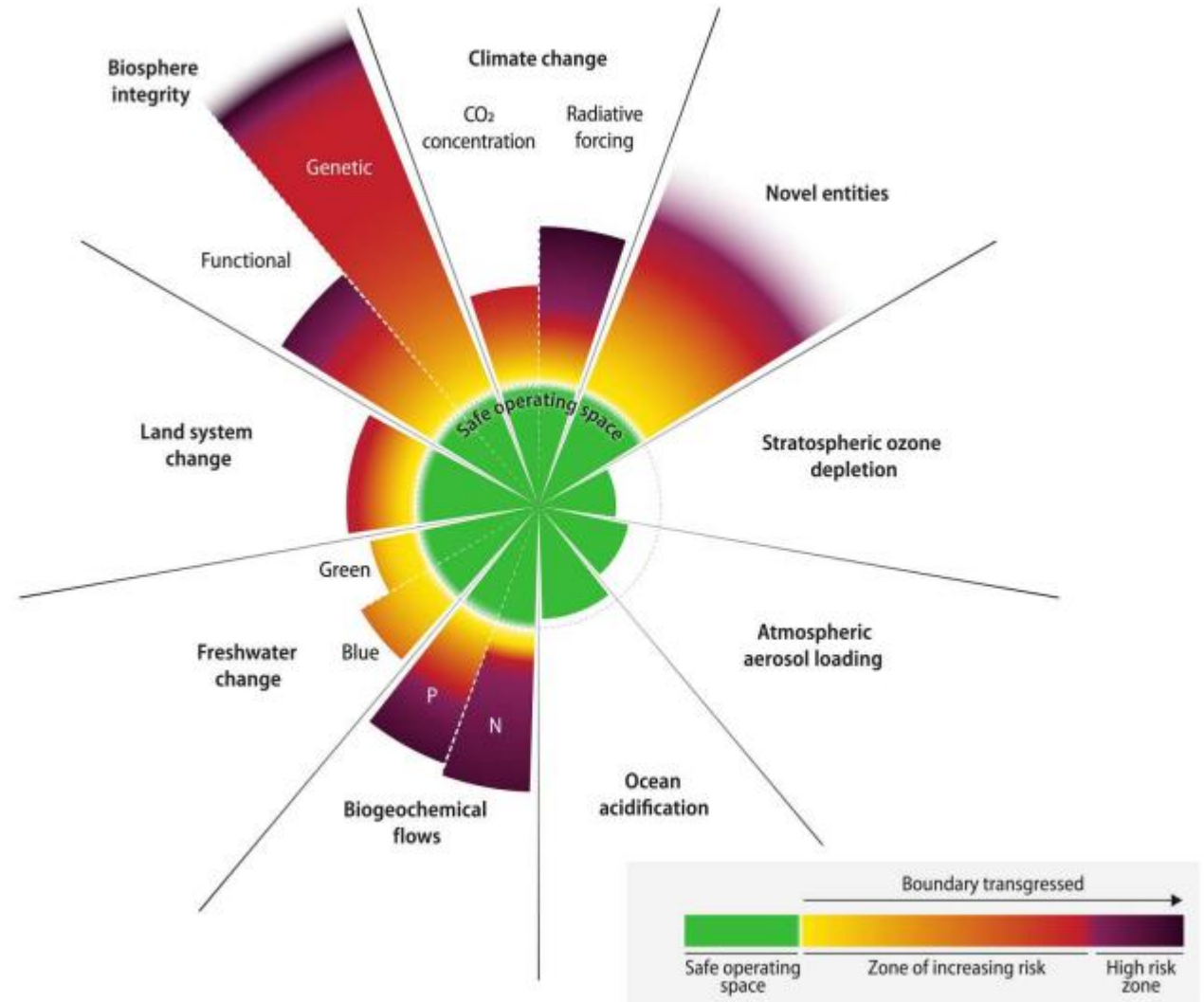
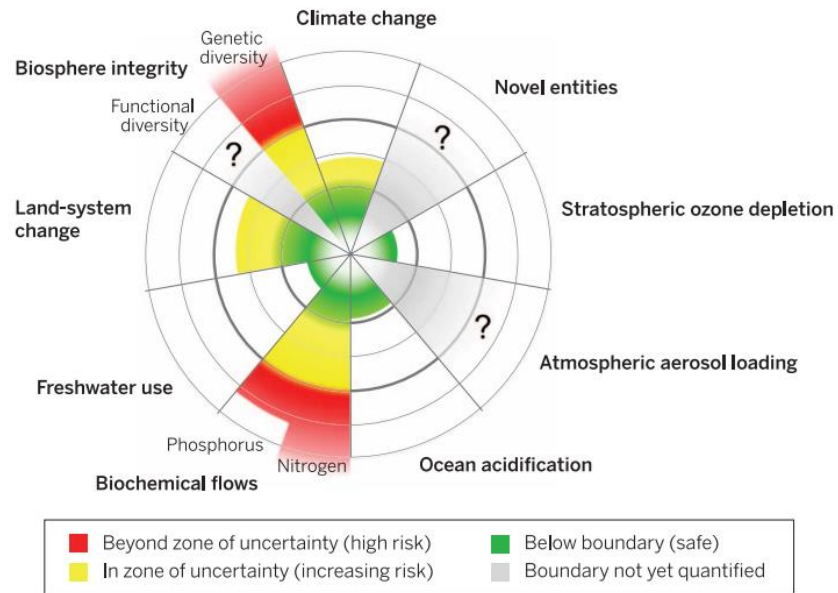
Earth-system process	Control variable(s)	Planetary boundary (zone of uncertainty)	Current value of control variable
Climate change (R2009: same)	Atmospheric CO ₂ concentration, ppm	350 ppm CO ₂ (350–450 ppm)	398.5 ppm CO ₂
	Energy imbalance at top-of-atmosphere, W m ⁻²	+1.0 W m ⁻² (+1.0–1.5 W m ⁻²)	2.3 W m ⁻² (1.1–3.3 W m ⁻²)
Change in biosphere integrity (R2009: Rate of biodiversity loss)	<i>Genetic diversity:</i> Extinction rate	< 10 E/MSY (10–100 E/MSY) but with an aspirational goal of ca. 1 E/MSY (the background rate of extinction loss). E/MSY = extinctions per million species-years	100–1000 E/MSY
	<i>Functional diversity:</i> Biodiversity Intactness Index (BII)	Maintain BII at 90% (90–30%) or above, assessed geographically by biomes/large regional areas (e.g. southern Africa), major marine ecosystems (e.g., coral reefs) or by large functional groups	84%, applied to southern Africa only
	Note: These are interim control variables until more appropriate ones are developed		

Science **2015**, 347, 1259855.
DOI: 10.1126/science.1259855

<https://www.co2.earth/daily-co2>

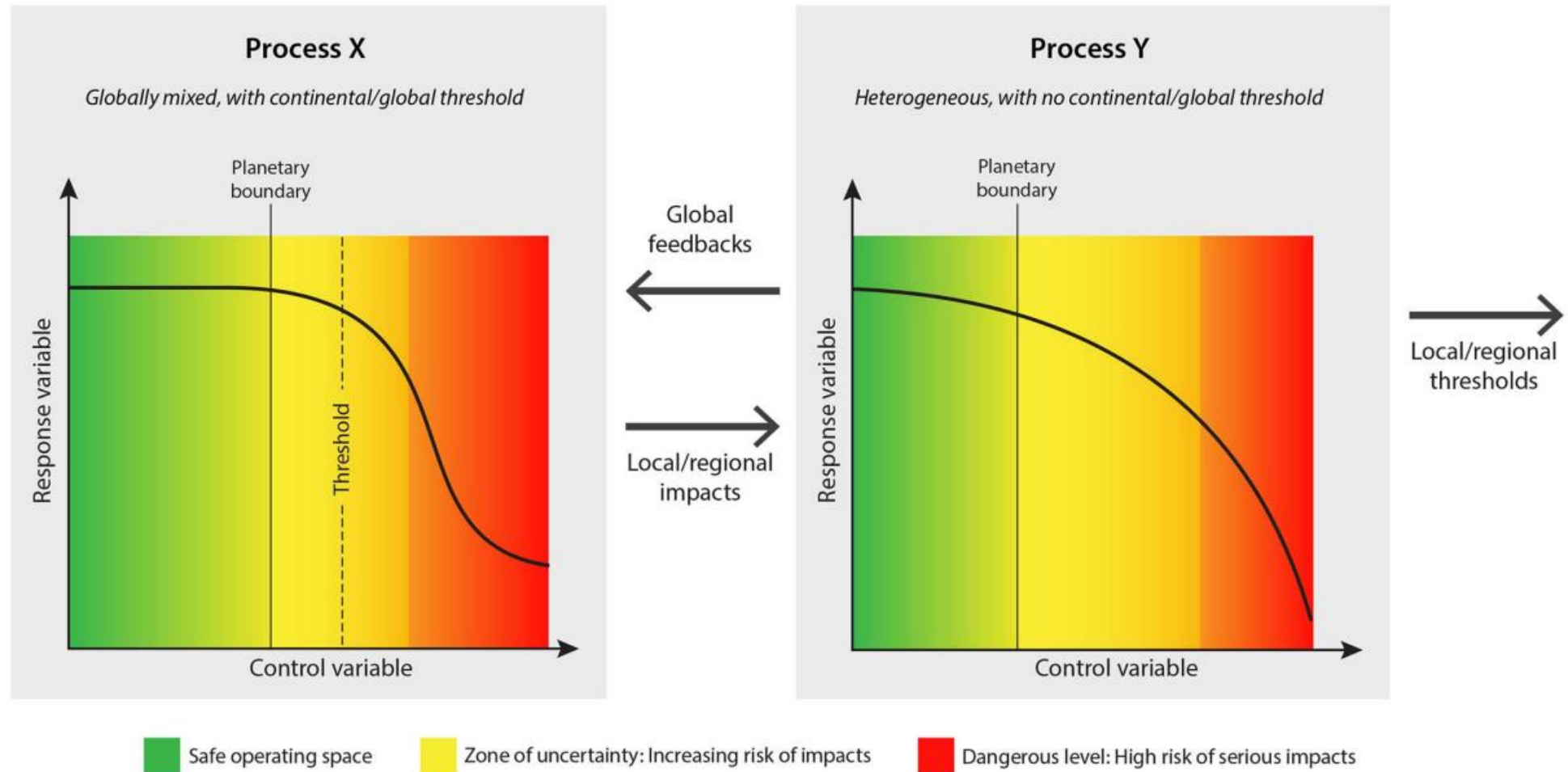
Planetary Boundaries

What does that means?



Science Adv. 2023, eadh2458.
<https://doi.org/10.1126/sciadv.adh2458>

Planetary Boundaries



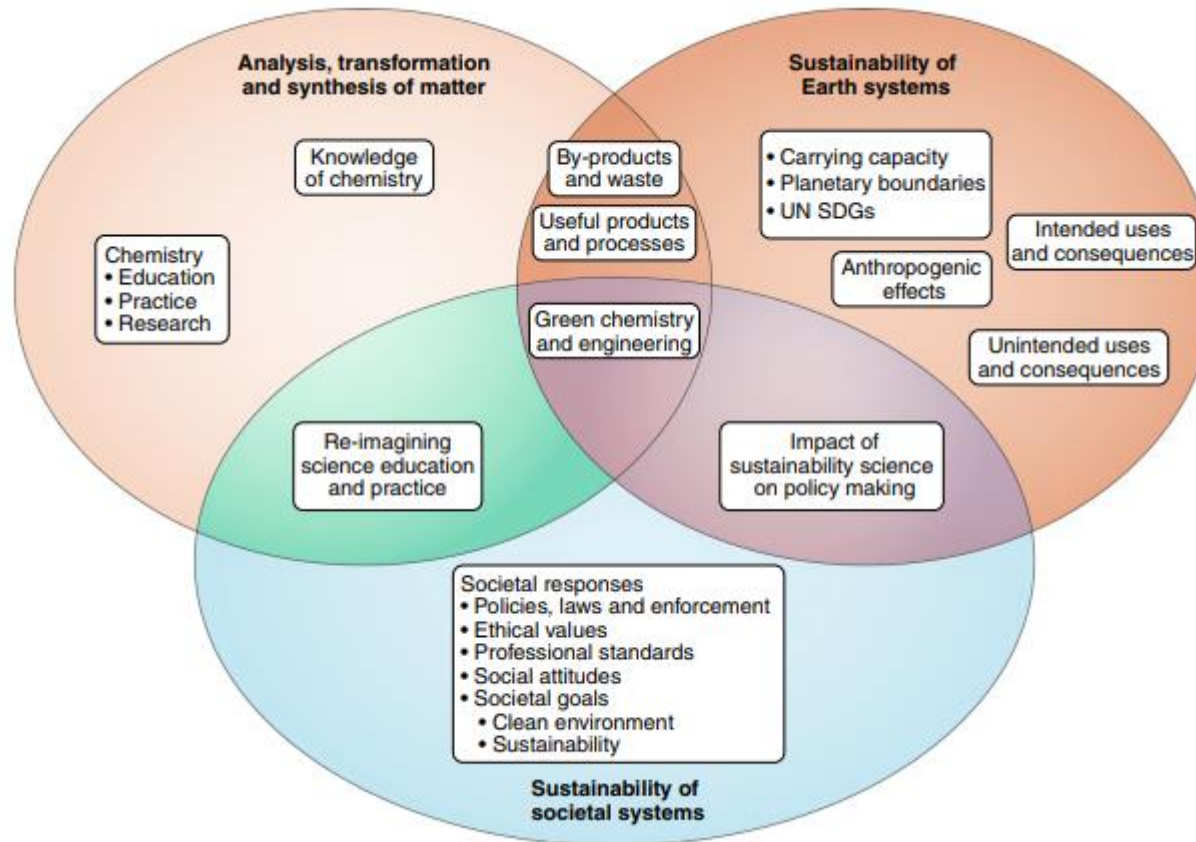
Science **2015**, 347, 1259855.

DOI: 10.1126/science.1259855

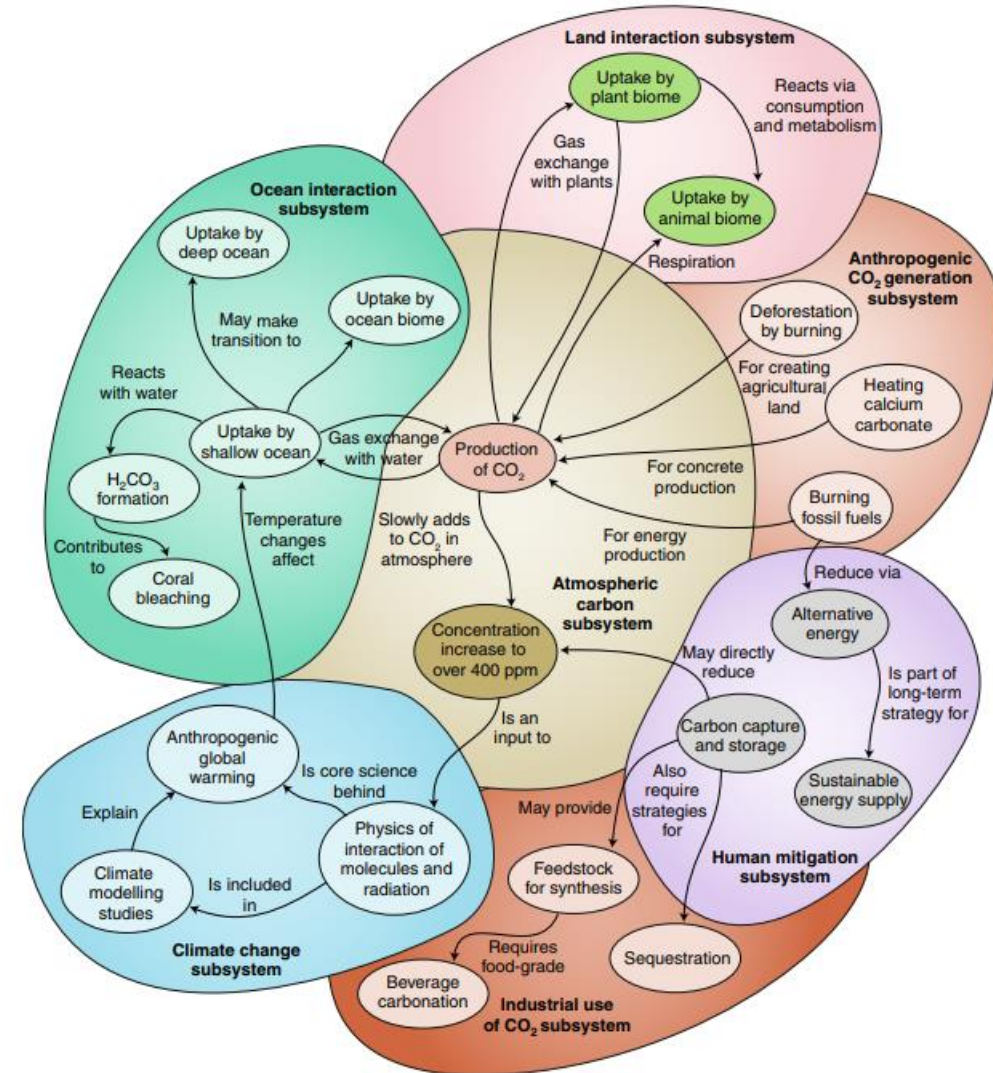
Systems Thinking

“The ability to understand and interpret complex systems” and involves: “visualizing the interconnections and relationships between the parts in the system; examining behaviors that change over time; and examining how systems-level phenomena emerge from interactions between the system’s parts”

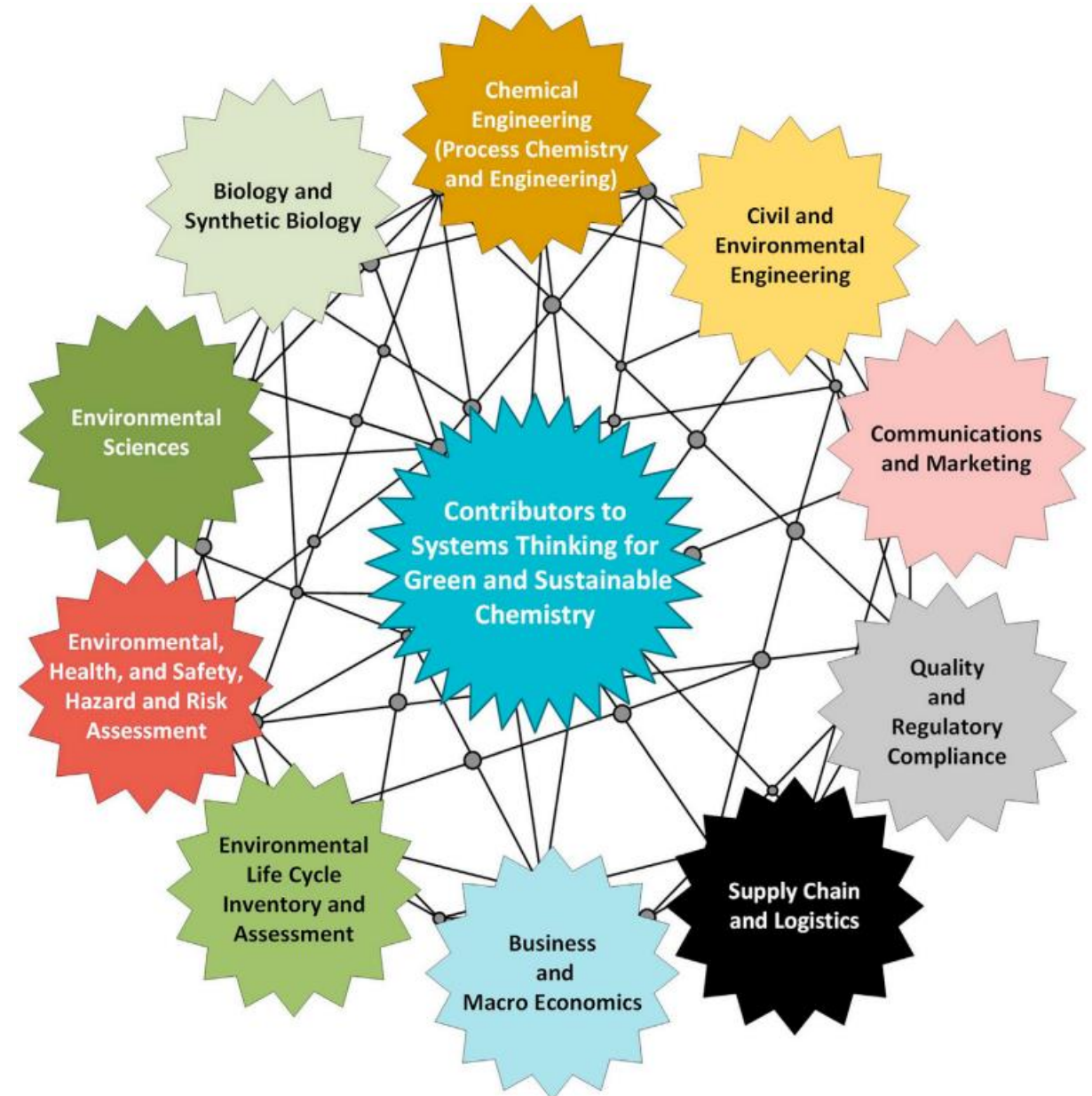
Systems Thinking



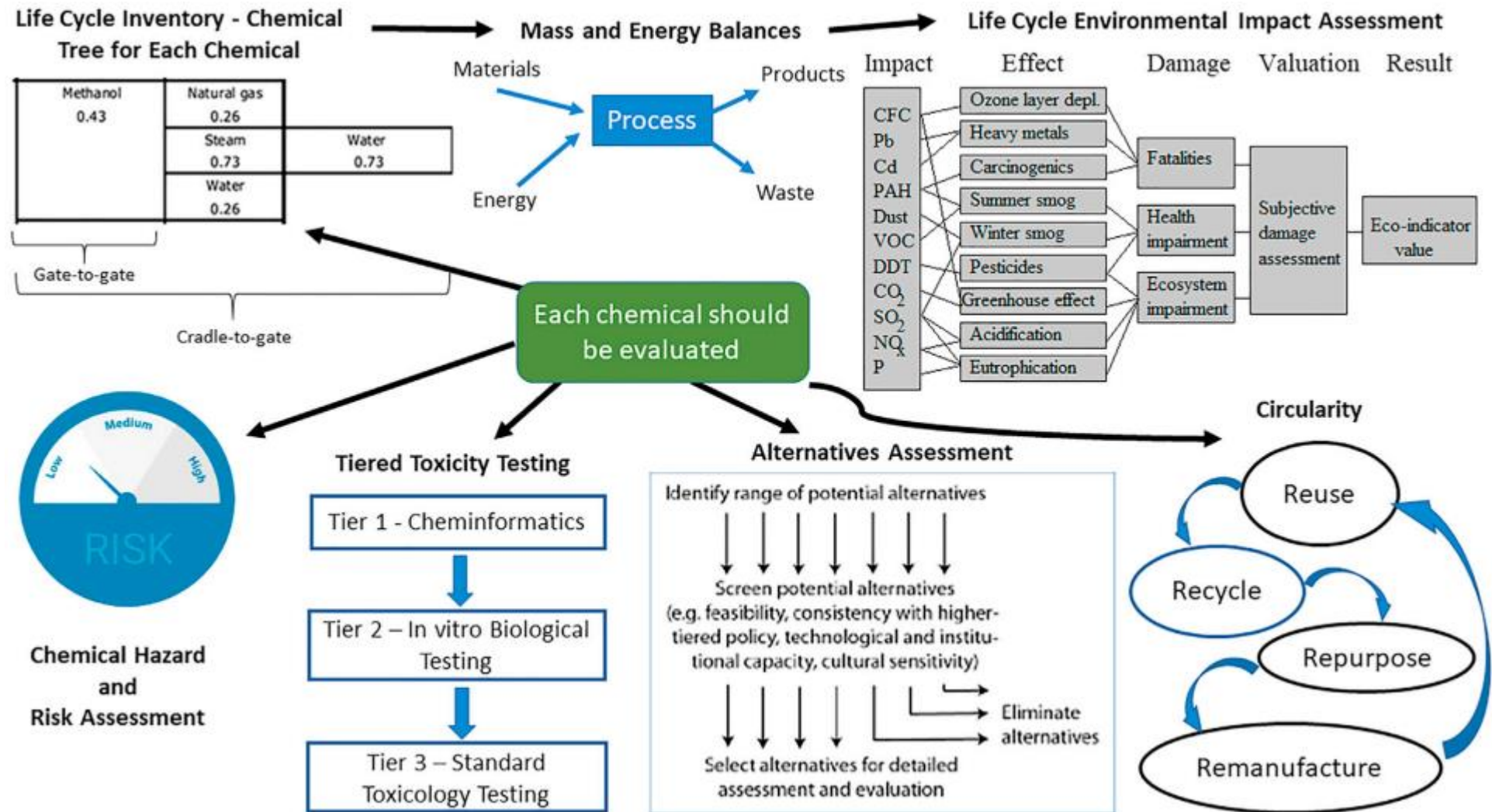
Systems Thinking



Systems Thinking



Systems Thinking



Green Metrics: Real-Life Tools

Green Chemistry has been defined as the use of chemistry for pollution prevention using suitable designs of products and processes, reducing and mainly, if possible, eliminating the use and generation of hazardous substances.

Anastas & Warner stated in 1998: «It is an approach that provides a fundamental methodology for changing the intrinsic nature of a chemical product or process so that it is inherently of less risk to human and the environment, to prevent pollution, and thereby solve environmental problems, promoting pollution prevention and industrial ecology»

Noyori expressed that “green chemistry is not just a catchphrase. It is an indispensable principle of chemical research that will sustain our civilized society in the twenty-first century and further into the future.”

Anastas, P.T.; Warner, J.C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, UK, **1998**.

Noyori, R. Synthesizing Our Future, *Nat. Chem.*, **2009**, *1*, 5–6.

Processes **2022**, *10*, 1274.

<https://doi.org/10.3390/pr10071274>

Green Metrics: Real-Life Tools

Green Chemistry

WHY ? DEFINITION?

Not everything that can be counted counts and not everything that counts can be counted

Einstein?

Green Metrics: Real-Life Tools

Green Chemistry: 12 Principles



Anastas, P. T.; Eghbali, N. Green Chemistry: Principles and Practice. *Chem. Soc. Rev.* **2010**, 39, 301.
Whitaker, G. T. *Org. Process Res. Dev.* **2019**, 23(10), 2109–2121.

Green Metrics: Real-Life Tools

Green Chemistry: 12 Principles

Condensed Principles of Green Chemistry

- P - Prevent wastes
- R - Renewable materials
- O - Omit derivatization steps
- D - Degradable chemical products
- U - Use safe synthetic methods
- C - Catalytic reagents
- T - Temperature, Pressure ambient
- I - In-Process Monitoring
- V - Very few auxiliary substances
- E - E-factor, maximise feed in product
- L - Low toxicity of chemical products
- Y - Yes, it is safe



Green Metrics: Real-Life Tools

Sustainable Chemistry is engaged toward the life cycle assessment (LCA), which is associated with the entire life cycle of a product, process, or activity.

OECD's definition: *"Sustainable chemistry is a scientific concept that seeks to improve the efficiency with which natural resources are used to meet human needs for chemical products and services. Sustainable chemistry encompasses the design, manufacture and use of efficient, effective, safe and more environmentally benign chemical products and processes."*

Benefits of Sustainable Chemistry

The **environmental** and **societal** benefits of sustainable chemistry include:

- Avoiding the use of persistent, bioaccumulative, toxic, and otherwise hazardous materials,
- Using renewable resources and decreasing consumption of non-renewable resources,
- Minimising negative environmental impacts of chemical processing and manufacturing,
- Providing technologies that are economically competitive for and advantageous to industry.

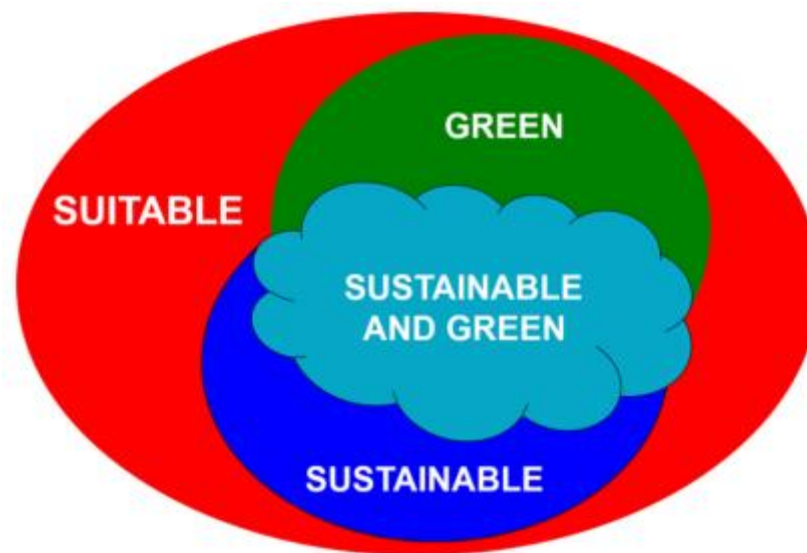
[OECD Sustainable Chemistry.](#)

Krasnodębski, M. An unlikely bifurcation: history of sustainable (but not Green) chemistry. *Found Chem* (2023).

<https://doi.org/10.1007/s10698-023-09474-x>

Green Metrics: Real-Life Tools

Green Chemistry & Sustainable Chemistry



The Molecular Basis of Sustainability

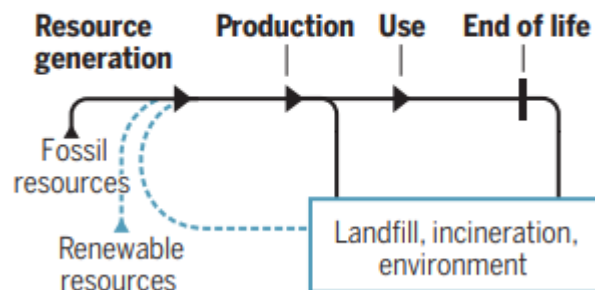
Chemistry as a central domain

Chemists have been responsible for deeply understanding the material world and how it functions.

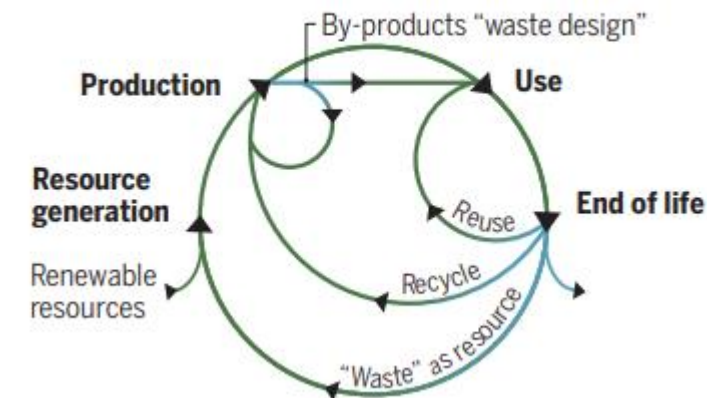
One accepted definition for Green Chemistry: green chemistry is the **design** of chemical products and processes that reduce or eliminate the use and generation of hazardous substances

Designing

Today's chemical sector



Tomorrow's chemical sector



- Mostly linear processes → Circular processes
- Fossil feedstocks → Renewable feedstocks
- Reactive, persistent, or toxic chemical reagents and products → Benign chemical reagents and products
- Catalysis using rare metals → Catalysis using abundant metals, enzymes, photons, or electrons
- Covalent bonds → Weak, noncovalent interactions
- Conventional solvents → Low toxicity, recyclable, inert, abundant, easily separable green solvents or solventless
- Material- and energy-consuming isolation and purification → Self-separating systems
- Large "waste" volume → Atom-, step-, and solvent-economical processes
- "Waste" treatment → "Waste" utilization
- Design exclusively for use phase with reliance on circumstantial control → Intentional molecule design for full life cycle
- Performance = maximize function → Performance = maximize function + minimize hazards
- Maximum chemical production for increased profit → Maximum performance with minimal benign material use for increased profit

The Molecular Basis of Sustainability

Chemistry as a central domain

Paradigm shift is needed

Box 1. Examples Contrasting Green Chemistry Principles with Traditional Chemical Approaches

Principle 1: avoid waste

Traditional: waste is something to be managed, measured, treated, and disposed of

Principle 3: reagents should be non-toxic

Traditional: toxic chemicals can be safely managed through circumstantial controls

Principle 5: feedstocks should be renewable

Traditional: chemical feedstocks are derived from finite and depleting sources

SDG Goals & Green Metrics

Millenium Development Goals: 8 focuses in 2000.....



<https://www.unaa.org.au/2017/01/19/the-united-nations-millennium-development-goals-successes-and-failures-from-2000-until-today/>

SDG Goals & Green Metrics

Sustainable Development Goals: 12 focuses on responsible and environmentally sustainable production and targets the substantial reduction of waste generation by 2030.



SDG Goals & Green Metrics

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Green Metrics: Real-Life Tools

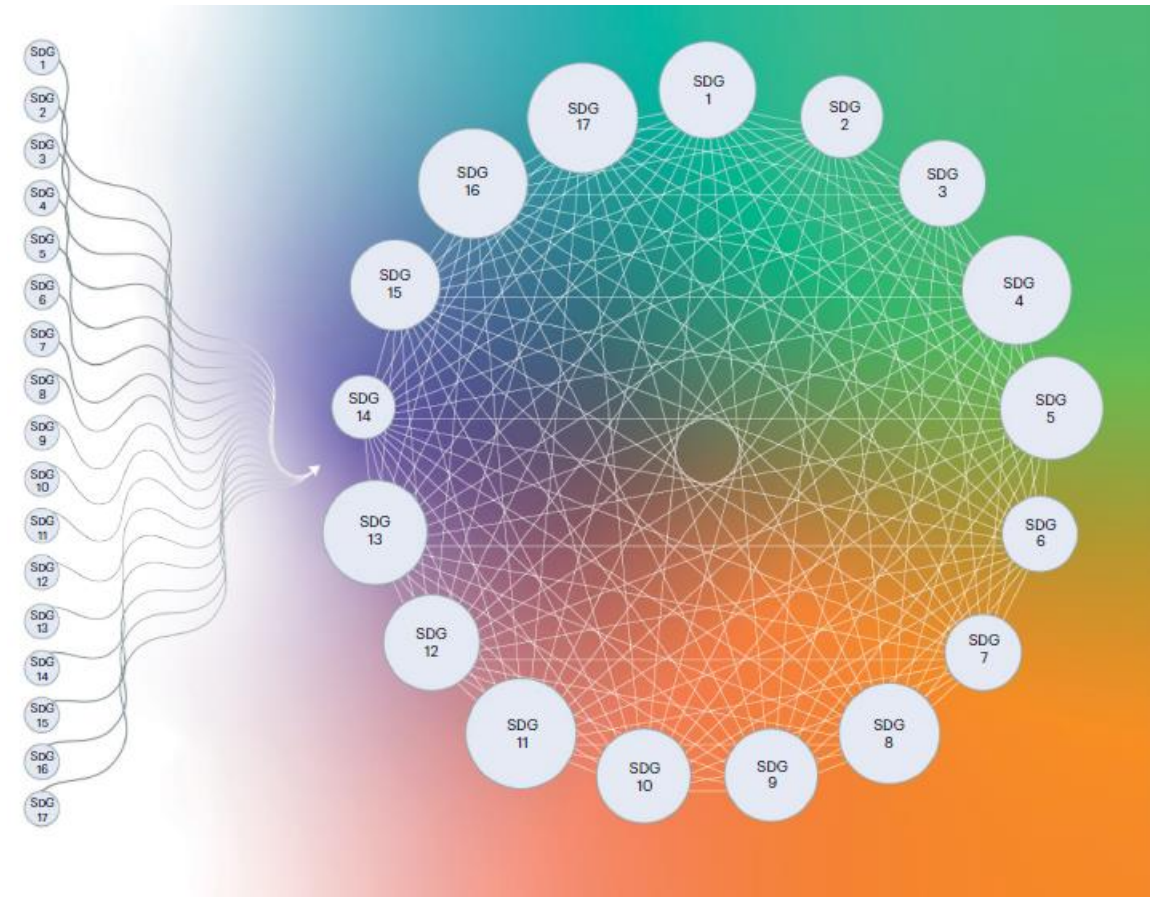
Sustainable Development Goals: 12 focuses on responsible and environmentally sustainable production and targets the substantial reduction of waste generation by 2030.

For example:

Climate action (SDG13)

Make consumption and production more sustainable (SDG12)

Systemic impact means accounting for each goal's positive and negative influence on all other goals.



Planetary Boundaries

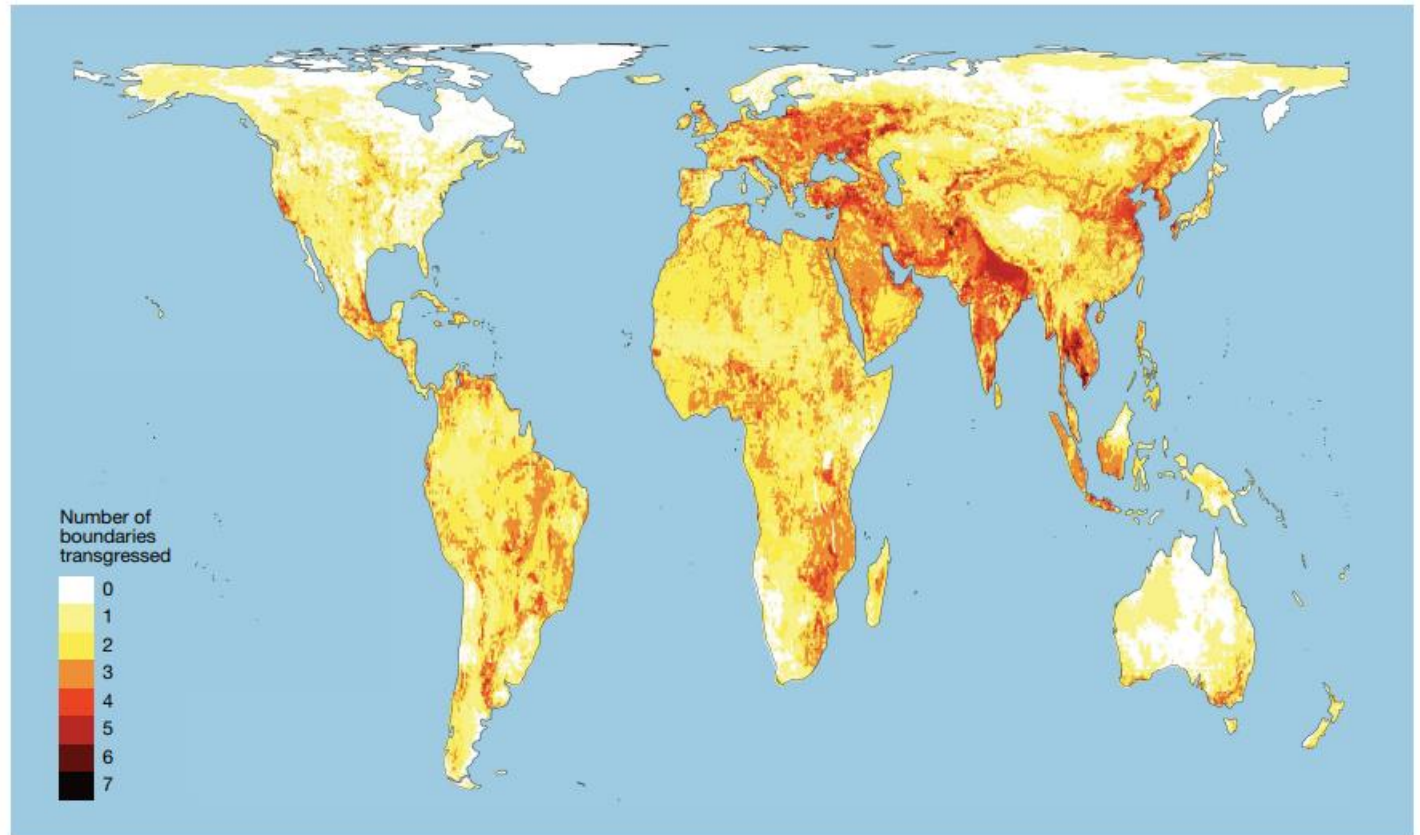


Fig. 3 | Hotspots of current ESB transgressions. The number of subglobal climate (two local exposure boundaries), functional integrity, surface water, groundwater, nitrogen, phosphorus and aerosol safe and just ESBs currently transgressed by location. No more than seven of these eight metrics have their ESBs transgressed in any one pixel. Since climate is a globally defined ESB, we use wet bulb temperatures of over 35 °C for at least 1 day per year and low-

elevation coastal zones (<5 m) exposed to sea-level rise as proxies for local climate transgression while acknowledging that the impacts of climate change are far more diverse. We also emphasize that exposure of a location does not necessarily imply responsibility for causing or addressing these environmental impacts. We invite the reader to investigate the consequences of different boundary values using the code in the code availability information.

Value of Nature

Plurality of values:

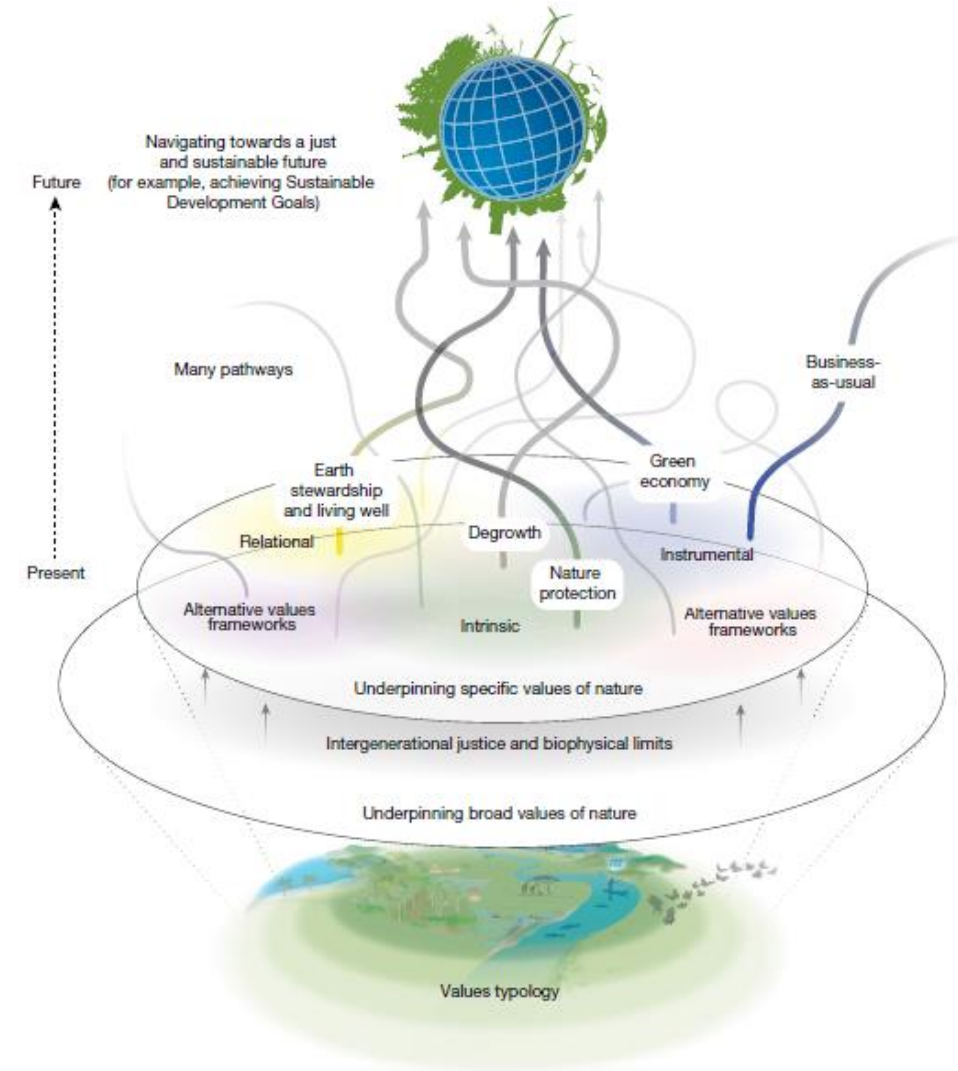
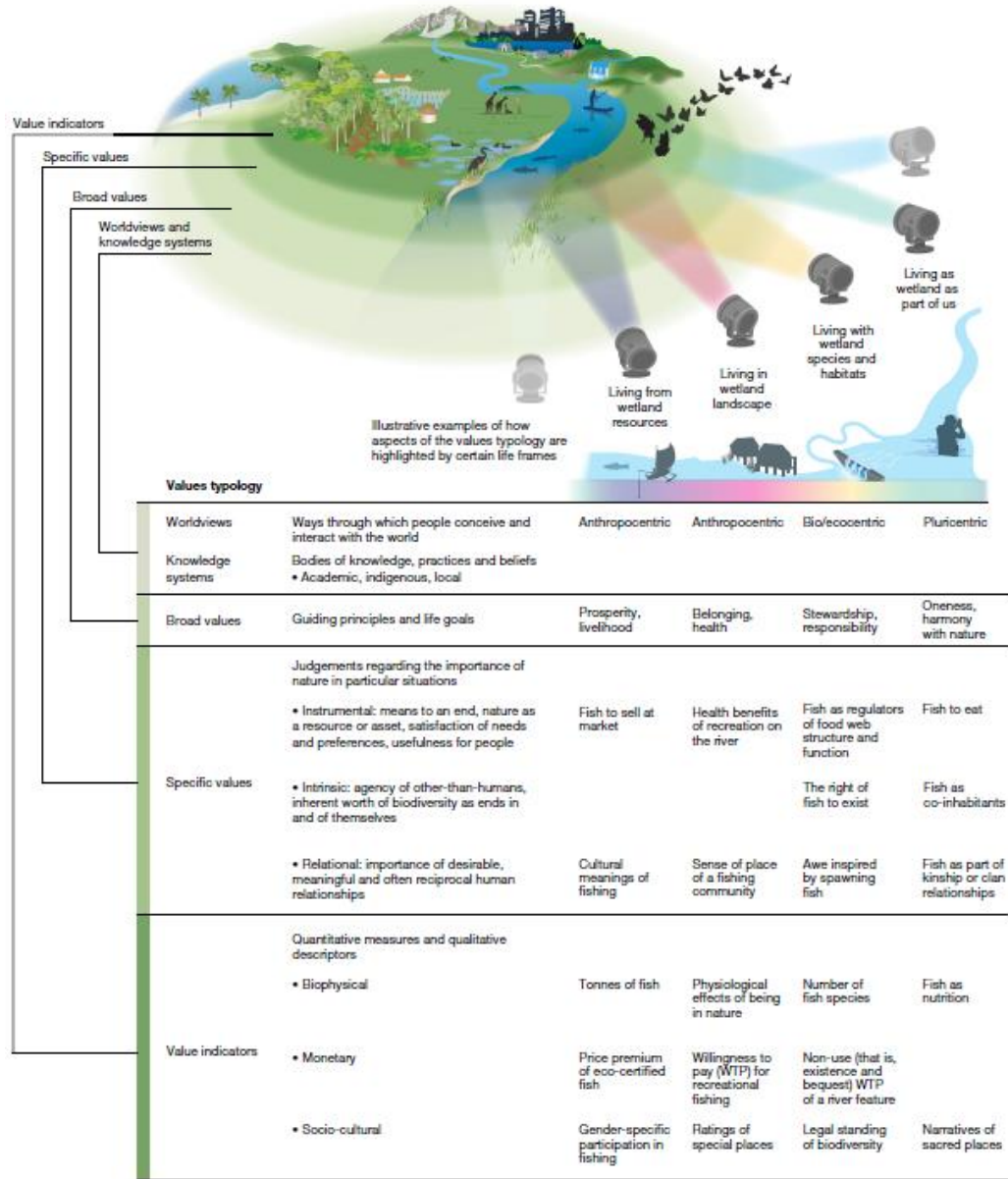
Postindustrial societies with high level of material security: increase in the value of wildlife

Global South: lower levels security; instrumental values...

Nature, **2023**, 620, 821.

<https://doi.org/10.1038/s41586-023-06406-9>

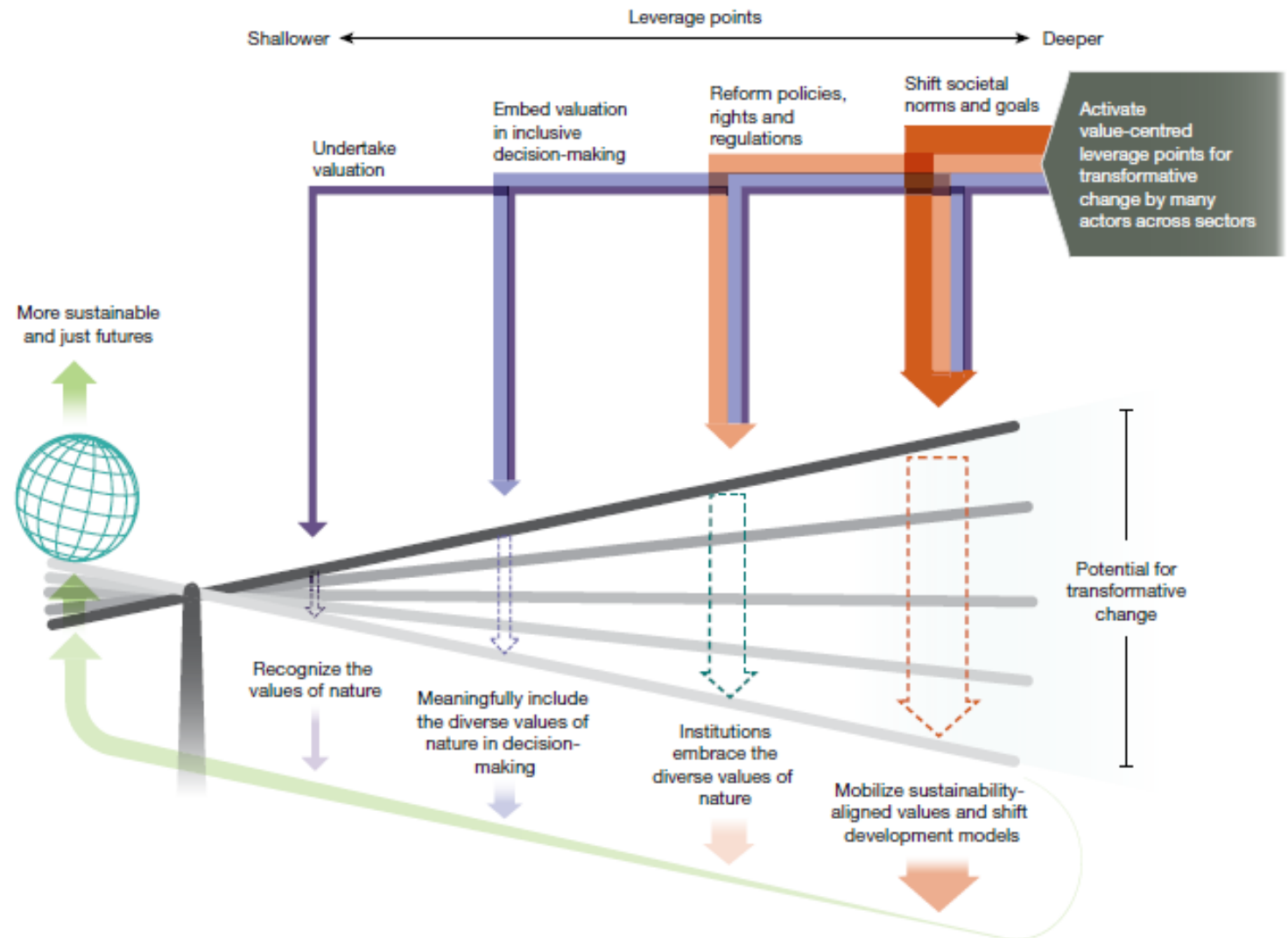
Value of Nature



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<https://doi.org/10.1038/s41586-023-06406-9>

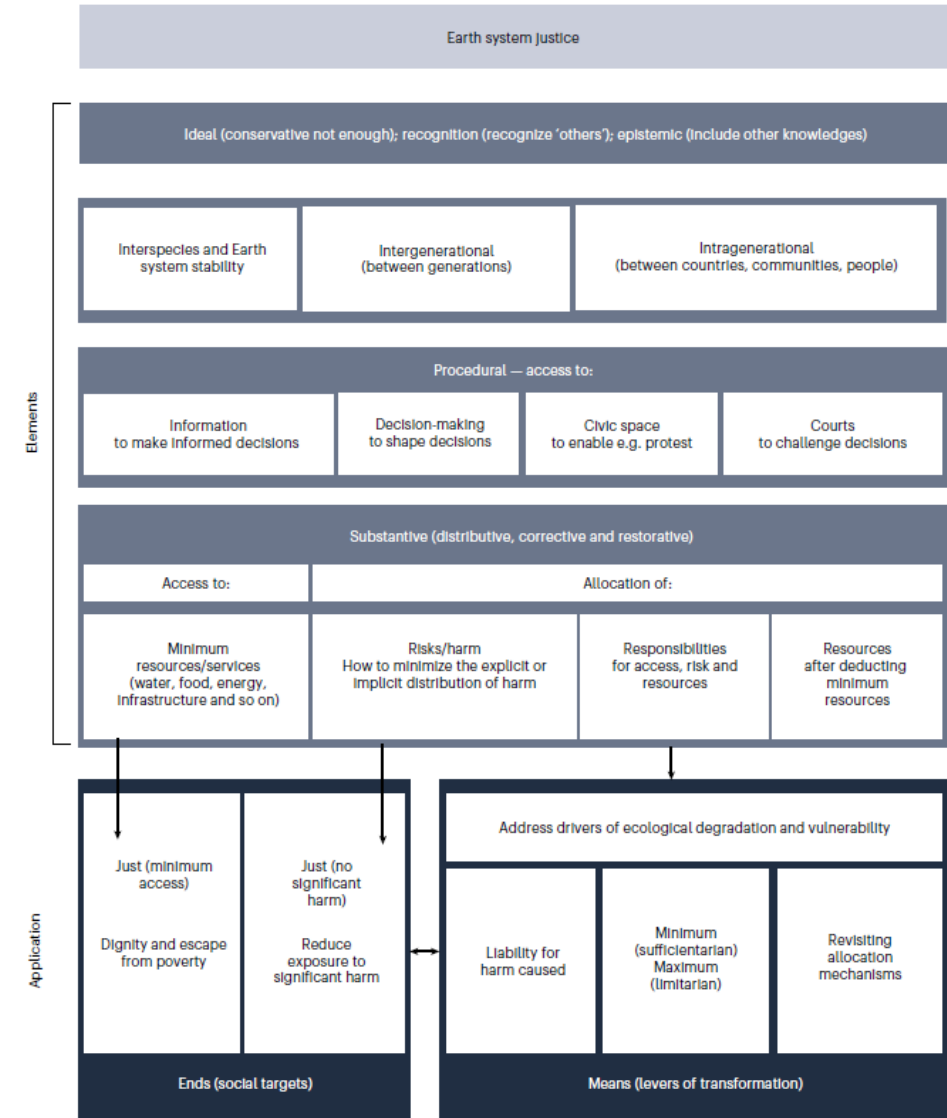
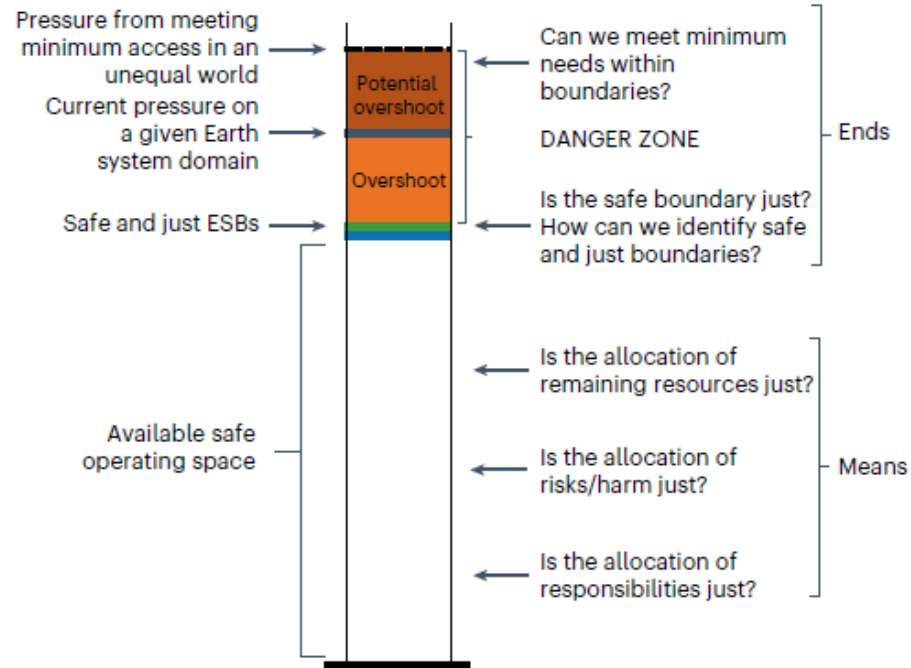
Value of Nature



Nature, **2023**, 620, 821.

<https://doi.org/10.1038/s41586-023-06406-9>

Justice?



Nature Sustainability, 2023

<https://doi.org/10.1038/s41893-023-01064-1>

Green Metrics: Real-Life Tools

“you can’t manage what you don’t measure”

Edwards Deming or Peter Drucker

«If you can’t measure it, you can’t improve it»

Lord Kelvin

“Nothing becomes more important just because you can measure it. It becomes more measurable, that’s all”

Edwards Deming

Green Metrics: Real-Life Tools

Historical context:

Back in 1956, Nobel Price Winner Robert B. Woodward stated: “synthesis must always be carried out by a plan, and the synthetic frontier can be defined only in terms of the degree to which realistic planning is possible, utilizing all of the intellectual and physical tools available”

Woodward, R. B. (1956) *In Perspectives in Organic Chemistry* (ed. Todd, A.), 155–184.

Corey, E. J., Cheng, X.-M. (1989) *The Logic of Chemical Synthesis*. John Wiley & Sons, New York.

Green Chemistry Metrics by Frank Roschangar and Juan Colberg

in *Green Techniques for Organic Synthesis and Medicinal Chemistry*, Second Edition. Edited by Wei Zhang and Berkeley W. Cue. © 2018 John Wiley & Sons Ltd

Green Metrics: Real-Life Tools

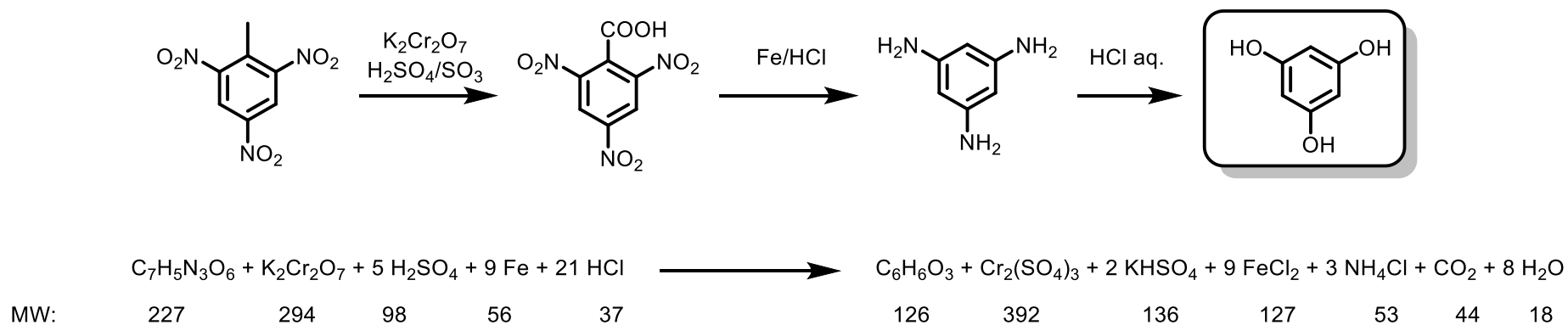
Historical context:

The ideal synthesis [...] may be defined as one in which the target molecule is prepared from readily available starting materials in one simple, safe, environmentally-acceptable, and resource-effective operation that proceeds quickly and in quantitative yield.”

Green Metrics: Real-Life Tools

Historical context:

In 1980 for the production of Phloroglucinol: 200 MT/y the synthesis starts from TNT !!

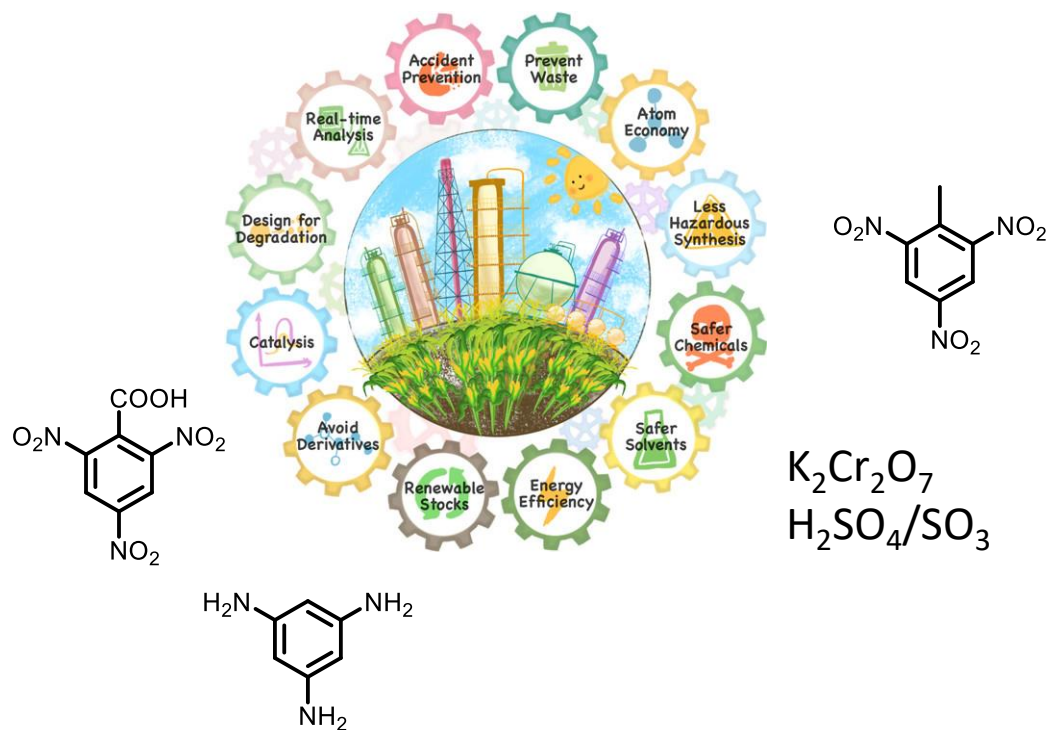


Green Metrics: Real-Life Tools

Historical context:

Production of Phloroglucinol: 200 MT/y

Atom Economy [AE]: $126 / (126 + 392 + 2 \cdot 136 + 9 \cdot 127 + 3 \cdot 53 + 44 + 8 \cdot 18) = 5,5\%$



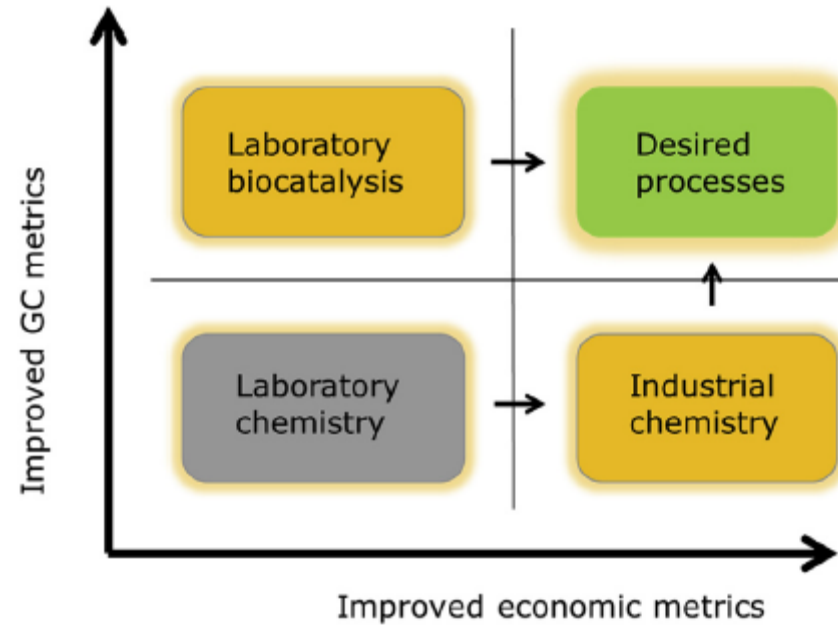
Green Metrics: Real-Life Tools

Can we measure the «greenness» of a Chemical Reaction or Process ?
How this could be done?

Can we compare 2 chemical steps or chemical processes and decide which one is «greener» ?

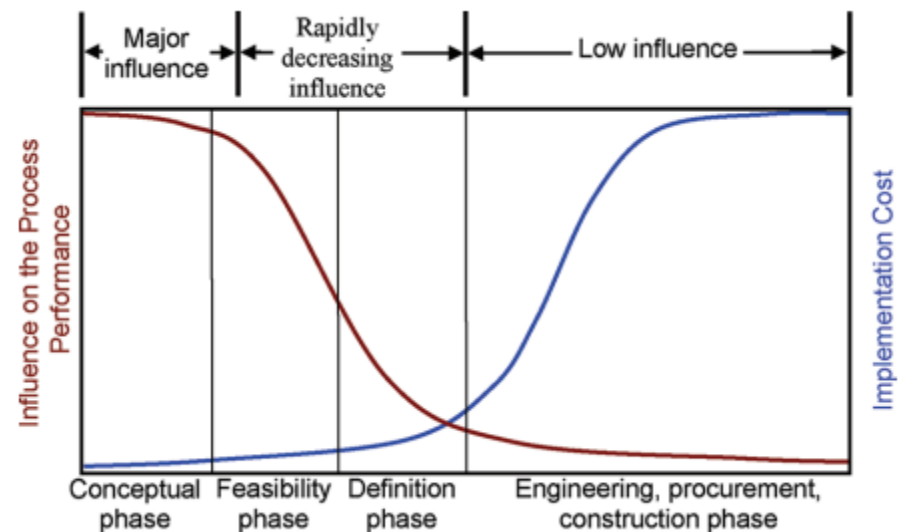
The accepted consensus for any metric is that it must be simple, easily measurable and clearly highlight the desired information

Green Metrics: Real-Life Tools



Green Metrics: Process Implementation

Material Flow Analysis



Green Metrics: Real-Life Tools

Historical context:

In 1991 Barry Trost defined:

The prime focal point in organic synthesis: Selectivity-chemo- (functional group differentiation), regio- (orientational control of two reacting partners), diastereo-(control of relative stereochemistry), and enantio- (control of absolute stereochemistry)

But **Atom Economy** defined as: how much of the reactants end up in the product has been overlooked!

$$AE = \frac{MW(Product) \times 100}{\sum MW(Raw\ Materials) + \sum MW(Reagents)}$$

Optimum Value= 100.

Trost, B. M. The atom economy—A search for synthetic efficiency. *Science*, **1991**, 254, 1471–1477.

Sheldon, R. A. (**1992**) Organic synthesis: Past, present and future. *Chem. Ind. (London)*, 23, 903-906.

Green Metrics: Real-Life Tools

Historical context:

In the 1992, Roger Sheldon defined the E-Factor

$$EFactor = \frac{\sum m(\text{Input Materials w.o. Water}) - m(\text{Product})}{m(\text{Product})}$$

Optimum Value= 0.

Sheldon, R. A. (1992) Organic synthesis: Past, present and future. Chem. Ind. (London), 23, 903-906.

Sheldon, R. A. Metrics of Green Chemistry and Sustainability: Past, Present, and Future ACS Sustainable Chem. Eng. 2018, 6, 32–48.

Green Metrics: Real-Life Tools

E Factor:

Industry Segment (Examples)	Annual Product Tonnage	E-Factor (kg waste/ kg product)	Total Annual Waste Tonnage	No. of Steps	Years of Development
Petrochemicals (Solvents, Detergents)	1,000,000– 100,000,000	~0.1	10,000,000	“Separations”	100+
Bulk Chemicals (Plastics, Polymers)	10,000– 1,000,000	<1–5	5,000,000	1–2	10–50
Fine Chemicals (Coatings, Electronic Parts, Pharmaceutical Raw Materials)	100–10,000	5–>50	500,000	3–4	4–7
Pharmaceuticals (Antibiotics, Drugs, Vaccines)	10–1,000	25–>100	100,000	6+	3–5

Green Metrics: Real-Life Tools

Historical context:

AE and E-Factor, pros vs cons:

AE assumed a chemical yield of 100% whereas E-Factor took it into account

AE does not consider selectivity of the reaction

E-Factor did not take into account water used

E-Factor considered all waste the same....1 kg NaCl vs 1kg of CrO_3

AE is easily applied to a one-step reaction whereas E-Factor allows a holistic assessment of a complete Process.

AE allows a rapid evaluation of waste between 2 processes.

E-Factor: What is a waste?

Acid gas scrubbing, pH adjustment in waste treatment plants, etc. included?

Is waste that is produced as a result of energy use (heating or cooling reactions, abatement technology, etc)

Is waste solvent passed on to a waste handler to be burned in a cement kiln included?

Both do not take into account: chemical toxicity, safety risks, energy consumption, etc.

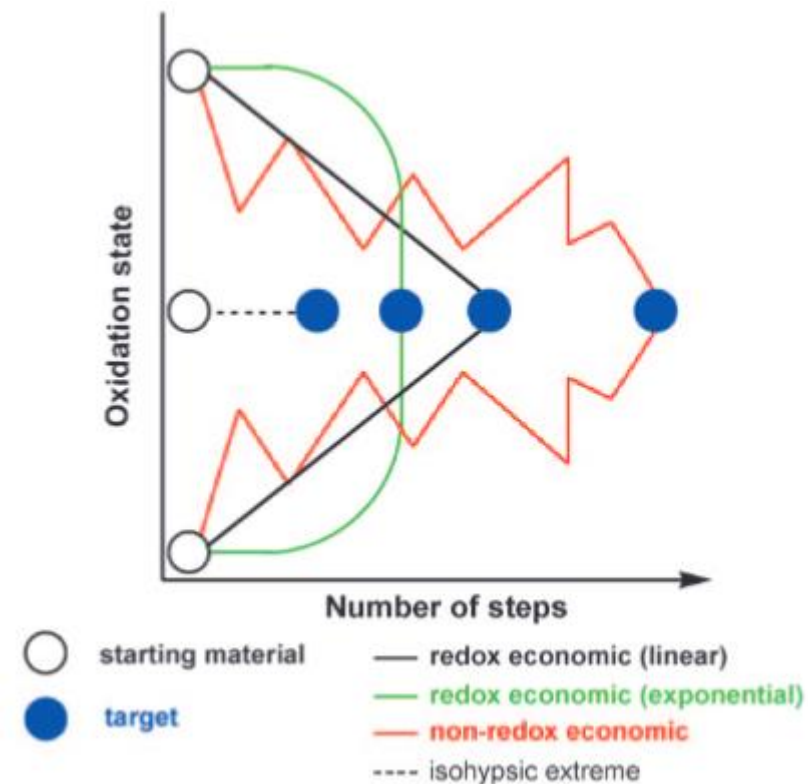
Green Metrics: Real-Life Tools

Ideality & Complexity:

$$\%ideality = \frac{[(\text{no. of construction rxns}) + (\text{no. of strategic redox rxns})]}{(\text{total no. of steps})} \times 100$$

Complexity = %ideality × total no. of reaction

Complexity = no. of construction reactions + no. of strategic redox reactions



Burns, N. Z.; Baran, P. S.; Hoffmann, R. W. Redox Economy in Organic Synthesis *Angew. Chem. Int. Ed.* **2009**, 48, 2854.

Gaich, T.; Baran, P. S. Aiming for the Ideal Synthesis *J. Org. Chem.* **2010**, 75, 4657.

Roschangar, F.; Sheldon, R. A.; Senanayake, C. H. *Green Chem.*, **2015**, 17, 752.

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

Need for others metrics

Reaction Mass Efficiency

included all reactant mass, yield & atom economy

$$\text{RME} = \frac{m(\text{Product}) \times 100}{\sum m(\text{Raw Materials})}$$

Optimum Value= 100.

But: does not include all the other materials: reagents, solvents, catalysts.

Curzons, A. D. *et al. Green Chem.* **2001**, 3, 1.

Constanble, D. J. C. *et al. Green Chem.* **2002**, 4, 521.

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

Mass Intensity & Process Mass Intensity:

$$\text{MI} = \frac{\text{Total mass used in a process step or a process (kg)(excl. water)}}{\text{Mass of Product (kg)}}$$

Optimum Value= 1.

$$\text{PMI} = \frac{\text{Total mass used in a process step or a process (kg)(incl. water)}}{\text{Mass of Product (kg)}}$$

Optimum Value= 1.

Curzons, A. D. *et al. Green Chem.* **2001**, 3, 1.

Constanble, D. J. C. *et al. Green Chem.* **2002**, 4, 521.

Jimenez-Gonzalez, C. *et al. Org. Process Res. Dev.* **2011**, 15, 912,

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

Process Mass Intensity:

$$\text{PMI} = \frac{\text{Total mass used in a process step or a process (kg)(incl. water)}}{\text{Mass of Product (kg)}}$$

Optimum Value= 1.

Good indicator of the efficiency of a step or a synthesis

Curzons, A. D. *et al. Green Chem.* **2001**, 3, 1.

Constanble, D. J. C. *et al. Green Chem.* **2002**, 4, 521.

Jimenez-Gonzalez, C. *et al. Org. Process Res. Dev.* **2011**, 15, 912,

Green Metrics: Real-Life Tools

Development of New Metrics: Pharma industries

PMI vs *cEFactor*

$$cEFactor = \frac{\sum m(\text{Input Materials incl. Water}) - m(\text{Product})}{m(\text{Product})}$$

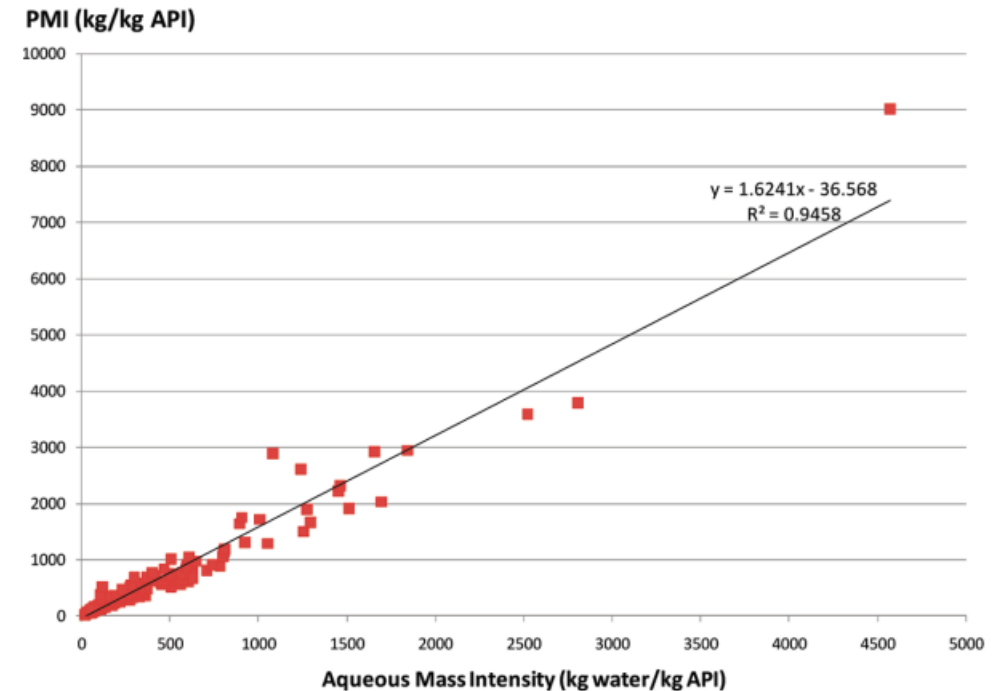
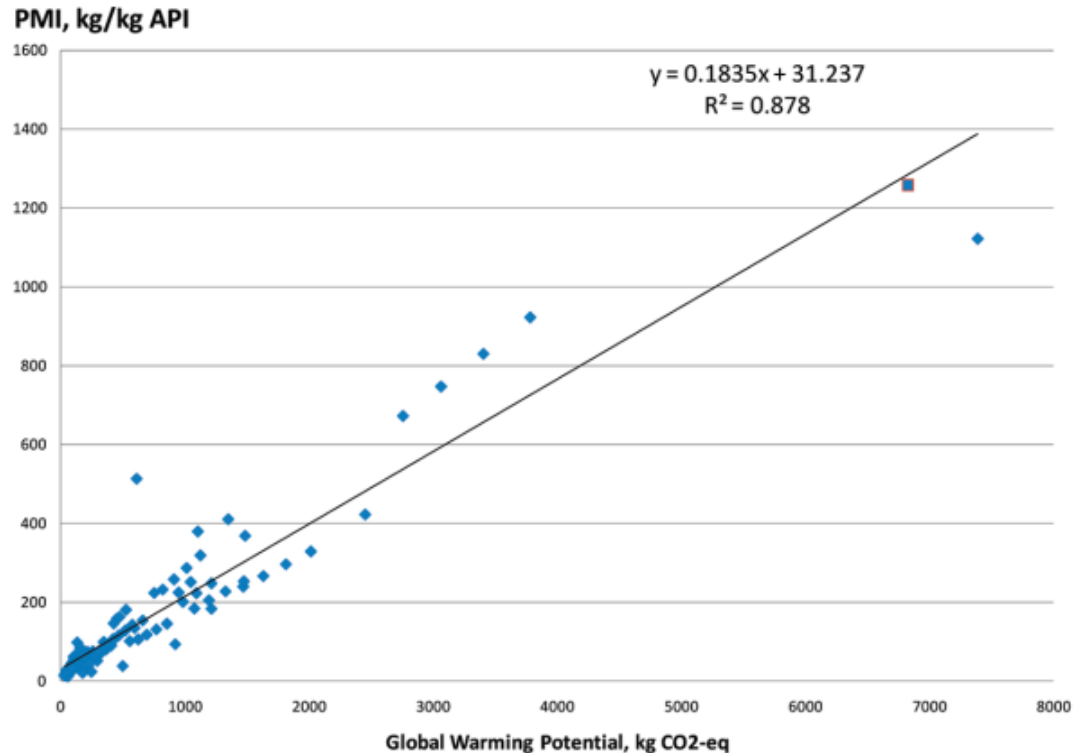
$cEFactor = PMI - 1$ There is more than «-1» !

“end-of-pipe view of waste-management philosophy from the 1980s”

Green Metrics: Real-Life Tools

PMI vs *cE*Factor

“Simply put, the good focus is on minimizing waste. The greater focus is on maximizing value and efficiency. If one maximizes value, waste reduction will be one of the benefits.”

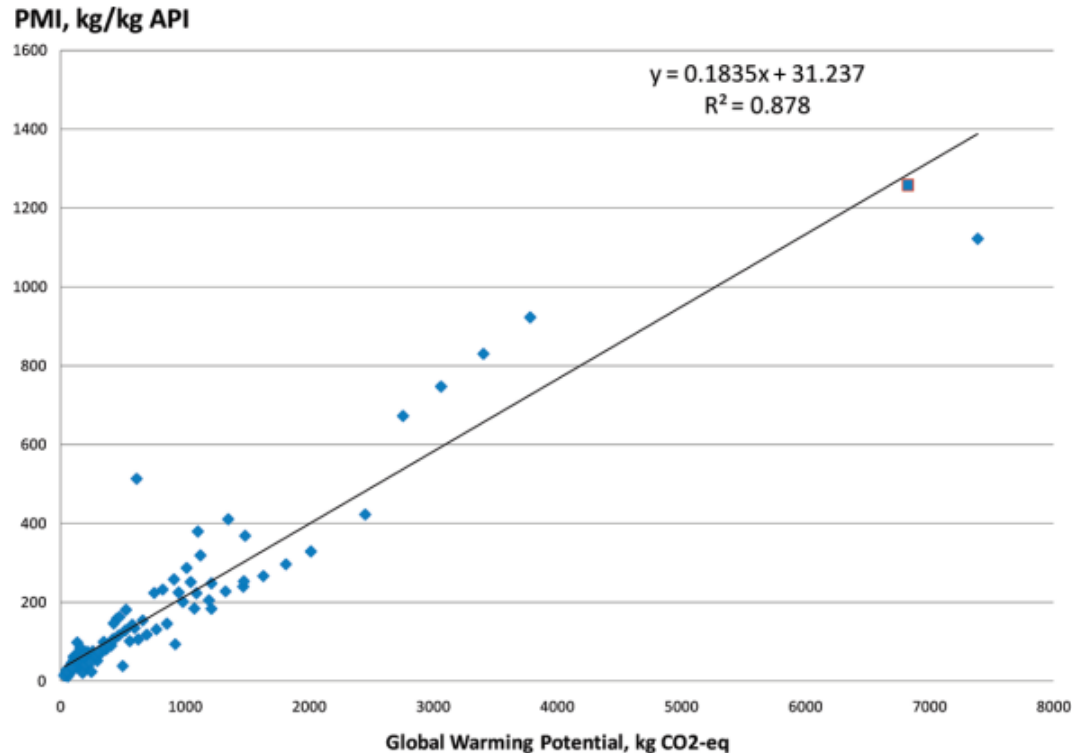


all development compounds in GlaxoSmithKline's portfolio (2011)

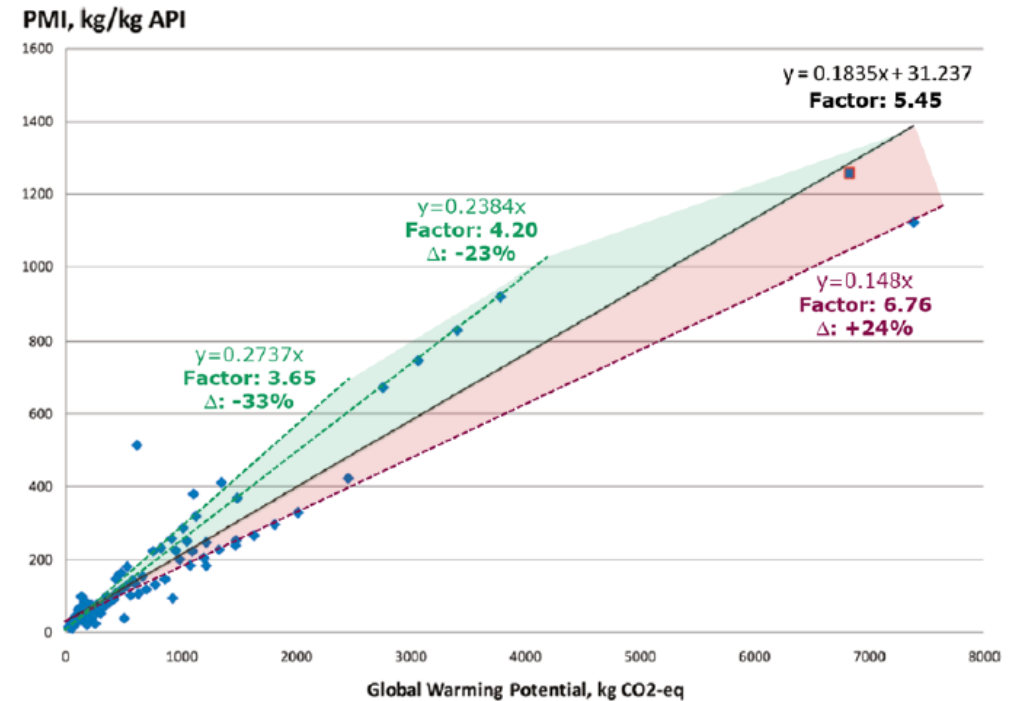
Green Metrics: Real-Life Tools

PMI vs *cE*Factor

“Simply put, the good focus is on minimizing waste. The greater focus is on maximizing value and efficiency. If one maximizes value, waste reduction will be one of the benefits.”



all development compounds in GlaxoSmithKline's portfolio (2011)



Colorful visualization of deviation from average PMI GWP correlation was performed at Merck KGA, Darmstadt, Germany for benchmarking

Internal Presentation.

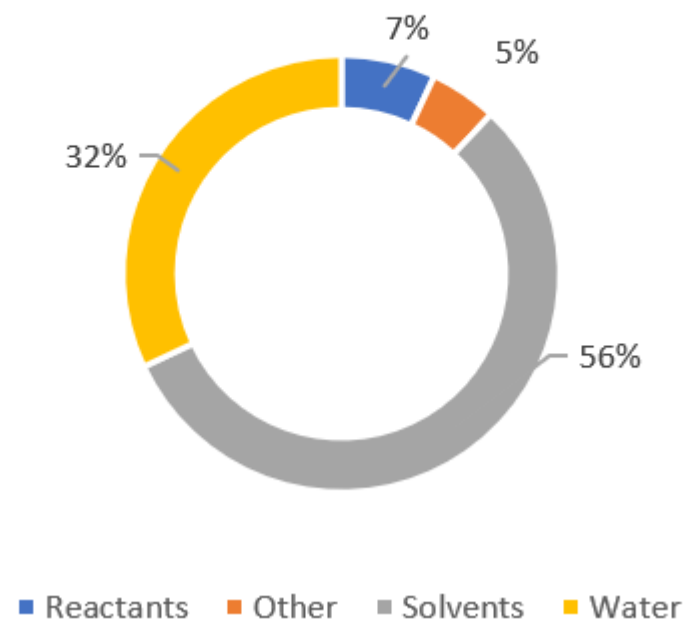
Green Metrics: Real-Life Tools

PMI

ACS GCI Pharmaceutical Roundtable 2008

Biggest waste contributor

Composition by Mass of the type of materials
used to manufacture API

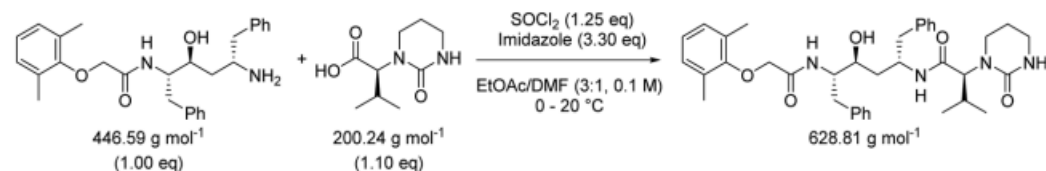


Jimenez-Gonzalez, C. et al. *Org. Process Res. Dev.* **2011**, 15, 912.

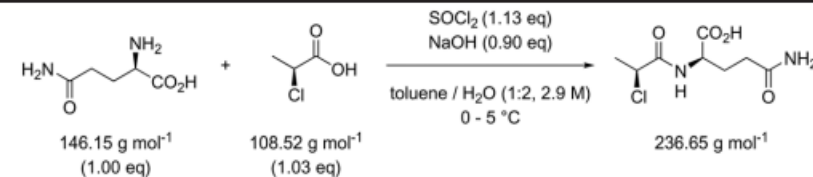
Monteith, E. R. et al. *Green Chem.* **2020**, 22, 123.

PMI

PMI Potential Pitfalls



Reaction 1

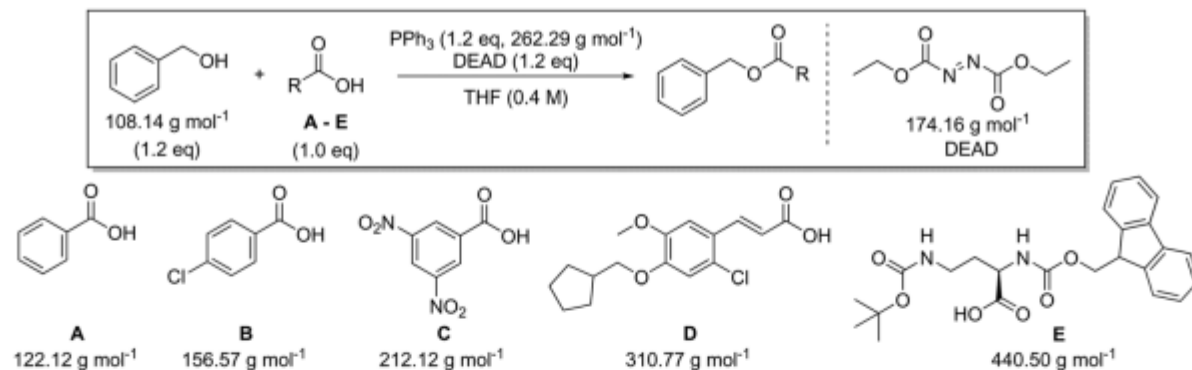


Reaction 2

	AE (%)	RME (%)	PMI (g g ⁻¹)	PMI _{RRC} (g g ⁻¹)	PMI _{Solv} (g g ⁻¹)	Yield (%)
Literature data reported						
Reaction 1: [Acid] = 0.1 M	97	87	17.3	1.8	15.5	92
Reaction 2: [Acid] = 2.9 M	93	75	3.9	2.2	1.7	81
Simulation A: [Acid] = 0.4 M, literature yield						
Reaction 1	97	87	5.7	1.8	3.9	92
Reaction 2	93	75	14.6	2.2	12.4	81
Simulation B: [Acid] = literature data, yield = 90%						
Reaction 1	97	85	17.7	1.8	15.8	90
Reaction 2	93	83	3.5	2.0	1.5	90
Simulation C: [Acid] = 0.4 M, yield = 90%						
Reaction 1	97	85	5.8	1.8	4.0	90
Reaction 2	93	83	13.2	2.0	11.2	90
Simulation D: [Acid] = 0.4 M, yield = 50%						
Reaction 1	97	47	10.5	3.3	7.2	50
Reaction 2	93	46	23.7	3.5	20.2	50

PMI

PMI Potential Pitfalls

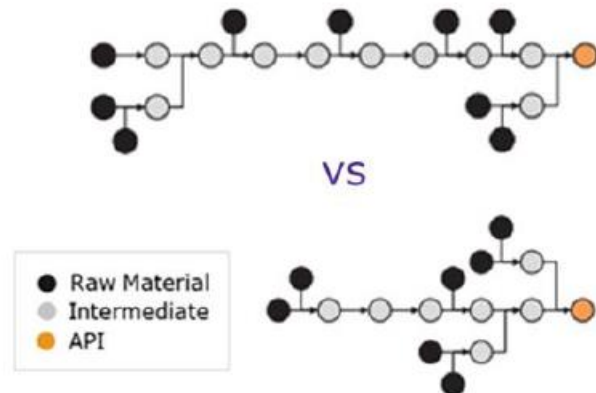


Carboxylic acid	AE (%)	RME (%)	PMI (g g ⁻¹)	PMI _{RRC} (g g ⁻¹)	PMI _{Solv} (g g ⁻¹)	Yield (%)
Simulation 1: [Acid] = 0.4 M, yield = 90%						
A	92	76	15.7	4.1	11.6	90
B	93	78	13.7	3.6	10.0	90
C	94	80	11.4	3.2	8.2	90
D	96	82	8.8	2.7	6.2	90
E	97	84	6.9	2.3	4.7	90
Simulation 2: [Acid] = 0.4 M, yield = 80%						
A	92	67	17.7	4.6	13.1	80
B	93	69	15.4	4.1	11.3	80
C	94	71	12.8	3.6	9.2	80
D	96	73	9.9	3.0	6.9	80
E	97	74	7.8	2.6	5.2	80
Simulation 3: [Acid] = 0.4 M, yield = 70%						
A	92	59	20.2	5.2	15.0	70
B	93	60	17.6	4.7	12.9	70
C	94	62	14.6	4.1	10.5	70
D	96	64	11.4	3.4	7.9	70
E	97	65	8.9	2.9	6.0	70

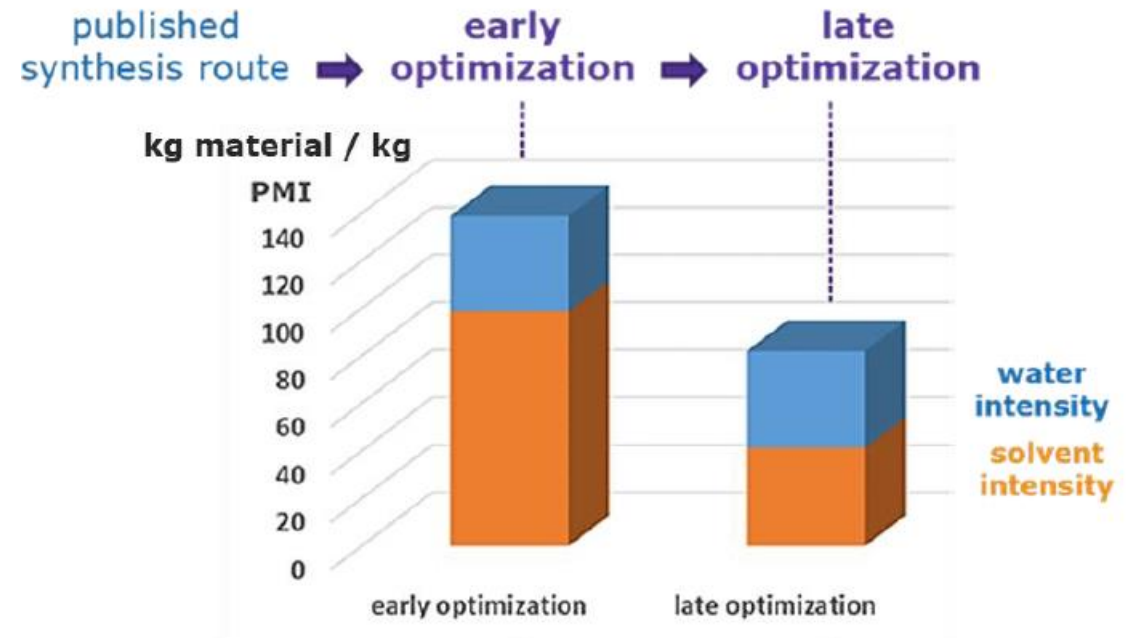
PMI

PMI: comparison of different routes & selection tool

How to compare 2 routes:
Metrics could help!



After selection: Optimization!



Safety and Hazard Metrics

Thermal Hazard
Reagent Hazard
Pressure
Hazardous by-product
Waste: metal, toxicity, upcycling

Solvent Usage: number, recovery
Mass Intensity of Solvent

Biodegradation, Bioaccumulation, Energy use

Curzons, A. D.; Constable, D. J. C.; Mortimera, D. N.; Cunningham, V. L. So you think your process is green, how do you know?—Using principles of sustainability to determine what is green—a corporate perspective *Green Chem.*, **2001**, 3, 1–6.

Specificity of Perfumery Ingredients

**Natural oil extraction
Biotechnology Processes**

**Metrics should be easy to understand by
our clients and final consumers**

**Our competitors are also our clients: Needs for metrics that could be asked or
guessed with the highest accuracy possible**

Green Metrics: Real-Life Tools

Solvents, Water:

Solvent Intensity:

$$SI = \frac{\sum m(\text{Solvents excl. Water})}{m(\text{Product})}$$

Optimum Value= 0.

Water Intensity:

$$WI = \frac{\sum m(\text{Water})}{m(\text{Product})}$$

Optimum Value= 0.

Solvents Guide

Solvent:

Required during a reaction:

- enable heat transfer
- mass transfer

Required during post-reaction processing and isolation of products

No solvent could be the ideal choice...

...but could participate in increasing the safety of chemical reactions

And also cleaning of the installations

Solvents Guide

GSK's guide

Solvent	Health	Safety	Env.	EHS flag	Sum ^a
Water	10	10	4	0	24
MeOH	5	5	4	0	14
EtOH	8	6	3	0	17
i-PrOH	8	6	3	0	17
n-BuOH	5	8	5	0	18
t-BuOH	6	6	3	0	15
Benzyl alcohol	7	7	6	0	20
Ethylene glycol	7	9	5	0	21
Acetone	8	4	3	0	15
MEK	8	4	3	0	15
MIBK	6	7	2	0	15
Cyclohexanone	6	8	6	0	20
Methyl acetate	7	4	3	0	14
Ethyl acetate	8	4	4	0	16
i-PrOAc	7	6	5	0	18
n-BuOAc	8	8	5	0	21
Diethyl ether	5	2	4	-8	3
DIPE	8	1	3	-8	4
MTBE	5	3	4	-8	4
THF	6	3	3	-8	4
Me-THF	4	3	4	0	11
1,4-Dioxane	4	4	3	0	11
Anisole	7	6	5	0	18
DME	2	4	4	-8	2
Pentane	8	2	5	-8	7
Hexane	4	2	3	-8	1
Heptane	8	3	3	0	14
Cyclohexane	7	2	5	0	14
Me-cyclohexane	8	3	5	0	16
Benzene	1	3	5	-8	1
Toluene	4	4	3	0	11
Xylenes	6	5	2	0	13
DCM	4	6	3	-8	5
Chloroform	3	6	3	-8	4
CCl ₄	3	4	4	-8	3
DCE	2	6	4	-8	4
Chlorobenzene	4	8	6	0	18
Acetonitrile	6	6	2	0	14
DMF	2	9	4	-8	7
DMAc	2	8	2	-8	4
NMP	3	8	4	-8	7
DMPU	4	7	3	0	14
DMSO	7	2	5	0	14
Sulfolane	6	10	5	0	21
Nitromethane	4	2	3	-8	1
Methoxy-ethanol	2	6	3	-8	3
Acetic acid	6	7	4	0	17
Ac ₂ O	4	6	5	0	15
Pyridine	4	7	2	-8	5
TEA	3	4	4	-8	3

Astra-Zeneca's guide

Solvent	Health	Safety	Envir.	Sum ^a
MeOH	5	7	7	19
EtOH	2	7	7	16
i-PrOH	3	7	6	16
n-BuOH	4	7	6	17
t-BuOH	6	7	7	20
Acetone	6	7	8	21
MEK	7	7	7	21
MIBK	6	7	9	22
Ethyl acetate	5	7	6	18
i-PrOAc	4	7	7	18
n-BuOAc	2	7	4	13
Diethyl ether	7	10	10	27
MTBE	9	7	8	24
THF	8	7	8	23
Me-THF	8	7	9	24
1,4-Dioxane	9	10	9	28
Anisole	2	10	6	18
DME	10	3	8	21
Hexane	6	10	10	26
Heptane	3	10	8	21
Cyclohexane	6	10	9	25
Toluene	5	10	7	22
Xylenes	2	10	7	19
DCM	9	1	10	20
Chlorobenzene	9	7	9	25
Acetonitrile	8	7	9	24
DMF	9	3	8	20
DMAc	9	3	8	20
NMP	9	1	8	18
DMSO	1	1	6	8
Sulfolane	1	1	7	9
Methoxy-ethanol	10	3	8	21
Formic acid	10	3	7	20
Acetic acid	8	3	6	17
Pyridine	9	7	10	26
TEA	10	7	3	23

Henderson. R. K. *et al. Green Chem.* **2011**, 13, 854.

Winterton, N. *Clean Technologies and Environmental Policy* **2021**, 23, 2499.

Solvents Guide

Solvents Guides:

Family	Solvent	AZ	GCI-PR	GSK	Pfizer	Sanofi ^a	Issues	Overall ^b
Water	Water	—	—	24	Preferred	Recommended	—	Recommended
Alcohols	MeOH	19	14	14	Preferred	Recommended	—	TBC
	EtOH	16	13	17	Preferred	Recommended	—	Recommended
	i-PrOH	16	16	17	Preferred	Recommended	—	Recommended
	n-BuOH	17	13	18	Preferred	Recommended	—	Recommended
	t-BuOH	20	15	15	Preferred	Subst. adv.	—	TBC
	Benzyl alcohol	—	11	20	—	Subst. adv.	—	TBC
Ketones	Ethylene glycol	—	13	21	Usable	Subst. adv.	—	TBC
	Acetone	21	15	15	Preferred	Recommended	—	TBC
	MEK	21	16	15	Preferred	Recommended	—	TBC
	MIBK	22	17	15	—	Recommended	—	TBC
	Cyclohexanone	—	14	20	—	Subst. adv.	—	TBC
Esters	Methyl acetate	—	14	14	—	Subst. adv.	—	TBC
	Ethyl acetate	18	15	16	Preferred	Recommended	—	Recommended
	i-PrOAc	18	13	18	Preferred	Recommended	—	Recommended
	n-BuOAc	13	14	21	—	Recommended	—	Recommended
Ethers	Diethyl ether	27	21	3	Undesirable	Banned	H224	HH
	Diisopropyl ether	—	—	4	Undesirable	Subst. adv.	Perox.	Hazardous
	MTBE	24	21	4	Usable	Subst. adv.	—	TBC
	THF	23	16	4	Usable	Subst. adv.	H351	TBC
	Me-THF	24	15	11	Usable	Recommended	—	Problematic
	1,4-Dioxane	28	21	11	Undesirable	Subst. req.	—	Hazardous
	Anisole	18	13	18	—	Recommended	—	Recommended
	DME	21	23	2	Undesirable	Subst. req.	H360	Hazardous
	Pentane	—	—	7	Undesirable	Banned	H224	Hazardous
	Hexane	26	21	1	Undesirable	Subst. req.	—	Hazardous
Hydrocarbons	Heptane	21	17	14	Usable	Subst. adv.	—	Problematic
	Cyclohexane	25	18	14	Usable	Subst. adv.	—	TBC
	Me-cyclohexane	—	17	16	Usable	Subst. adv.	—	Problematic
	Benzene	—	21	1	Undesirable	Banned	H350	HH
	Toluene	22	18	11	Usable	Subst. adv.	H351	Problematic
	Xylenes	19	15	13	Usable	Subst. adv.	—	Problematic
	DCM	20	18	5	Undesirable	Subst. adv.	H351	TBC
	Chloroform	—	18	4	Undesirable	Banned	—	HH
Halogenated	CCl ₄	—	19	3	Undesirable	Banned	H420	HH
	DCE	—	19	4	Undesirable	Banned	H350	HH
	Chlorobenzene	25	16	18	—	Subst. adv.	—	Problematic
	Acetonitrile	24	14	14	Usable	Recommended	—	Problematic
	DMF	20	17	7	Undesirable	Subst. req.	H360	Hazardous
Aprotic polar	DMAc	20	16	4	Undesirable	Subst. req.	H360	Hazardous
	NMP	18	16	7	Undesirable	Subst. req.	H360	Hazardous
	DMPU	—	—	14	—	Subst. adv.	—	Problematic
	DMSO	8	15	14	Usable	Subst. adv.	—	Problematic
	Sulfolane	9	13	21	—	Subst. adv.	—	Recommended
	Nitromethane	—	—	1	—	Banned	Explo.	HH
	Methoxy-ethanol	21	20	3	—	Subst. req.	H360	Hazardous
Miscellaneous	Formic acid	20	15	—	—	Subst. req.	—	TBC
	Acetic acid	17	15	17	Usable	Subst. adv.	—	TBC
	Ac ₂ O	—	16	15	—	Subst. adv.	—	TBC
Amines	Pyridine	26	16	3	Undesirable	Subst. adv.	—	TBC
	TEA	23	18	3	—	Subst. req.	—	Hazardous

^a Subst. adv.: substitution advisable; Subst. req.: substitution requested. ^b TBC: to be confirmed; HH: highly hazardous.

Prat, D. *et al. Green Chem.* **2014**, 16, 4546.

Winterton, N. *Clean Technologies and Environmental Policy* **2021**, 23, 2499.

Solvents Guide

Solvents Guide:

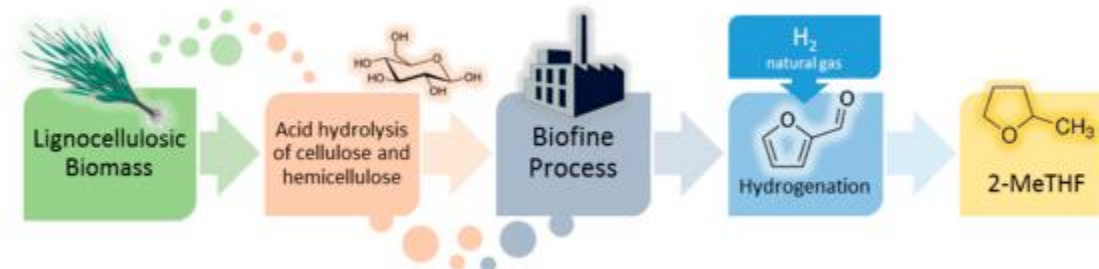
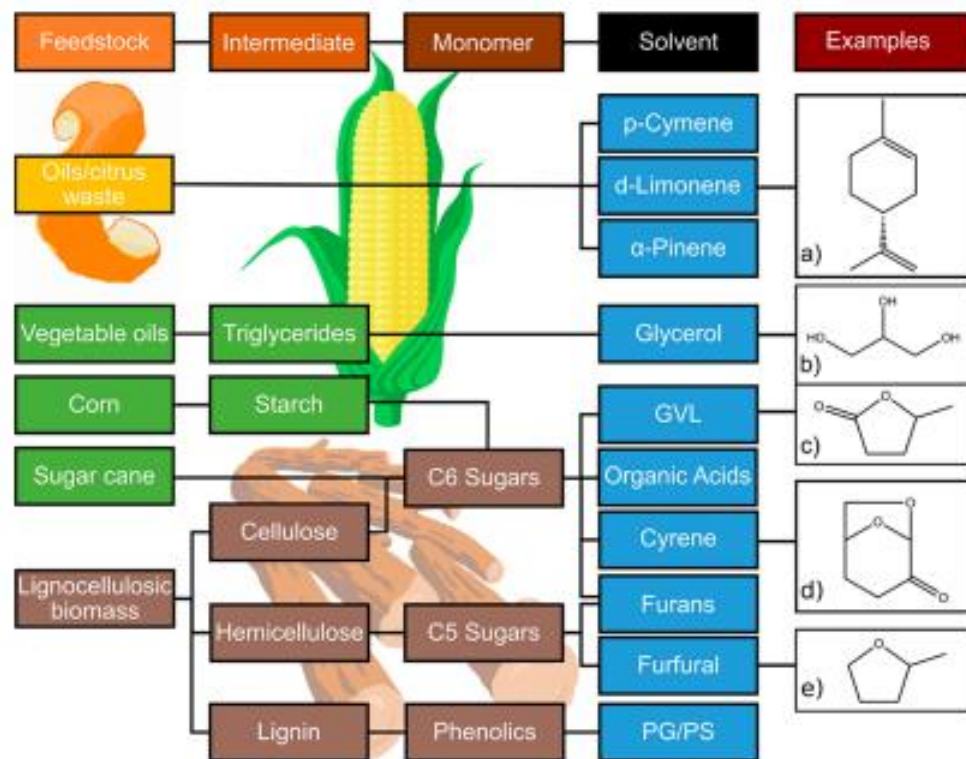
Recommended	Water, EtOH, i-PrOH, <i>n</i> -BuOH, EtOAc, i-PrOAc, <i>n</i> -BuOAc, anisole, sulfolane.
Recommended or problematic?	MeOH, <i>t</i> -BuOH, benzyl alcohol, ethylene glycol, acetone, MEK, MIBK, cyclohexanone, MeOAc, AcOH, Ac ₂ O.
Problematic	Me-THF, heptane, Me-cyclohexane, toluene, xylenes, chlorobenzene, acetonitrile, DMPU, DMSO.
Problematic or hazardous?	MTBE, THF, cyclohexane, DCM, formic acid, pyridine.
Hazardous	Diisopropyl ether, 1,4-dioxane, DME, pentane, hexane, DMF, DMAc, NMP, methoxy-ethanol, TEA.
Highly hazardous	Diethyl ether, benzene, chloroform, CCl ₄ , DCE, nitromethane.

Prat, D. *et al. Green Chem.* **2014**, 16, 4546.

Winterton, N. *Clean Technologies and Environmental Policy* **2021**, 23, 2499.

Solvents Guide

Solvents Biosourced:



Solvents Guide

Solvent recycling:

Key properties affecting recyclability:

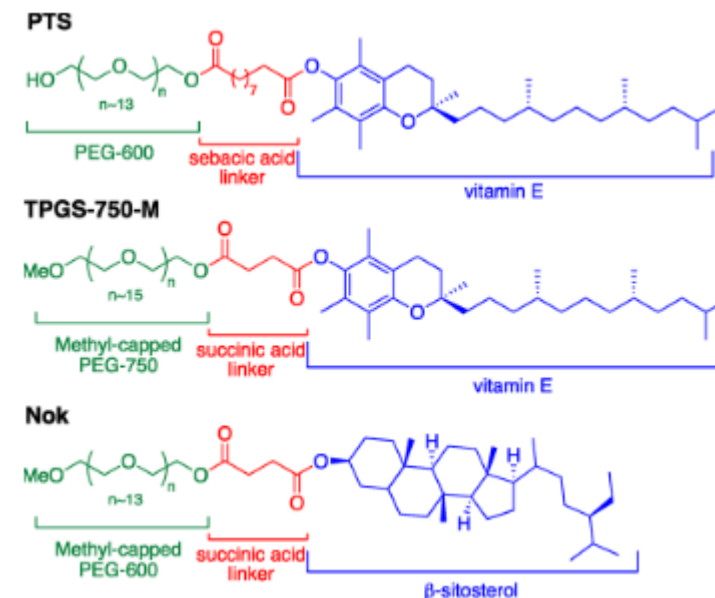
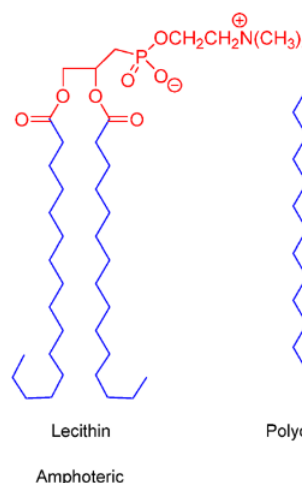
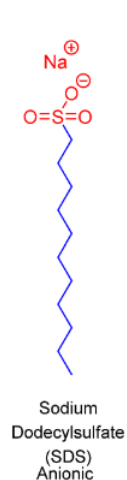
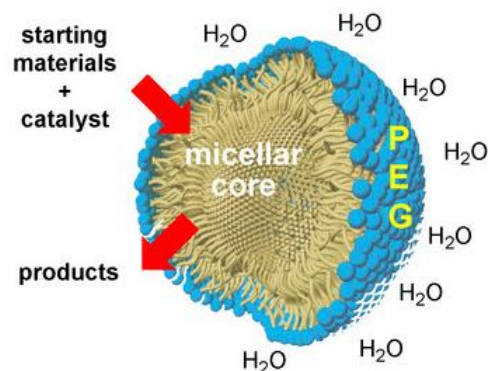
- Boiling point (i.e., ease of distillation)
- Number of solvents with a boiling point within 10°C (influencing ease of solvent separability)
- Number of azeotropes with other solvents
- Relative ease of drying (most solvents are needed dry)
- Risk on recovery (e.g., via peroxide formation)
- Reactivity (e.g., esters may hydrolyze)
- Water solubility (affecting the potential loss in aqueous streams) Issues

But risk of contamination !

Solvents Guide: What about water?

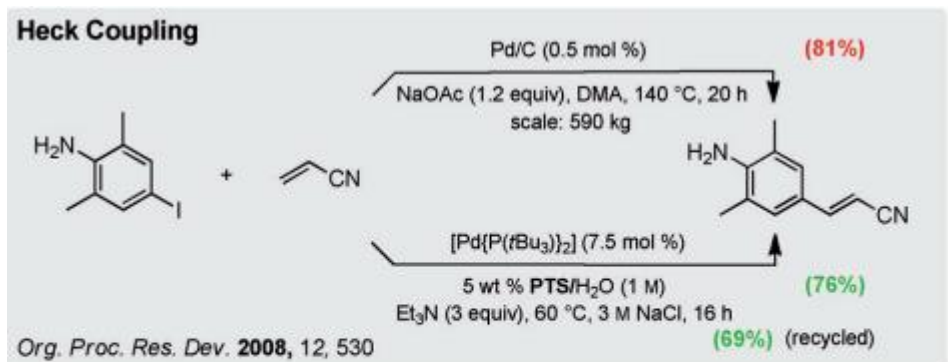
Chemistry in Water:

Seminal work by Prof. Breslow: Diels-Alder Reaction accelerated «on-water»
Further developement with micellar-type chemistry using Surfactants + catalysis

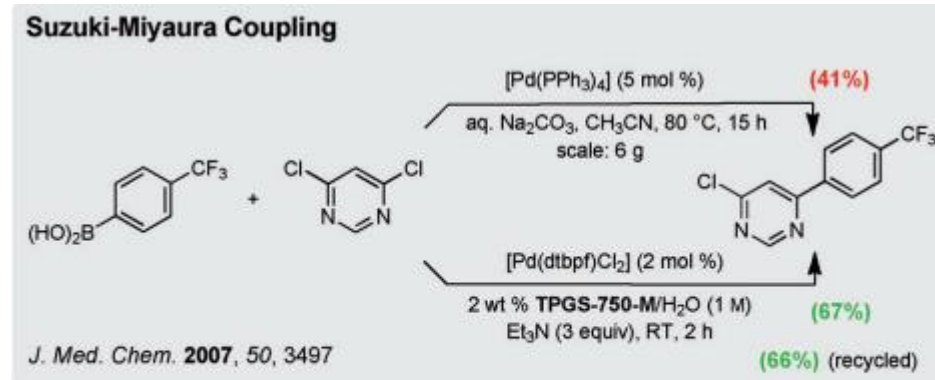


Solvents Guide: What about water?

Chemistry in Water:



	based on:	pharma	this work	with recycle
E Factors	total organic solvent	16.7	2.5	2.8
	aqueous workup included	31.1	10.2	2.8



	based on:	pharma	this work	with recycle
E Factors	total organic solvent	22.0	1.9	1.9
	aqueous workup included	50.0	7.6	1.9

E-Factor calculations: Lipschutz, B. H. *et al. Angew. Chem. Int. Ed.* **2013**, 52, 10952 & Lipschutz, B. H. *et al. Green Chem.* **2014**, 16, 3660.

Kitanosono, T. *et al. Chem. Rev.* **2018**, 118, 679.

Stevens, A. *Synthesis* **2019**, 51, 2632.

Margery C.-C. *et al. Chem. Eur. J.* **2018**, 24, 6672 & *Chem. Sci.*, **2021**, 12, 4237.

Fleck, N *et al. Org. Process Res. Dev.* **2023**, 27, 822.

Renewability

Renewables Intensity

$$RI = \frac{\sum m(\text{All Renewably derived materials used})}{m(\text{Product})}$$

Optimum Value= 1.

$$R \text{ percentage} = \frac{RI}{PMI} \times 100$$

Biosynthesis/Biocatalysis/Bio-based Products

Evaluation of the Impact:

New questions and parameters

Energy consumption

CO₂ Footprint

Supply Chain

Common mistake: Bio-based products are they synonymous with the term “sustainable” ?

Biosynthesis/Biocatalysis/Bio-based Products

Nagoya Protocole:

Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity

Adopted in 2010

Entered in force in 2014

In 2022, ratified by 137 states

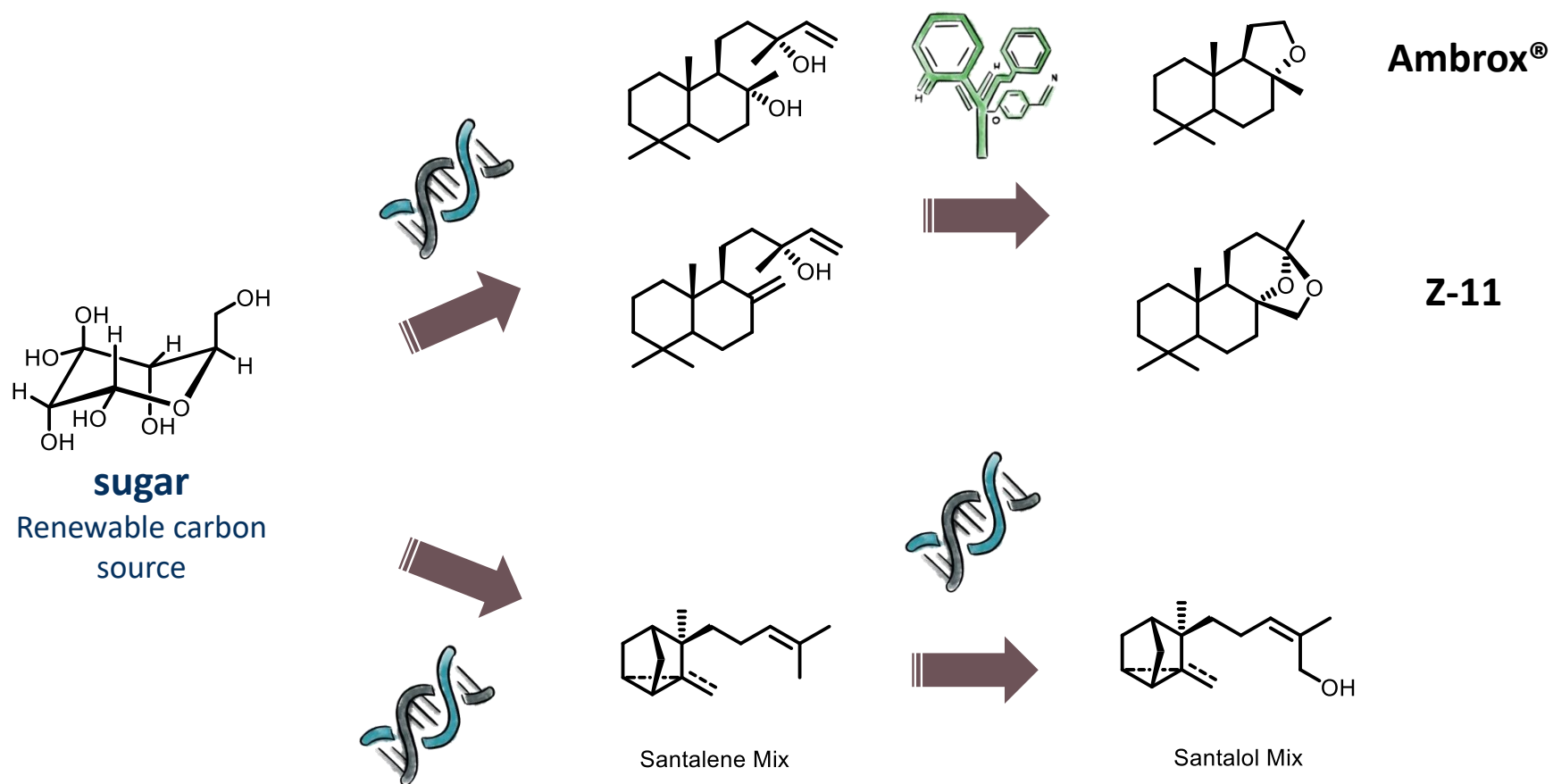
Benefit-sharing obligations

Compliance obligations

<https://www.cbd.int/abs/doc/protocol/nagoya-protocol-fr.pdf>

Biosynthesis/Biocatalysis/Bio-based Products

Evaluation of Biotechnology Processes



Biosynthesis/Biocatalysis/Bio-based Products

Evaluation of Biotechnology Processes: Pros vs Cons

Claim	Rationale
Reduced utilities	Mild reaction conditions (temperature)
Safe operation	Mild reaction conditions (pressure, pH)
Reduced waste	High selectivity
Renewable catalyst	Biocatalyst produced by fermentation based on sugar, air, and water

- Operates in water (thus replacing organic solvents)
- Has highly selective catalysis, including regio- and stereoselectivity (thus reducing E-factors)
- Operates in mild conditions, avoiding the need for protection (thus reducing E-factors)
- Overcomes the use of some hazardous materials (resulting in improved LCA)
- Uses renewable resources (resulting in improved LCA)
- Can be modified, that is, the biocatalyst properties can be altered to suit the process (thus improving the ease of processing)
- Is rarely endo- or exo-thermic (thus reducing energy requirements)
- Provides a high yield as a result of selectivity and mild conditions (thus improving the efficiency of processing)
- Is catalytic rather than stoichiometric (thus improving the ease of processing)

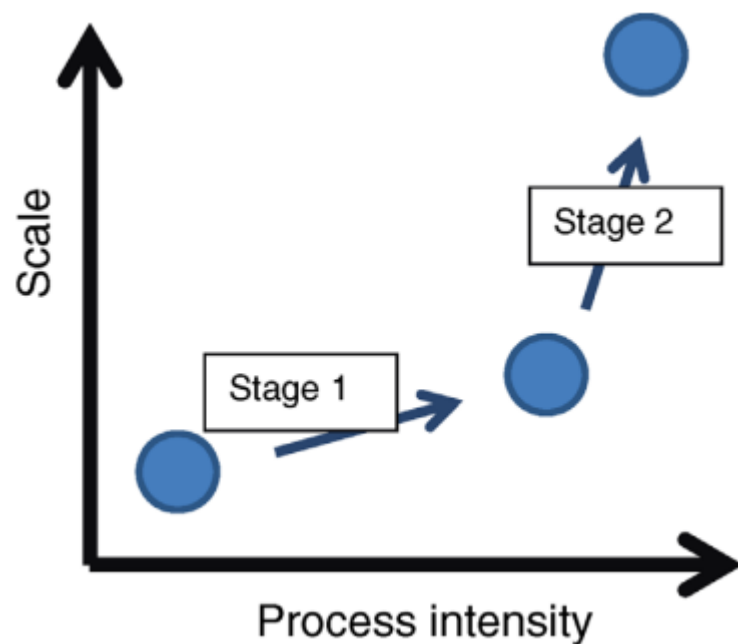
Biosynthesis/Biocatalysis/Bio-based Products

Evaluation of Biotechnology Processes: Pros vs Cons

Performance	Potential limitation
Selective	Enzyme
Reaction rate	Amount of catalyst
	Mass transfer
Reaction yield	Thermodynamics
	Stoichiometry

Biosynthesis/Biocatalysis/Bio-based Products

Evaluation of Biotechnology Processes



Stage	Benchmarking objective	Methodology
1	Route feasibility	<i>In silico</i> metrics: AE; CME
2	Biocatalyst and reaction development	<i>In vitro</i> metrics: PMI; SI; WI; E-factor

Biosynthesis/Biocatalysis/Bio-based Products

Metrics used for Bioprocesses:

Metric	Definition
Economic metrics	
Productivity ($\text{g l}^{-1} \text{h}^{-1}$)	Amount of product made as a function of the reactor volume and time
Yield of product on substrate (g g^{-1})	Amount of product (grams) made as a function of the amount of substrate (grams) added in the reaction
Turnover (mol mol^{-1})	Amount of product made as a function of the amount of biocatalyst added in the reaction
Green chemistry metrics	
Atom economy (g mol^{-1} per g mol^{-1})	Molecular weight of the desired product as a function of the sum of the molecular weight of all products
E factor (g g^{-1})	Amount of waste made as a function of the amount of product made
C factor (g g^{-1})	Amount of CO_2 equivalents as a function of the amount of product made
Process mass intensity (g g^{-1})	Amount of raw material input as a function of the amount of desired product made

Bell, E.L., Finnigan, W., France, S.P. *et al.* Biocatalysis. *Nat Rev Methods Primers* **2021**, 1, 46.

Woodley, J. M. New frontiers in Biocatalysis for sustainable synthesis. *Curr. Opin. Green. Sustain. Chem.* **2020**, 21, 22.

Biopharmaceuticals/Biologics

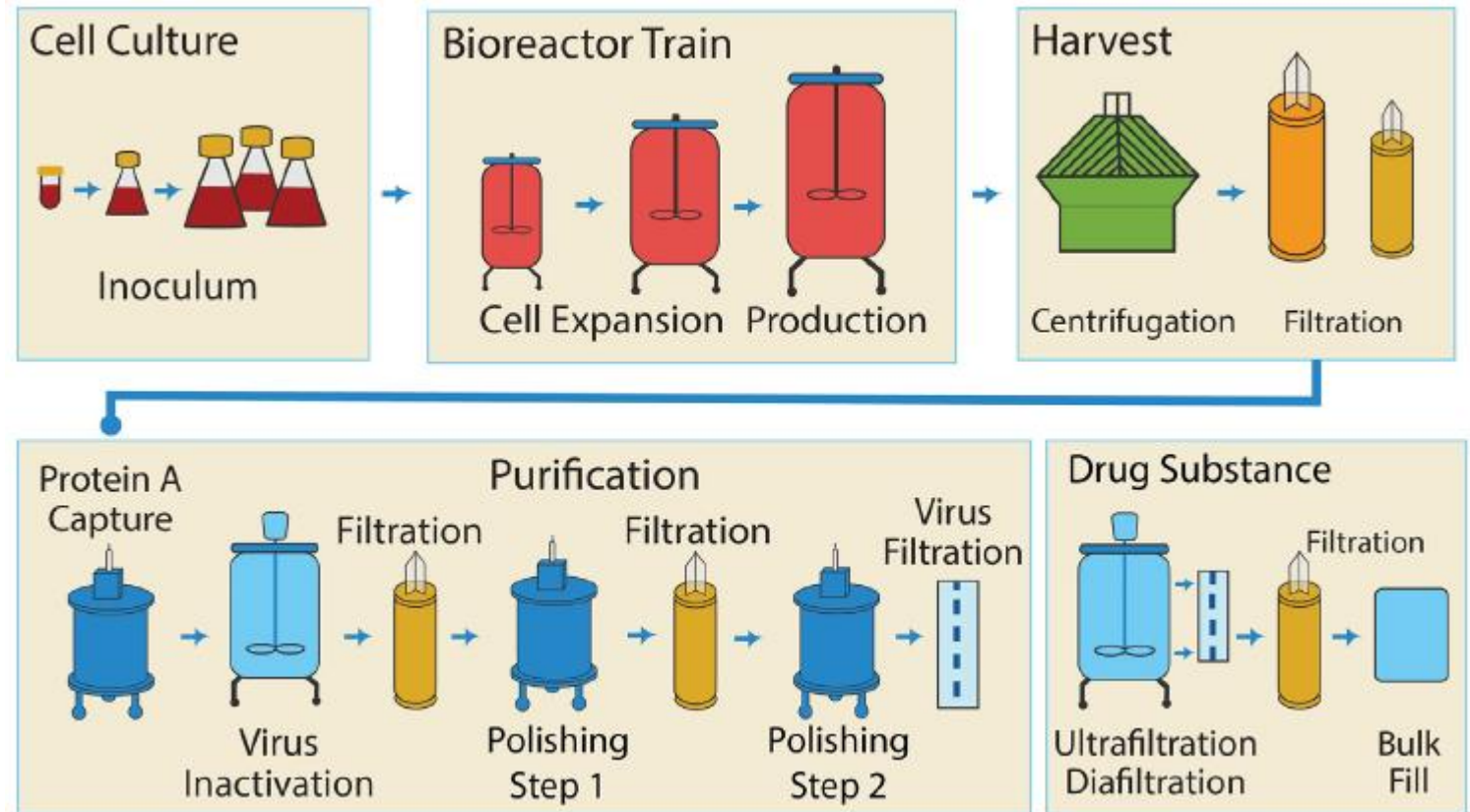
Metrics used for biologics:

Cleaning and sanitization but increases the amount of waste generated

Highly purified water: Energy!

65% of the carbon footprint is attributable to the energy required to maintain the clean room facility that houses the operation

single use systems (SUS) made of mixed plastics which are sterilized by gamma irradiation



Budzinski, K. et al. *New Biotechnology* **2019**, 49(25), 37-42.

Argoud, S. et al. *Current Opinion in Green and Sustainable Chemistry* **2022**, 35, 100614.

For the energy of water purification: Cataldo, A. L. et al. Water related impact of energy: cost and carbon footprint analysis of water for biopharmaceuticals from tap to waste. *Chem Eng Sci X* **2020**, 8, 100083. <https://doi.org/10.1016/j.cesx.2020.100083>

Biosynthesis/Biocatalysis/Bio-based Products

Further Developements for Bringing Benefits to Sustainability of Biocatalysis:

Sustainability Benefits	
Reaction Intensification	Reduced Downstream costs
Flow Biocatalysis	Reduced <i>E</i> Factor
Multi-step Catalysis	Reduction in Reactor Footprint
	Better control
	Reduction in Isolation steps and Solvent swap

Bio-based Products

New metrics proposed:

Feedstock Intensity:
$$FI = \frac{M_{raw\ Mat}}{M_{main\ Prod} + M_{co\ Prod}}$$

Circular Process Feedstock Intensity:
$$CPFI = \frac{M_{raw\ mat}}{M_{Main\ Prod} + M_{Co\ Prod} + M_{Rec\ Mat}}$$

Also the Process Material Circularity, Energy Intensity, Circular-Process Energy Intensity, ...

Bio-based Products

New metrics proposed:

Waste Factor:

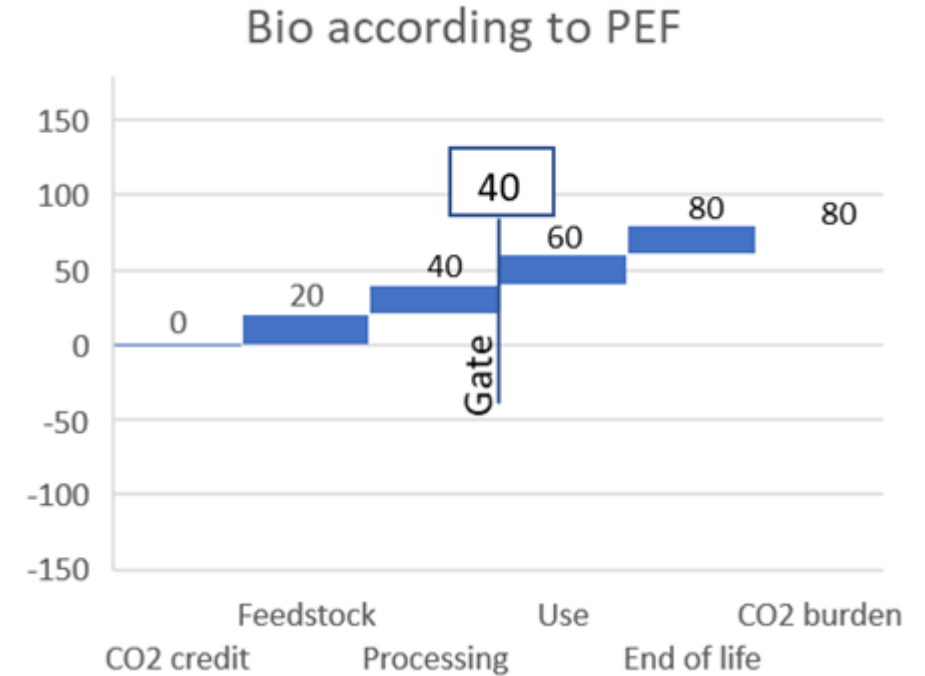
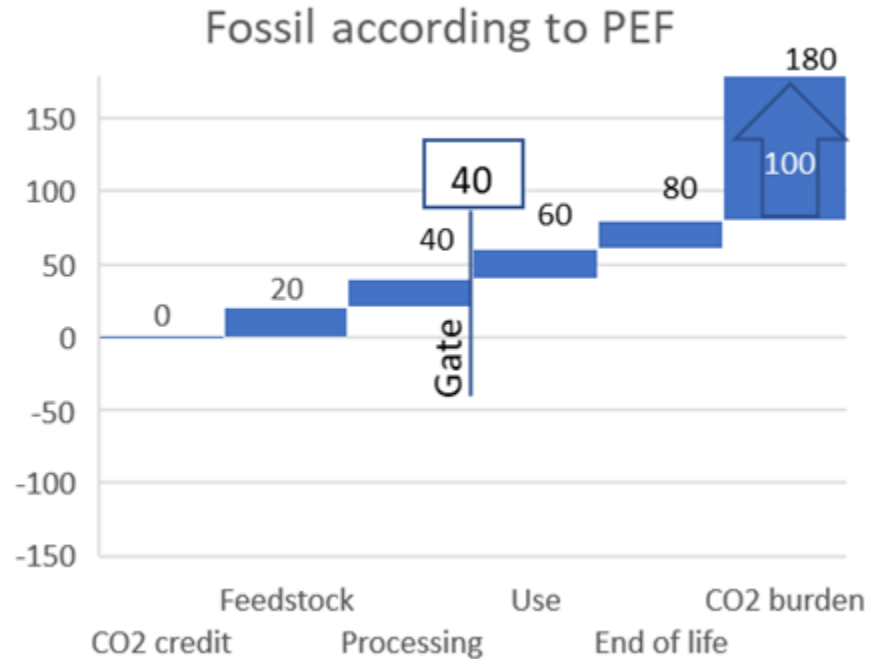
$$WF = \frac{M_{Tot\ Waste}}{M_{Prod} + M_{co\ Prod}}$$

Circular Process Waste Factor:

$$CPWF = \frac{M_{Tot\ Waste}}{M_{Prod} + MCo_{Prod} + MRec_{Mat}}$$

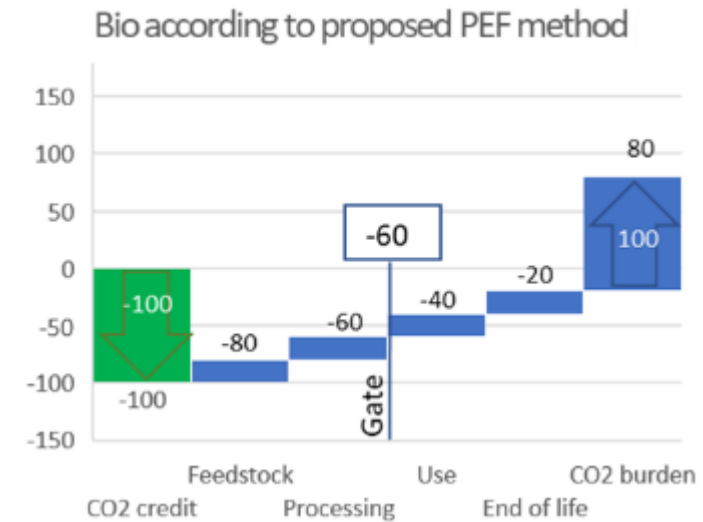
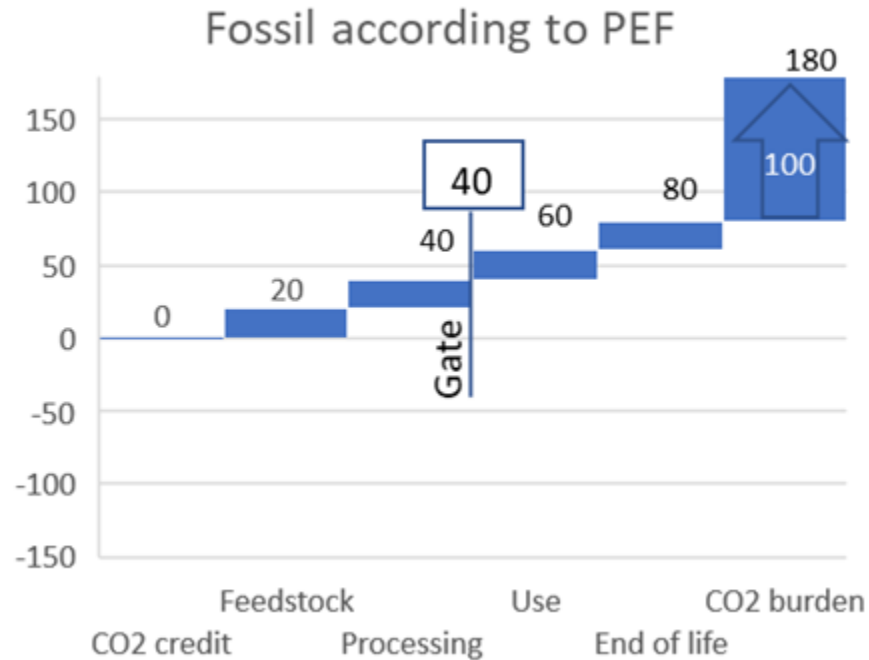
Bio-based Products

Carbon footprint of Bio-based Products: proposition of the CEFIC [European Chemical Industry Council]



Bio-based Products

Carbon footprint of Bio-based Products:



Bio-based Products

Carbon footprint of Bio-based Products:

Facilitate the development and adoption of international sustainability indicators for Biobased Products that are science-based, unambiguous and validated. These should consider factors such as:

- Energy balance, including non-renewable and renewable energy use.
- All greenhouse gas reduction over product life cycles.
- Bio-based content as an indicator of renewability.
- Anticipated product life.
- Water and solvent use during the different stages of production and impacts on biodiversity during feedstock production and subsequent processing.
- Direct and indirect land use for feedstock production.
- All aspects of end of product life.
- Conventional as opposed to alternative bio-based production economics.
- Impact on human and environmental health.

Upcycling of Waste Stream

Different Methods for Different Wastes:

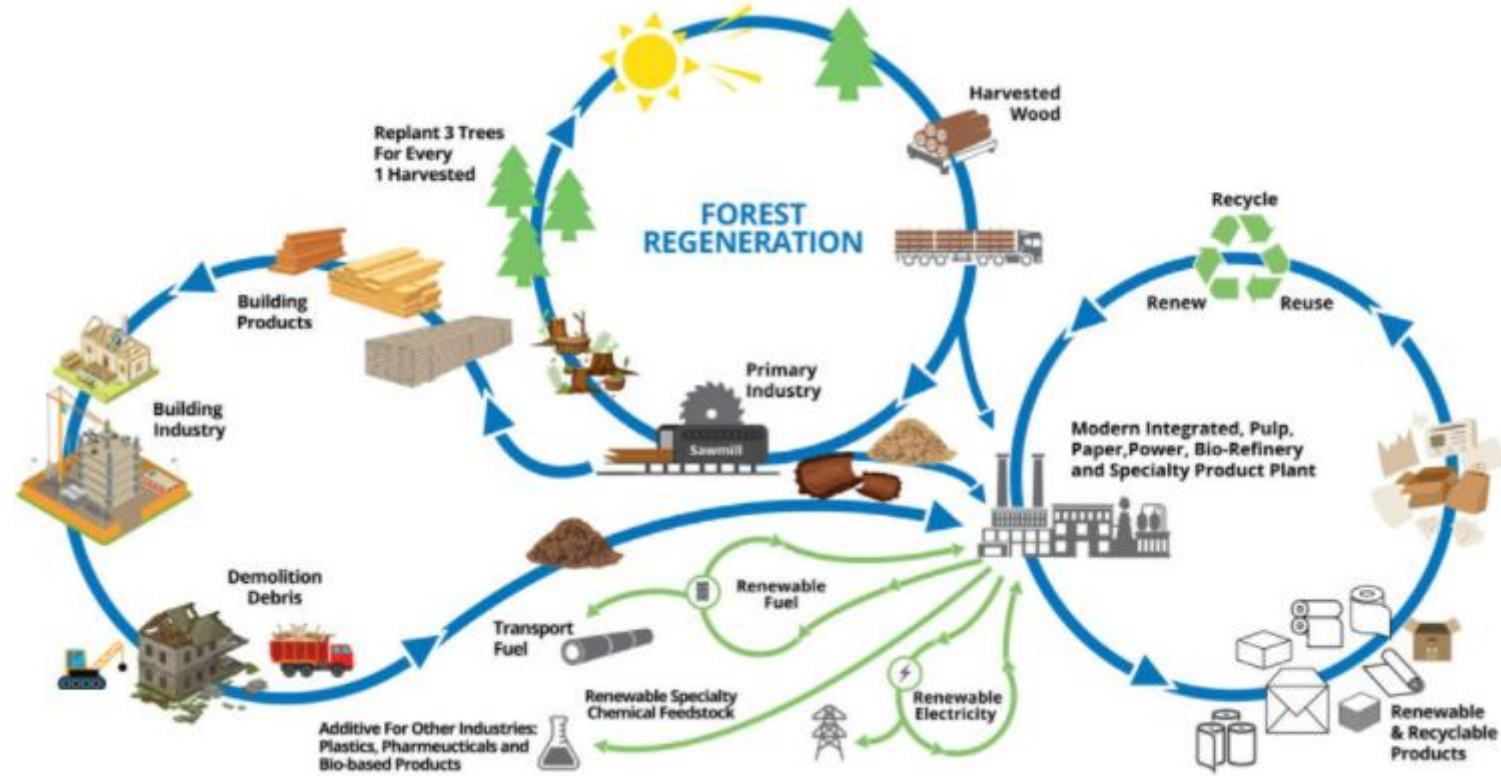
2 types of waste:

Bio-waste: from agriculture, paper industry, ...

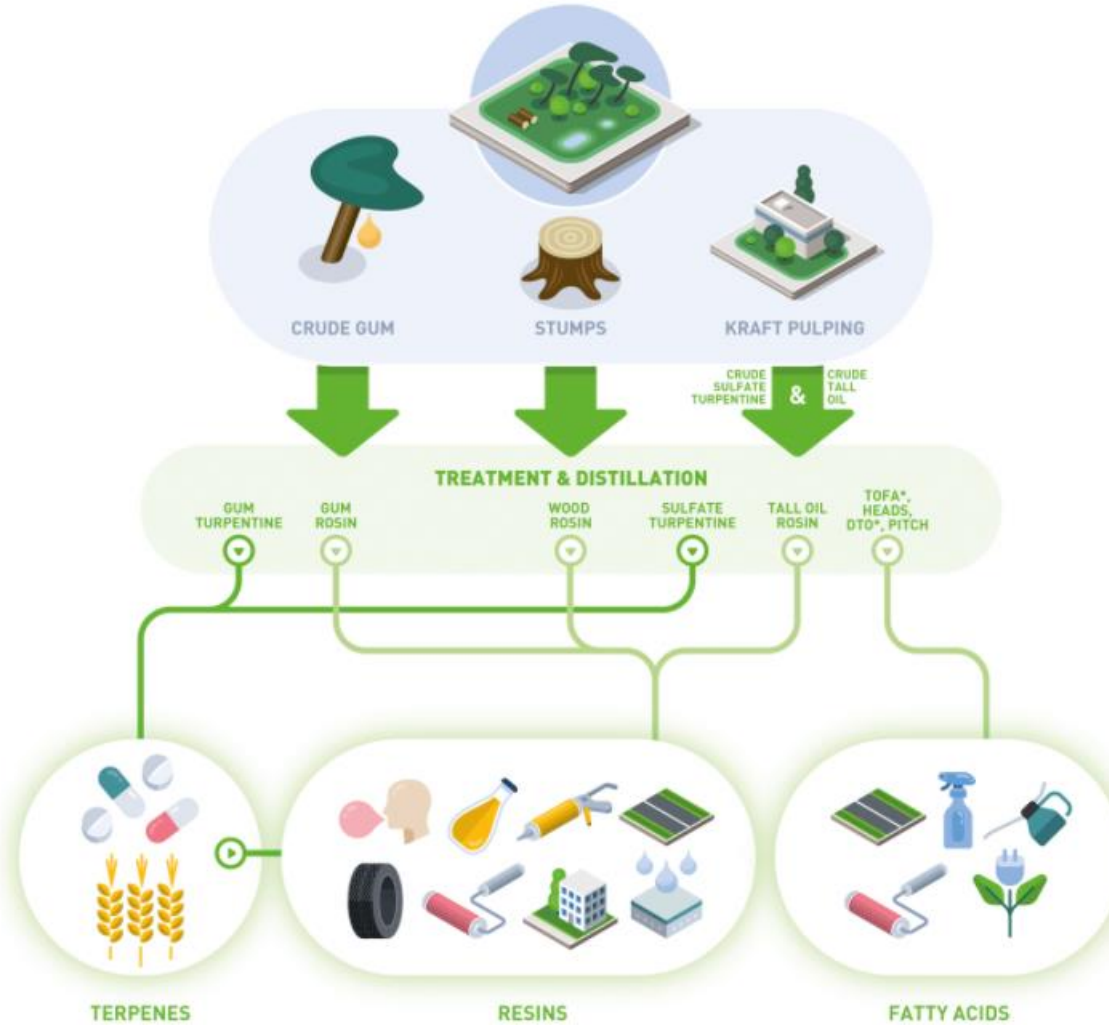
«chemical» waste: Polymers, ...

Different types of extraction methods: Organic Solvents, Supercritical CO₂, Steam, Mechanical extraction,...

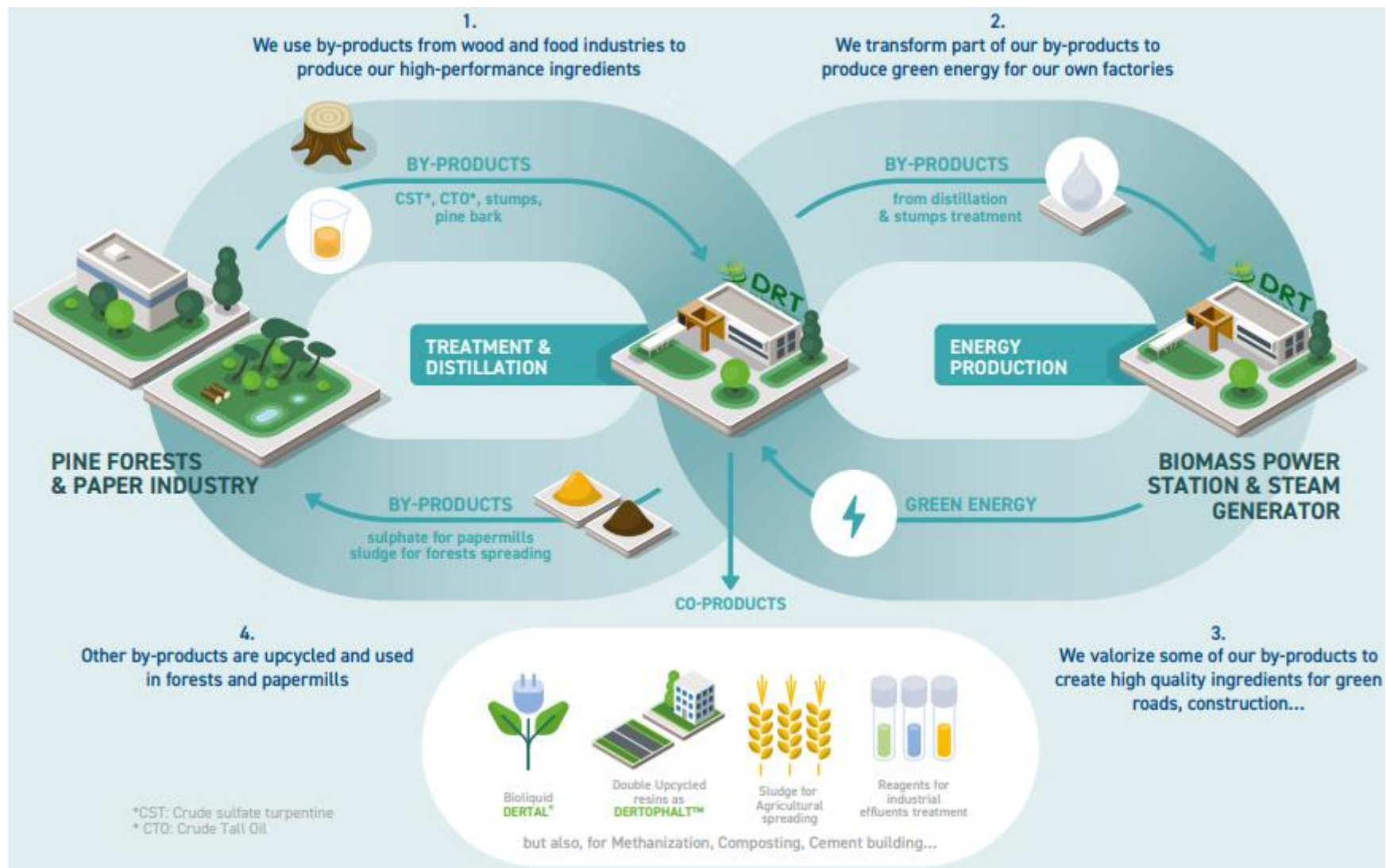
From Paper Industry



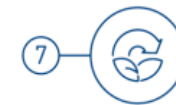
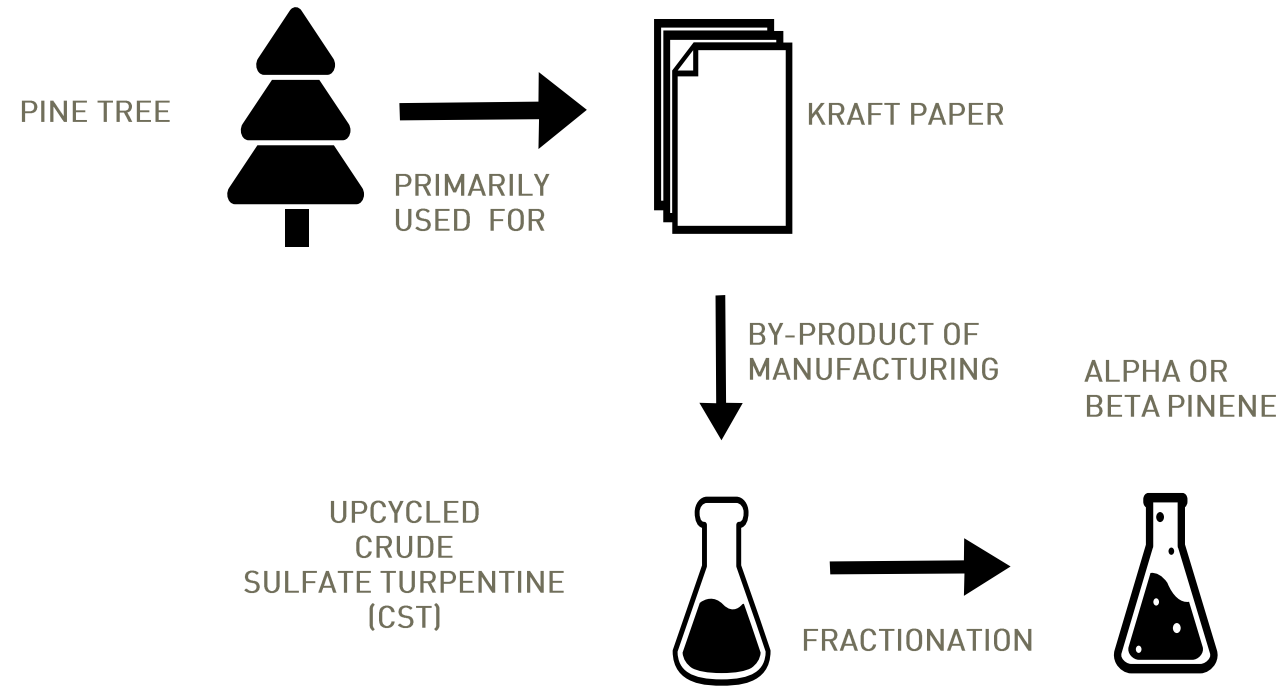
From Paper Industry



Circularity in practice: Vieille-St-Giron

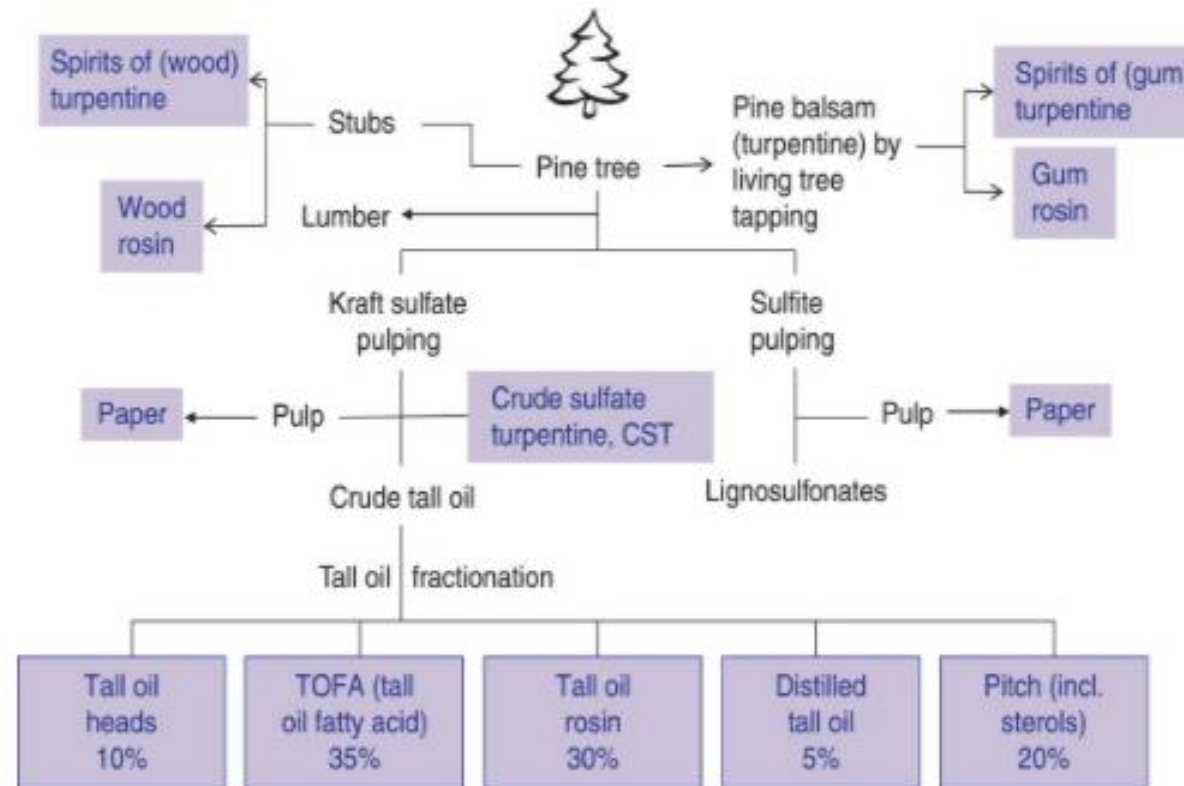


Circularity in practice: Vieille-St-Giron



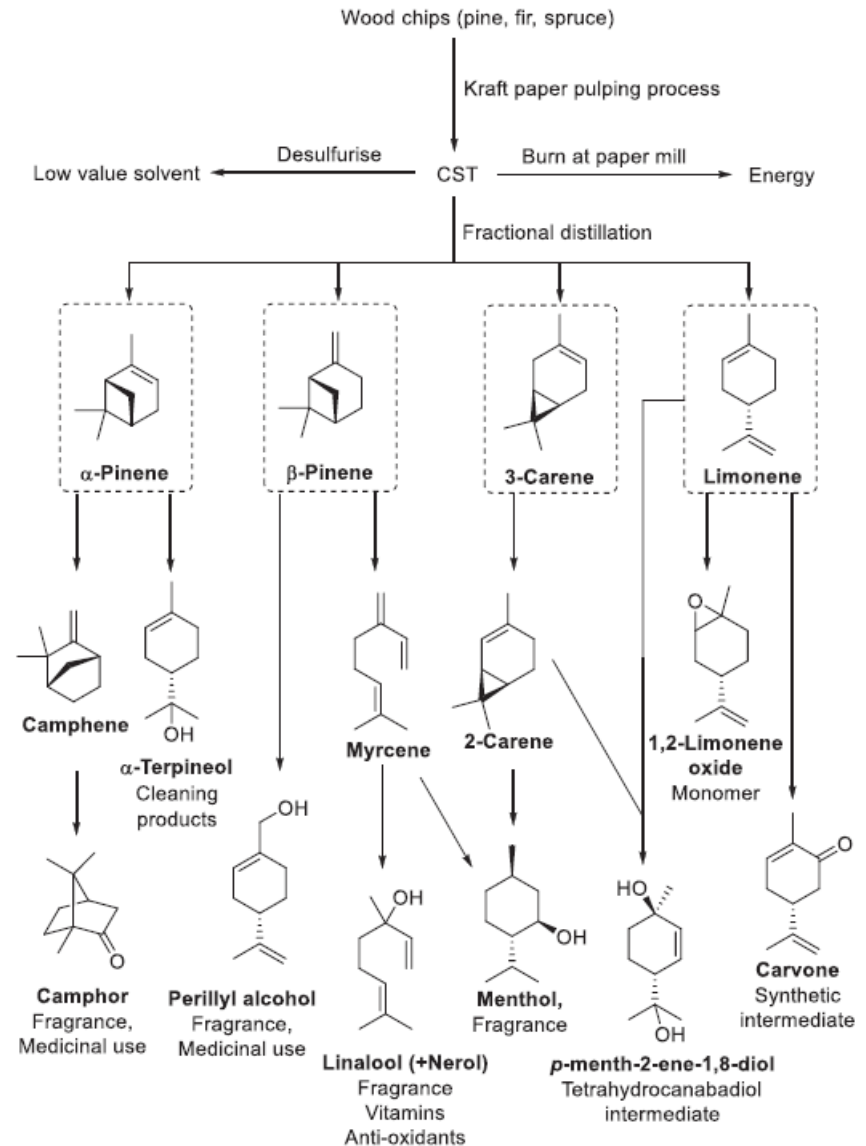
Principle 7:
Renewable feedstock

From Paper Industry



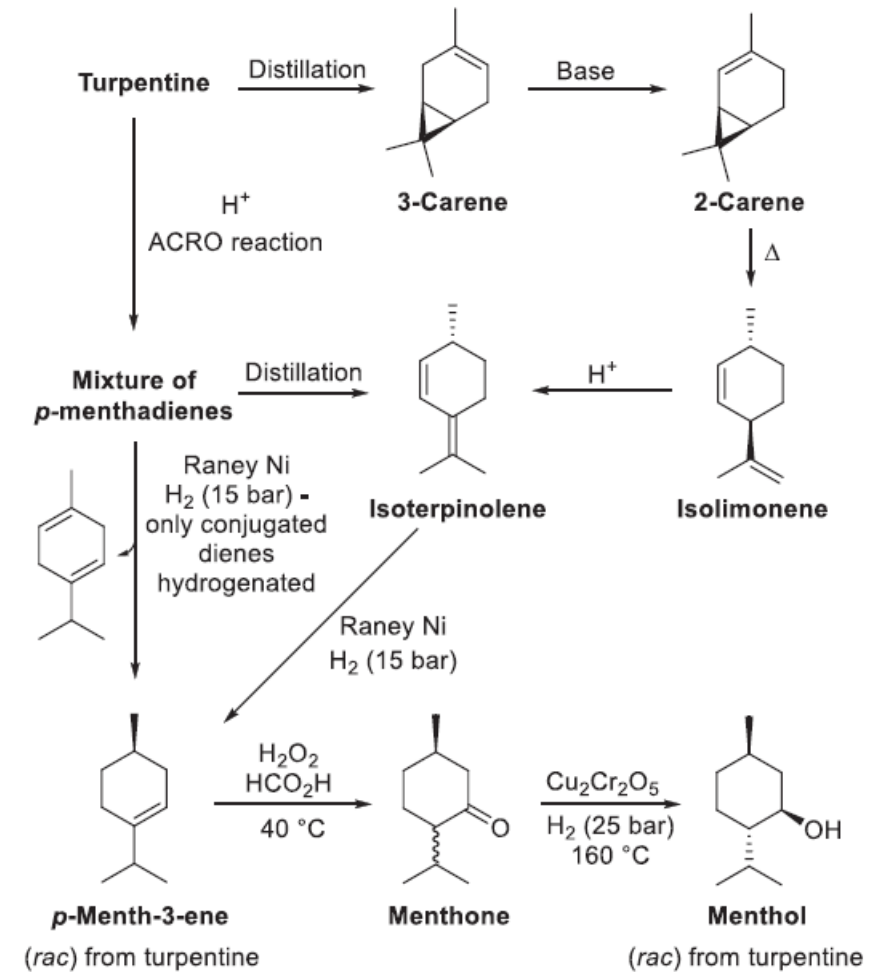
From Paper Industry

High Value Chemicals:



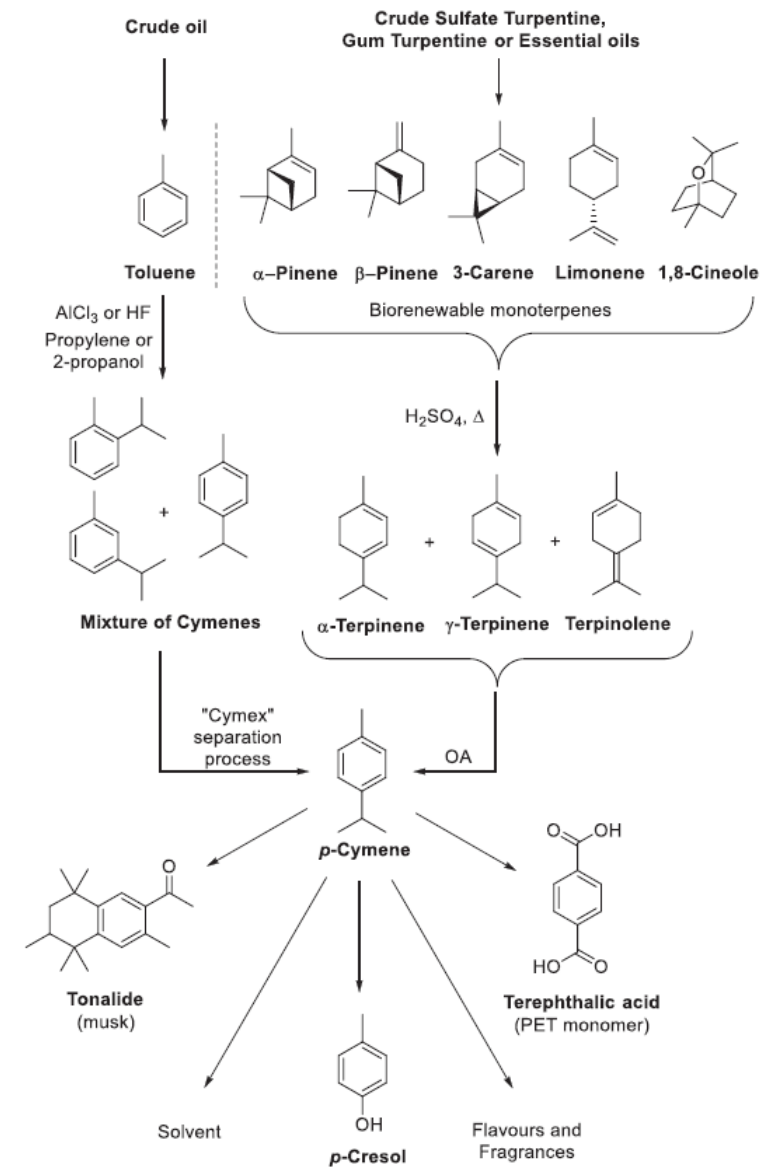
From Paper Industry

High Value Chemicals:



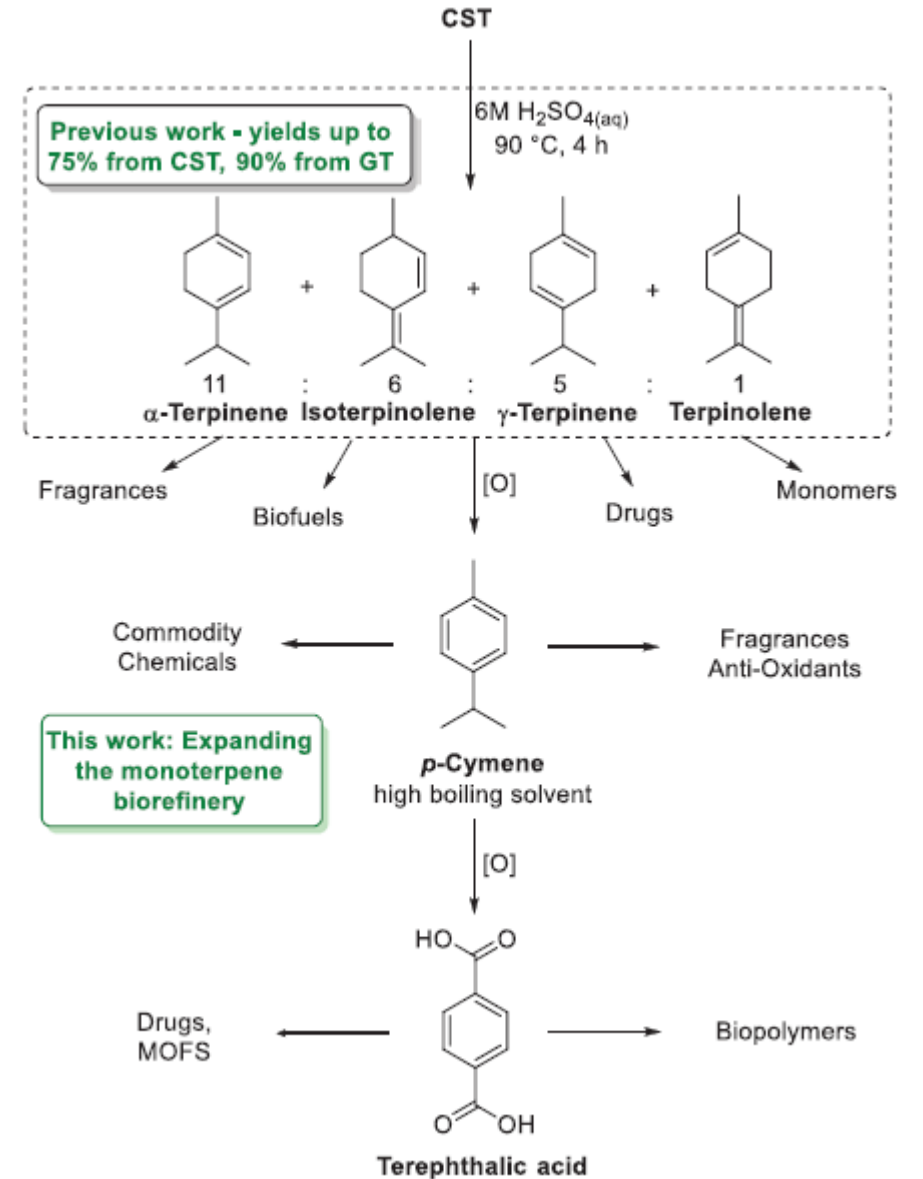
From Paper Industry

High Value Chemicals:



From Paper Industry

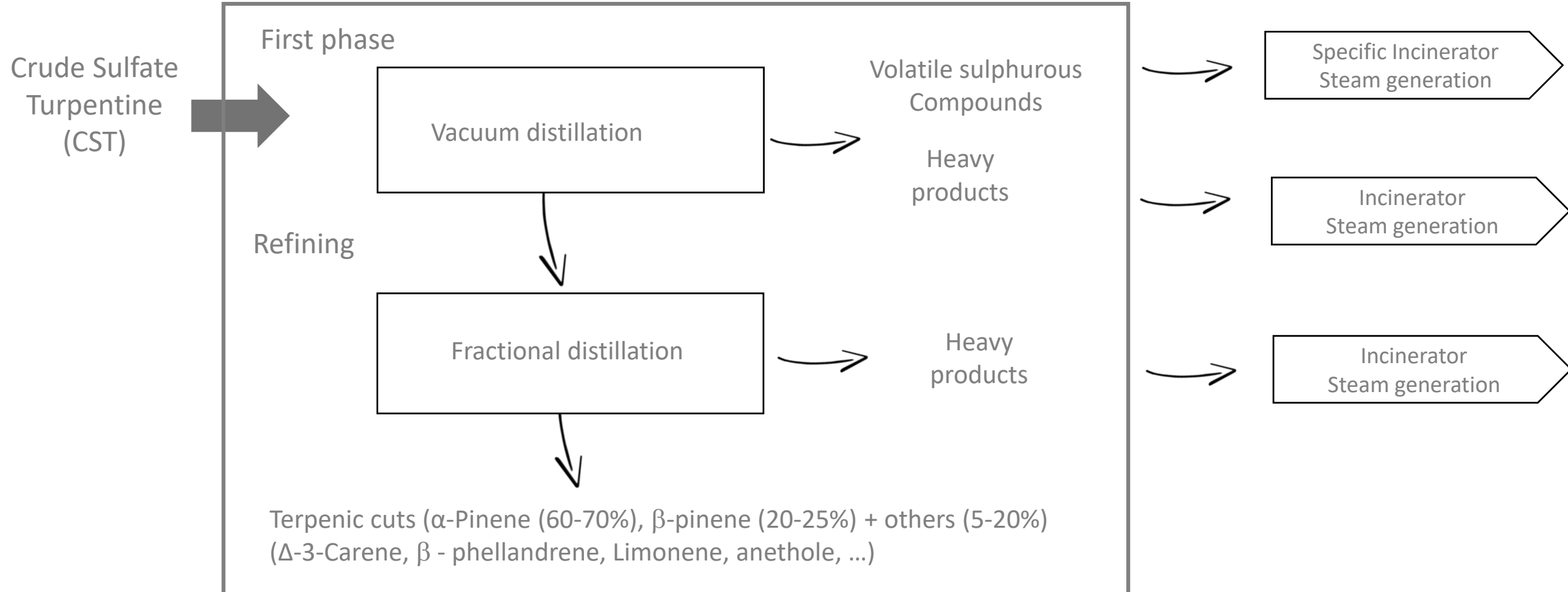
High Value Chemicals:



From Paper Industry

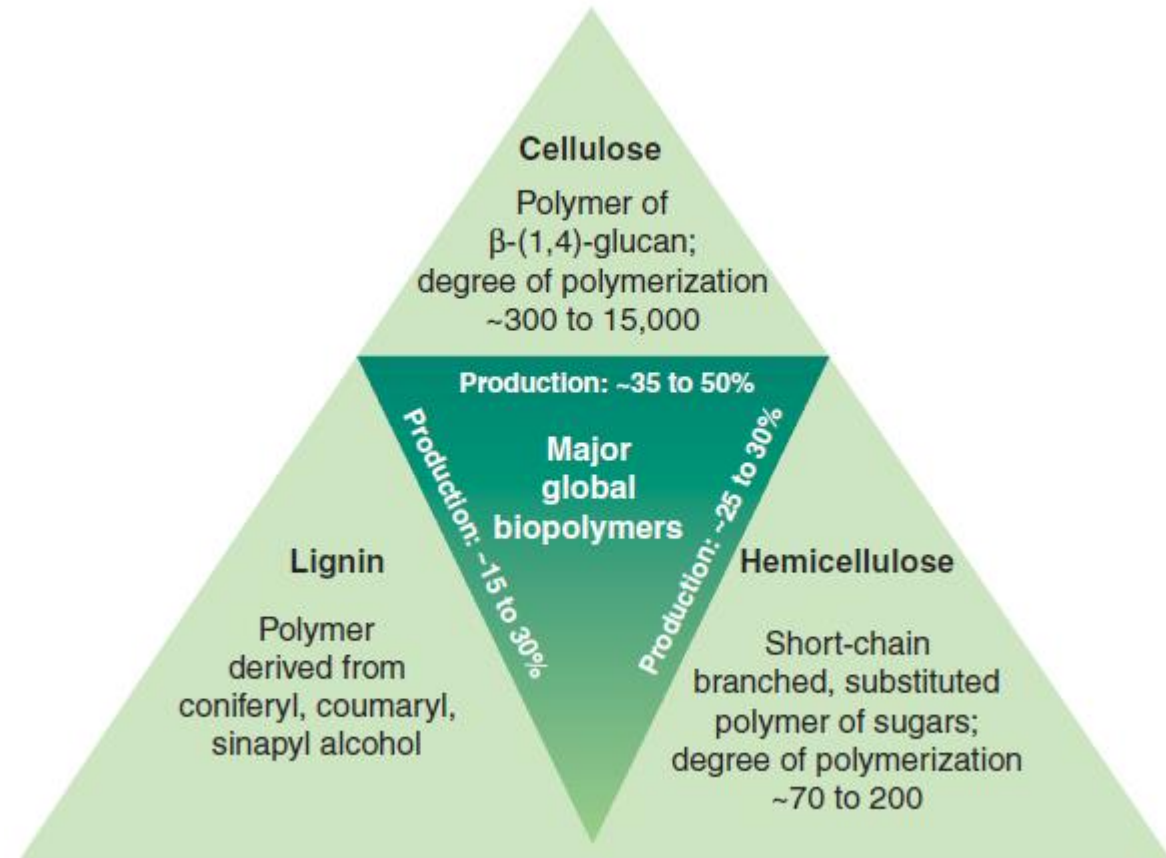
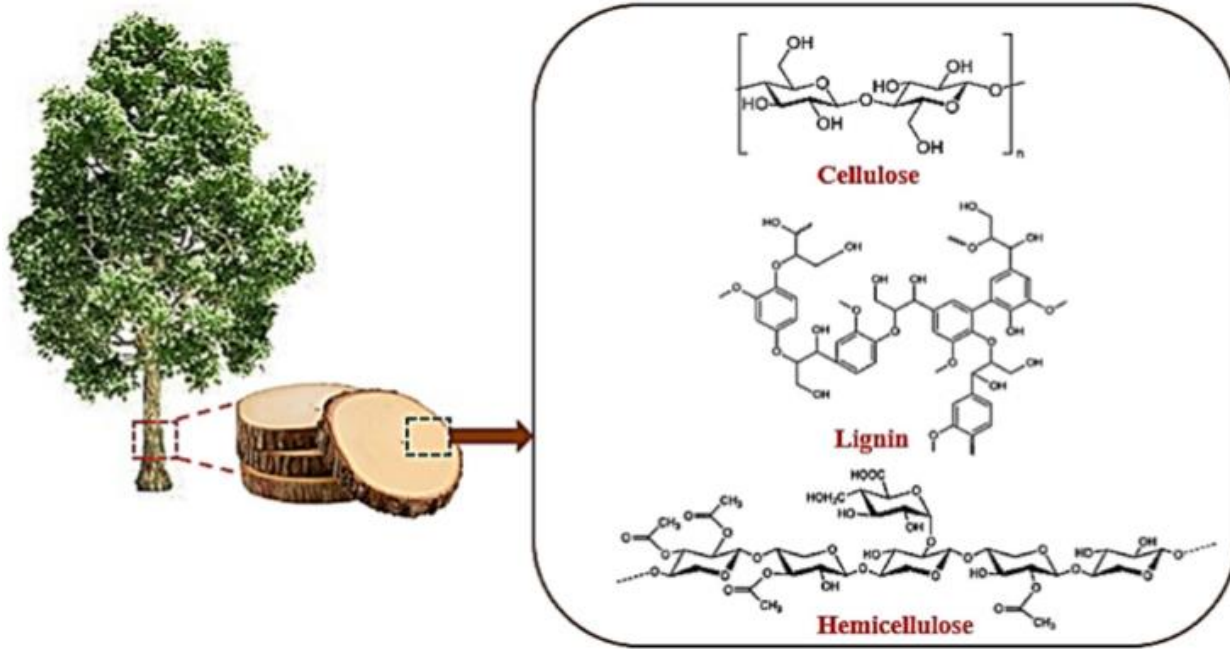


High Value Chemicals:



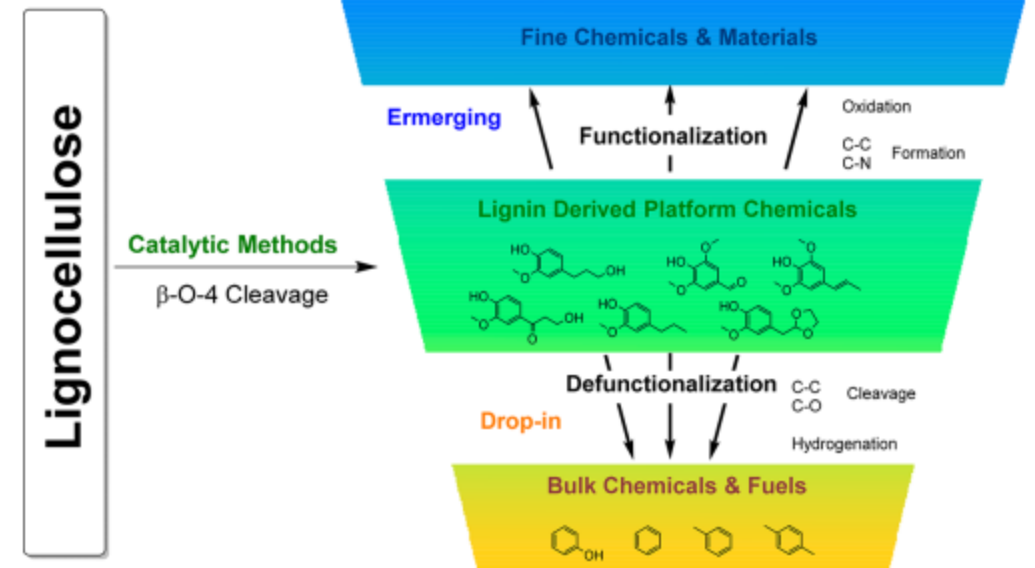
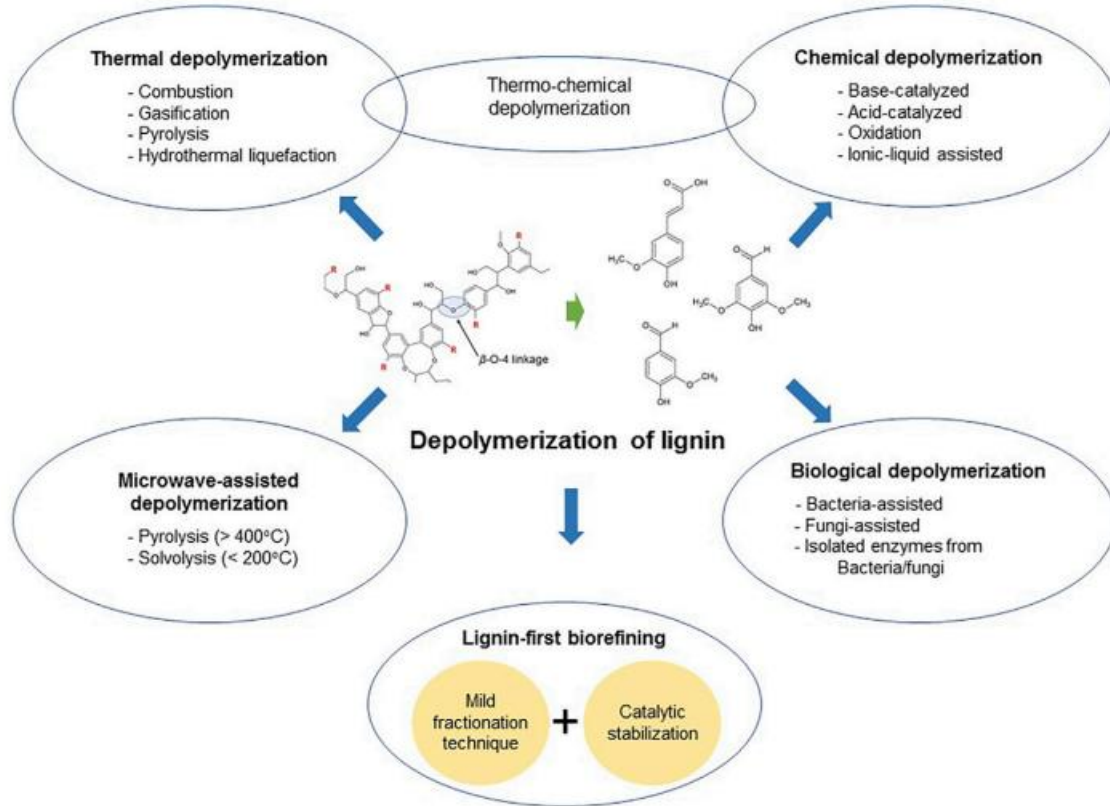
Key Global Biomass Resources

Agricultural residues, wood, and herbaceous energy crops:



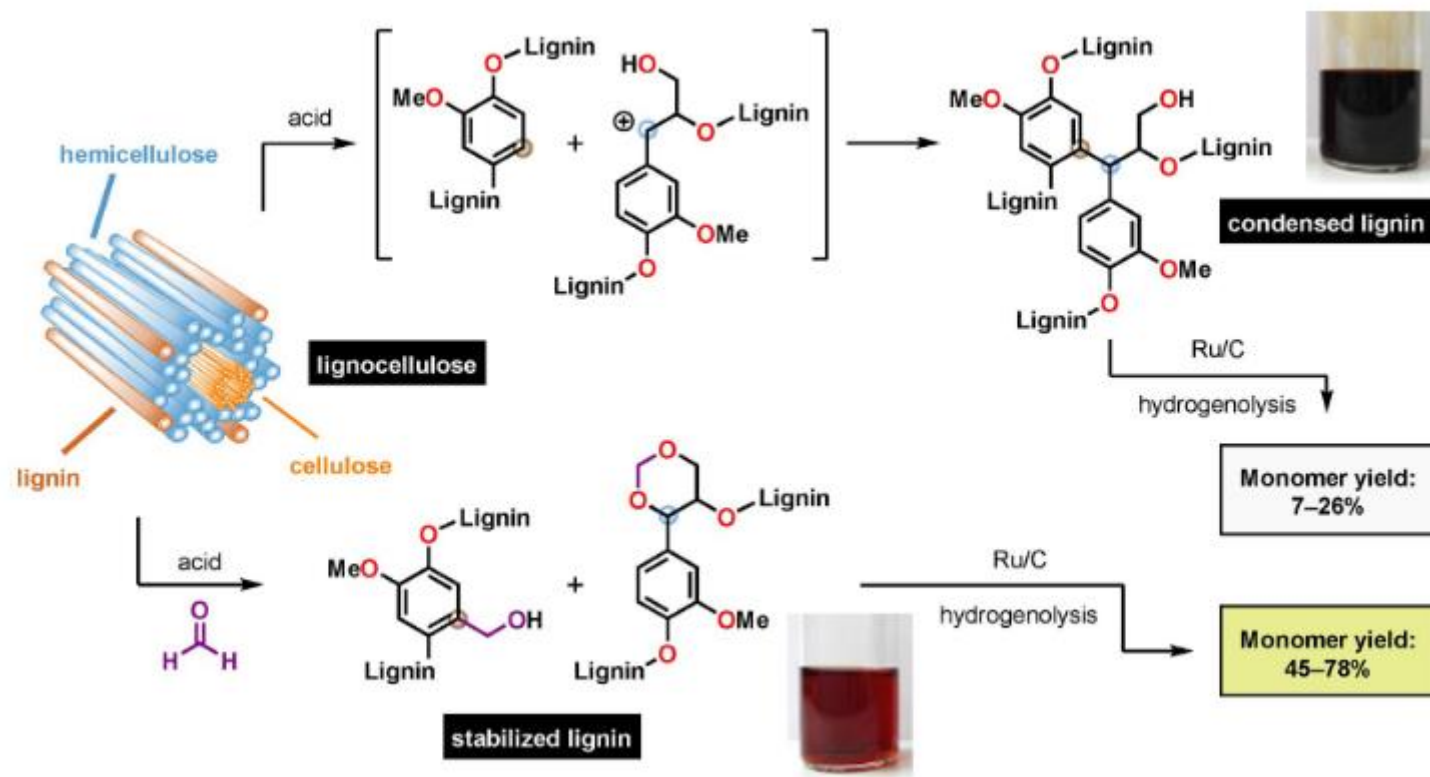
From Lignin

Depolymerization of Lignin:



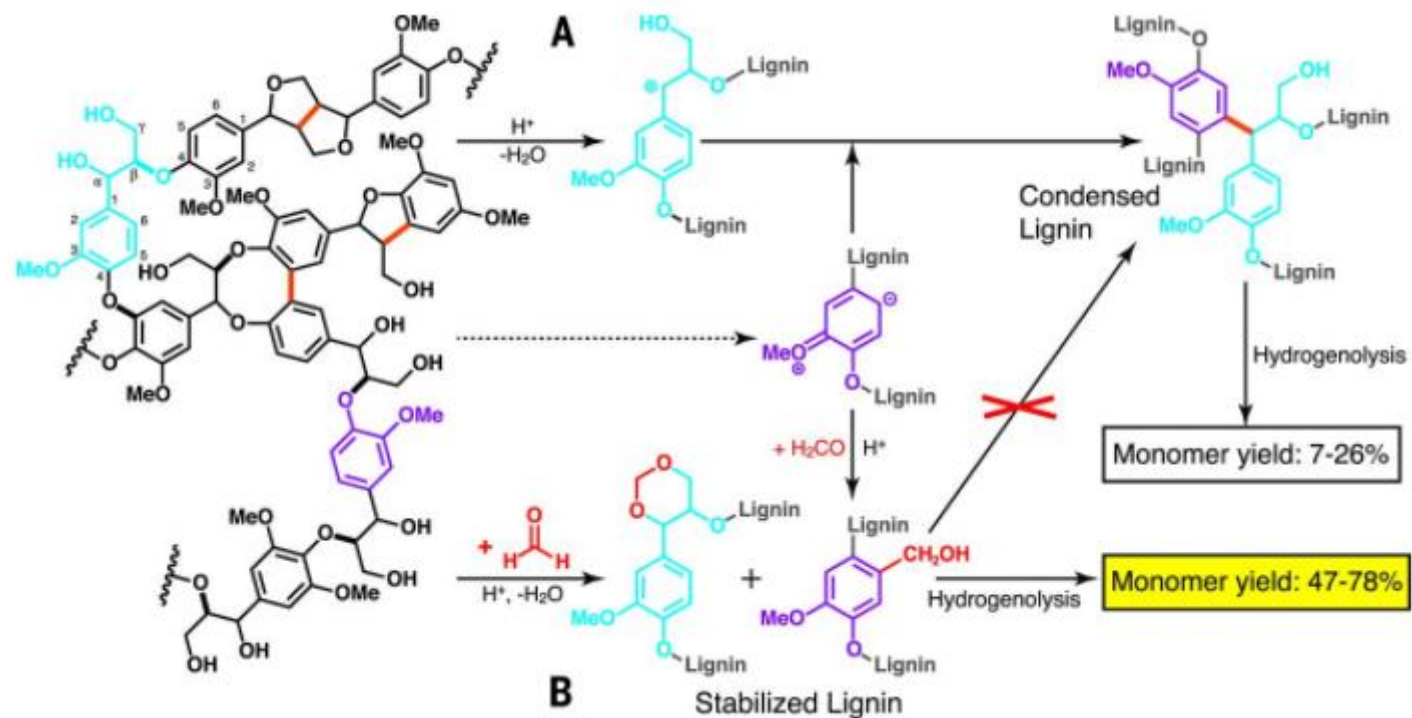
From Lignin

One Example from Bloom Biorenewables:



From Lignin

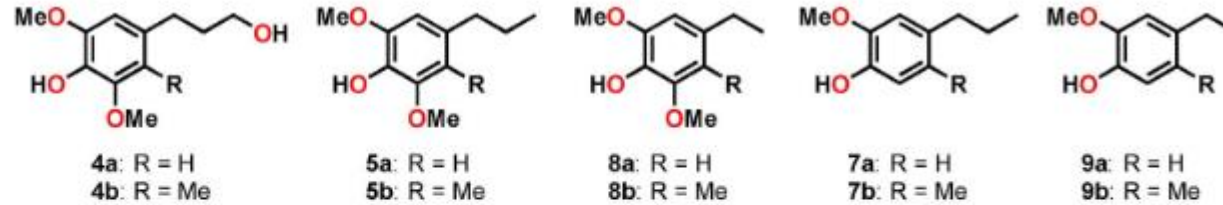
One Example from Bloom Biorenewables:



From Lignin

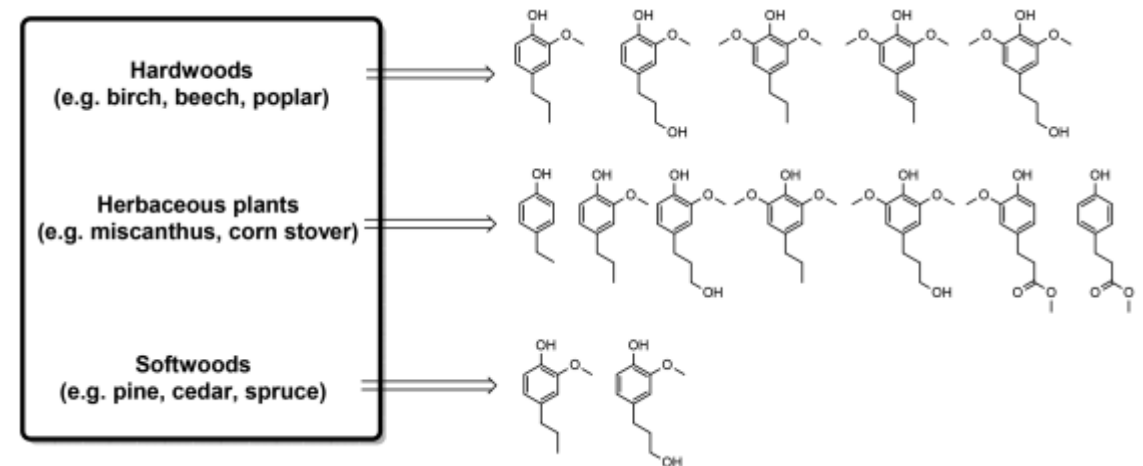
High Value Chemicals:

Product distribution



Beech wood^[a] (F5H poplar^[b])

● with formaldehyde	4a, 5.67% (16.45%) 4b, 3.60% (9.08%)	5a, 13.31% (18.57%) 5b, 9.44% (8.97%)	8a, 2.05% (15.24%) 8b, 1.07% (5.50%)	7a, 7.01% (1.98%) 7b, 2.27% (0.65%)	9a, 0.64% (1.22%) 9b, – (–)
● without formaldehyde	4a, 2.00% (2.57%) 4b, – (–)	5a, 1.82% (5.48%) 5b, – (–)	8a, 2.07% (14.86%) 8b, – (–)	7a, 0.66% (–) 7b, – (–)	9a, 0.55% (1.31%) 9b, – (–)



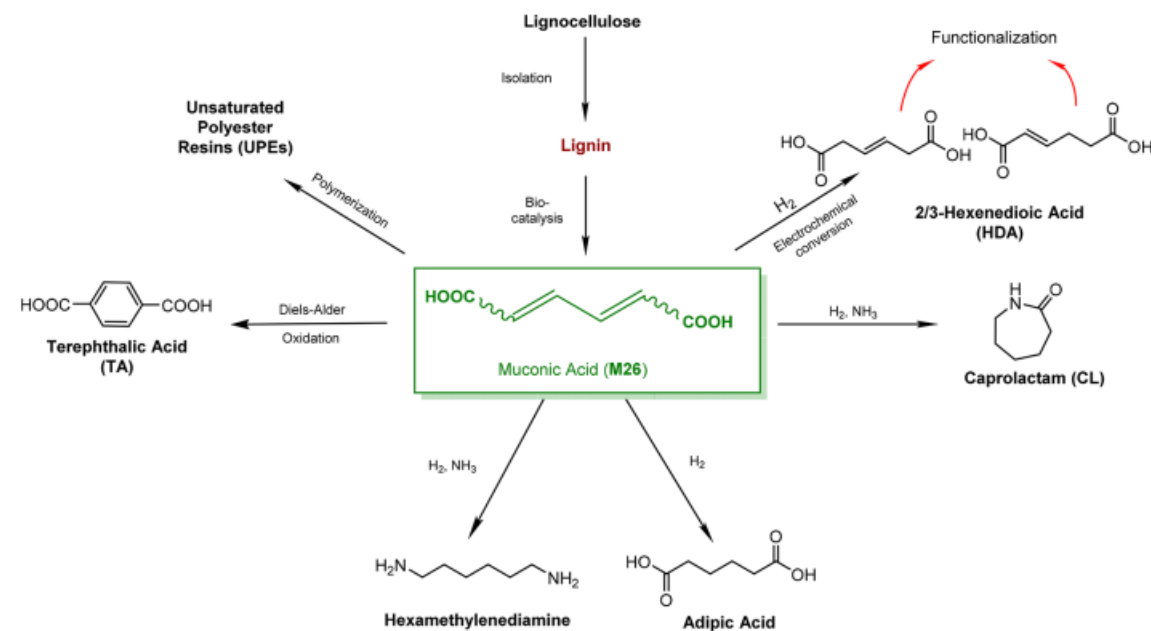
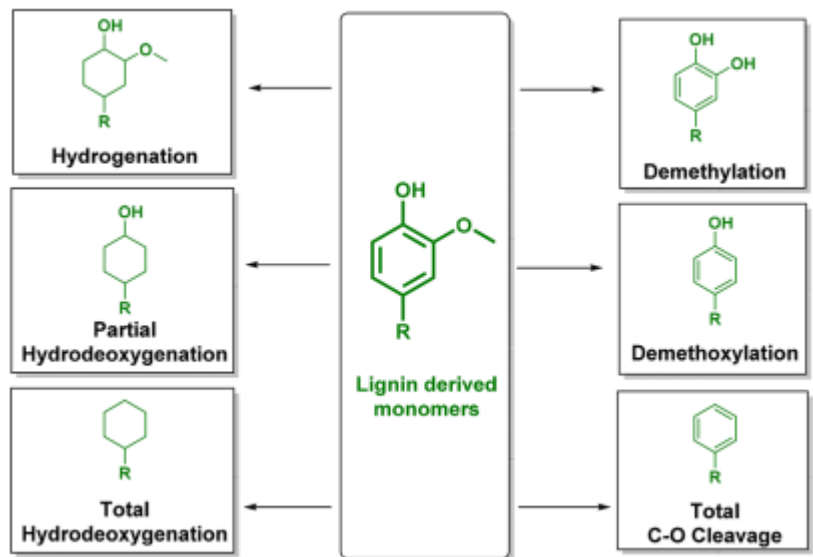
Luterbacher, J. S. & co. *Science* **2016**, 354, 329.

Kärkäs, M. D. *ChemSusChem* **2017**, 10, 2111.

Tibbetts, J. D.; Bull, S. D. *Adv. Sustainable Syst.* **2021**, 5, 2000292.

From Lignin

High Value Chemicals:

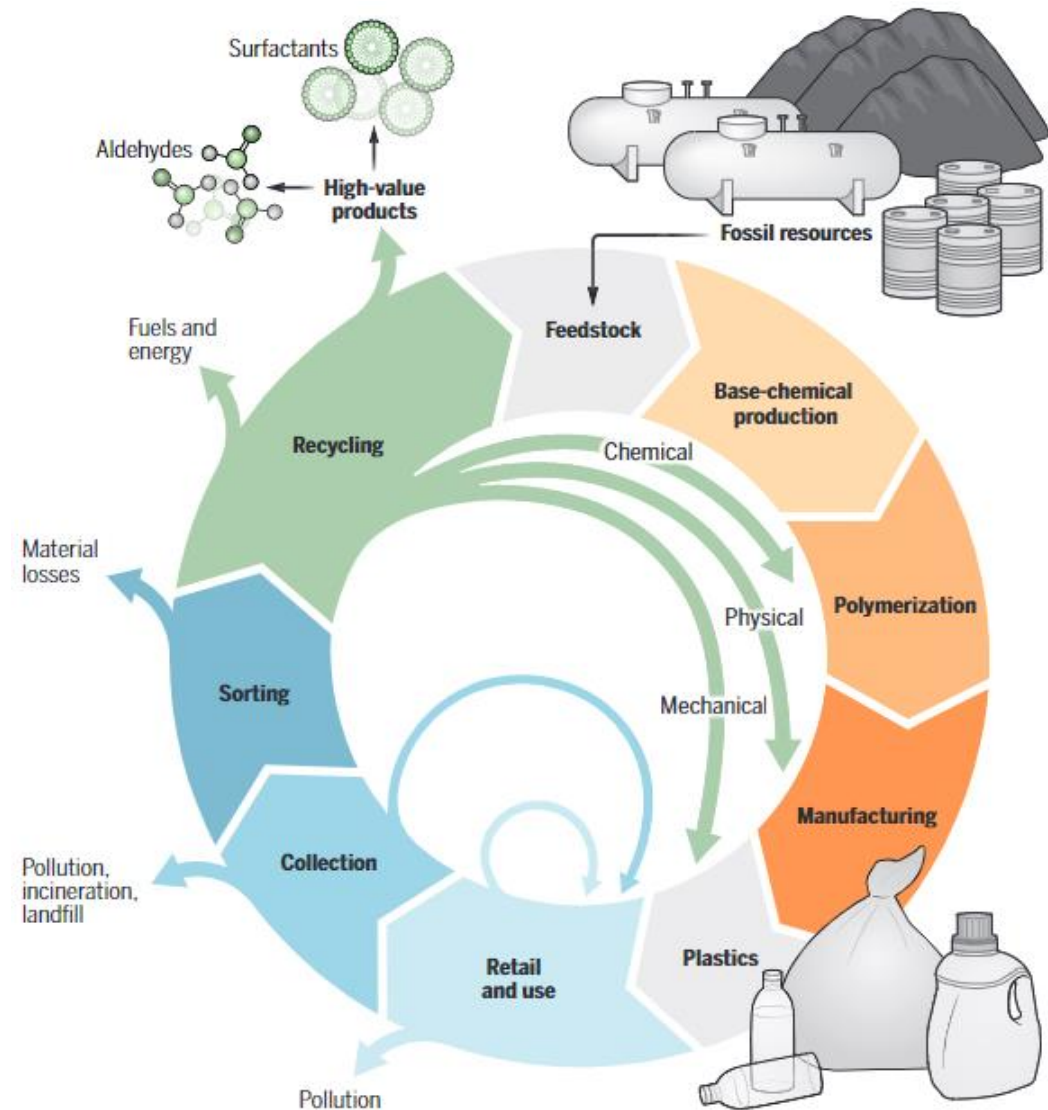


Kärkäs, M. D. *ChemSusChem* **2017**, *10*, 2111.

Sun, Z *et al. Chem. Rev.* **2018**, *118*, 614.

From Plastics

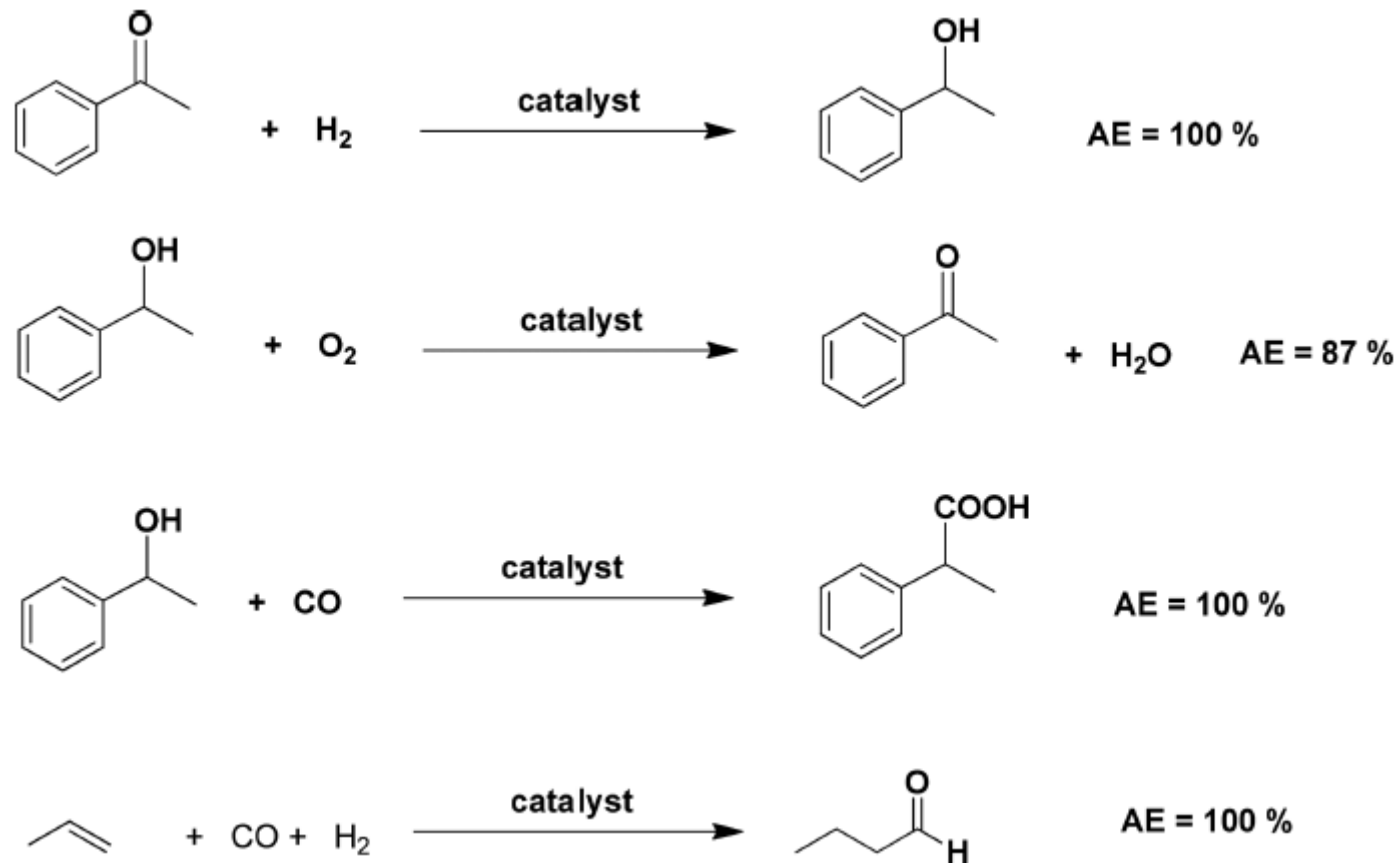
High Value Chemicals:



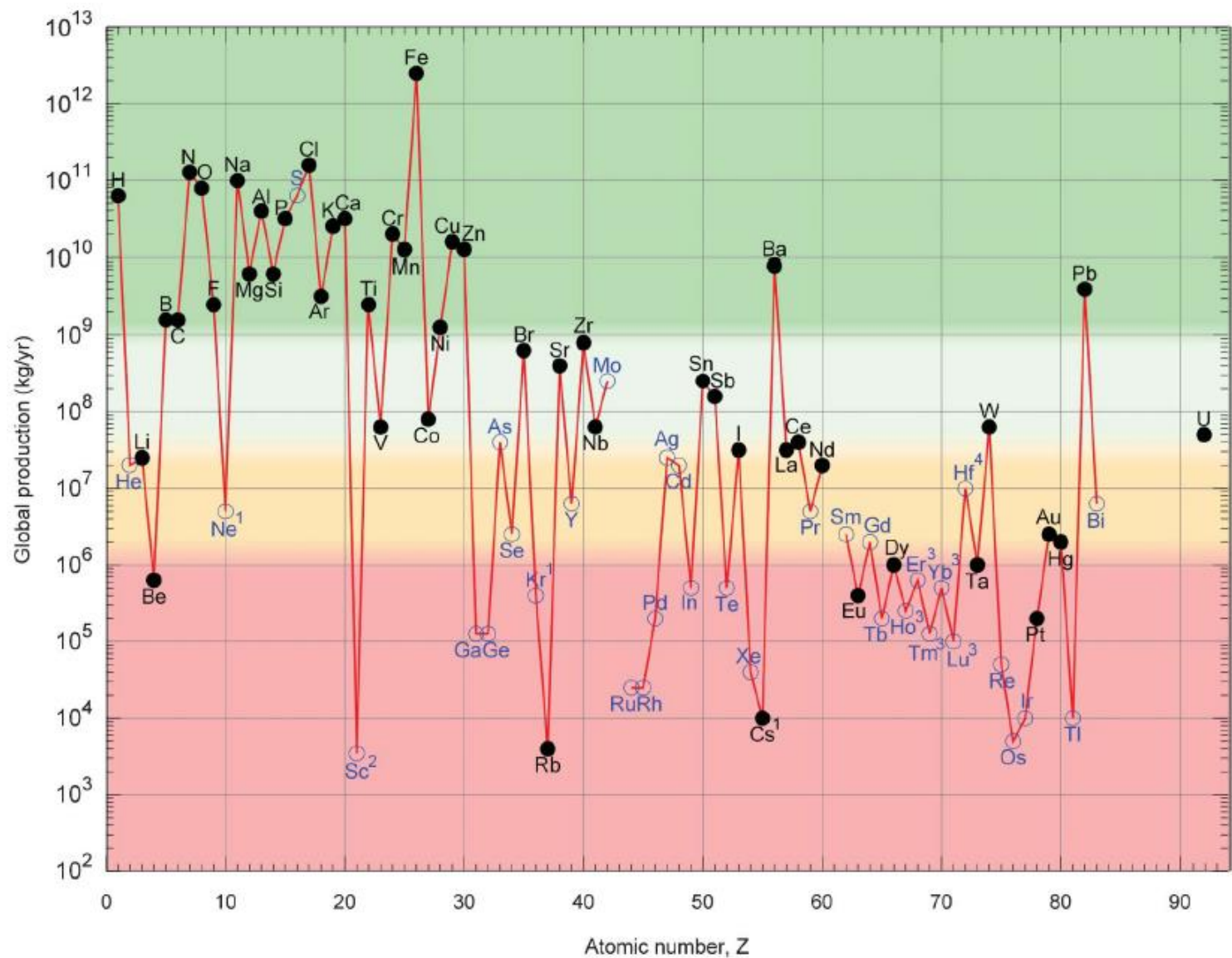
Chemical Catalysis

Chemical Catalysis:

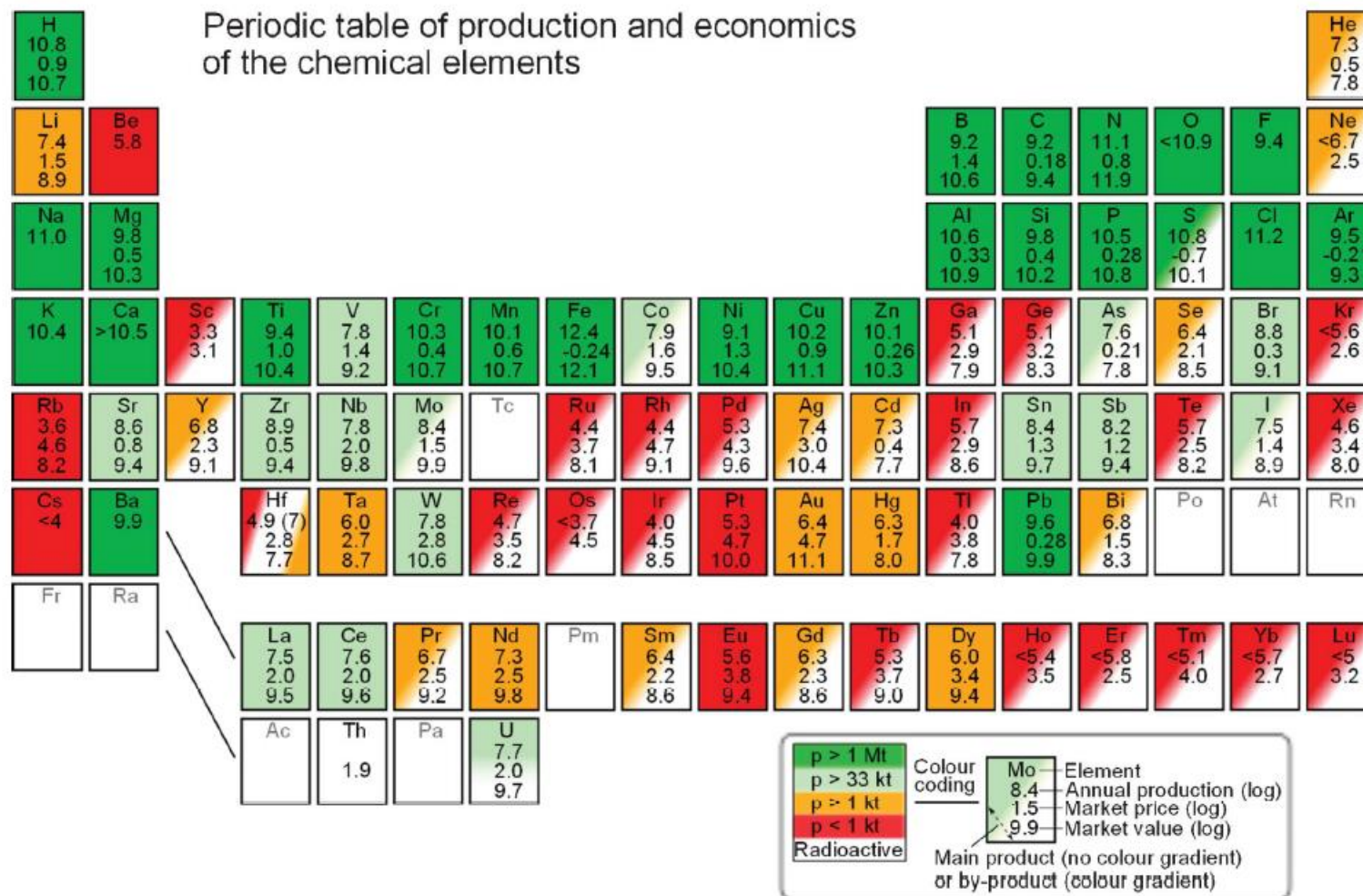
Pros & Cons
Metrics?
Issues?



Chemical Catalysis

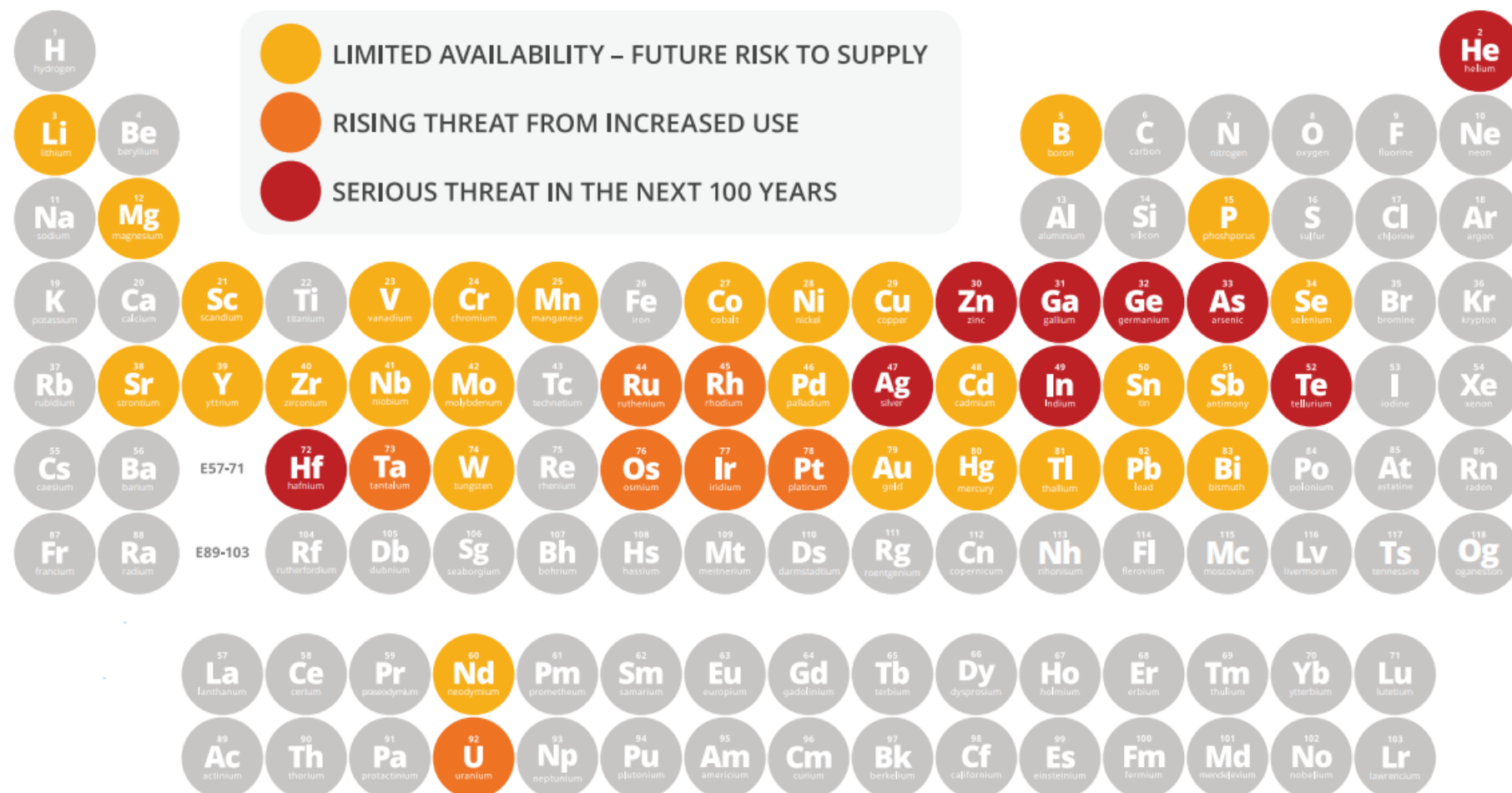


Chemical Catalysis



Chemical Catalysis

THE PERIODIC TABLE'S ENDANGERED ELEMENTS



<https://www.acs.org/greenchemistry/research-innovation/endangered-elements.html>

SOURCE: CHEMISTRY INNOVATION KNOWLEDGE TRANSFER NETWORK

Catalysis

Chemical Catalysis:

Synthesis of Ligands or Metallic Precursors? Green ? Sustainable?

From a sustainability, systems, and life cycle perspective:

- Type and chemical nature of the catalyst matters.
- Where and how the metals, the reagents, chemicals, and solvents are sourced.
- The reaction conditions required for the catalysis to proceed.
- The disposition of these components in use disposal.

No clear metric available.

But the impact of the catalysis during process development could be evaluated via: E-Factor, PMI, etc.

Hazardeous Score

Hazardeous Reactants & Reagents:

Hazard vs risk ?

A hazard is any source of potential damage, harm or adverse health effects on something or someone

Risk is the chance or probability that a person will be harmed or experience an adverse health effect if exposed to a hazard

Chemists have to recognize functional groups and structural motifs that lead to hazardous properties (environmental, safety, and human health) in order to avoid them.

Chemists should recognize and pursue ways to change the chemistry system to one that has minimal adverse impacts and promotes a more sustainable planet.

Hazardeous Score

Hazardeous Reactants & Reagents:

Fire/Explosion:

- Oxidizer
- Combustible

Reaction/Decomposition:

- Thermal Stability:
- Incompatibility
- Exothermic Reaction

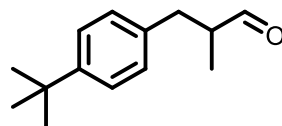
Toxicity Acute or Chronic:

- Carcinogenicity
- Mutagenicity
- Reproductive Tox.
- Sensitization
- Other

**And finally what about the final ingredient?
And by-product during the synthesis?**

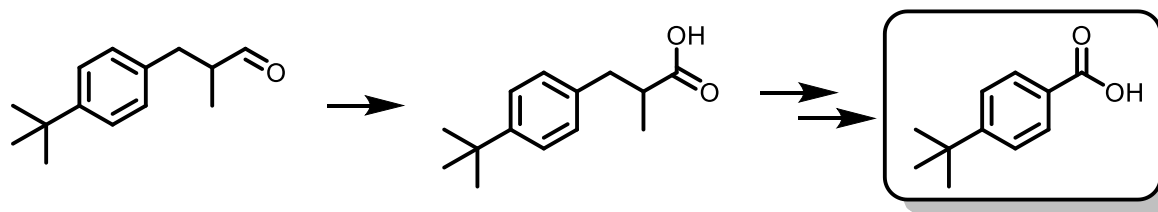
Hazardeous Score

Example from Perfumery Industry: Lyrar Case Study



Lyrar, widely used perfumery ingredient
Lilly-of-the-valley smell

Toxicity of Metabolized Lyrar:



Further link to CoA and as a consequence: impair male reproduction.

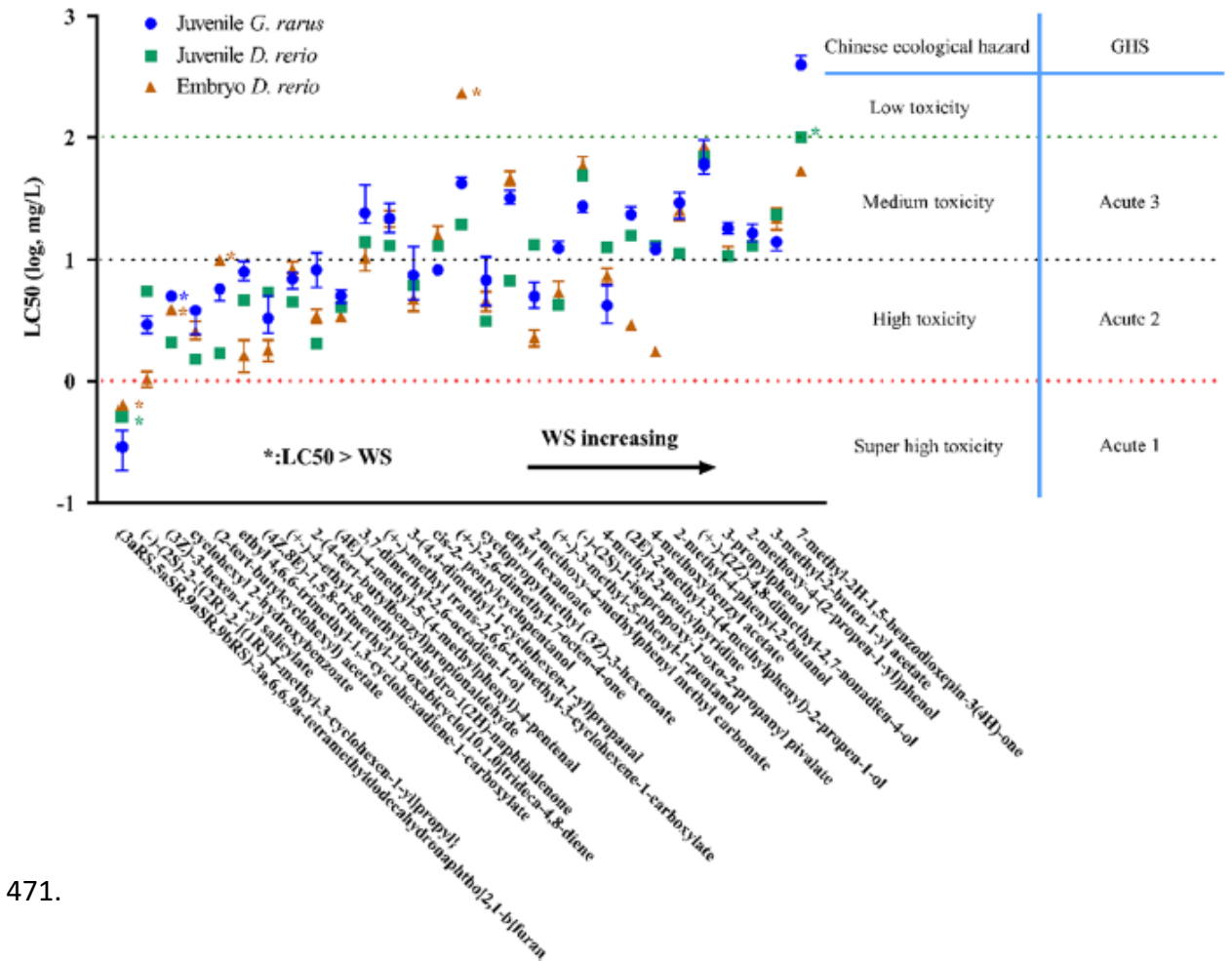
Hazardous Score

Example from Perfumery Industry:

Toxicity of perfumery Ingredients on 2 different Zebrafish

29 ingredients: different physical properties, structures

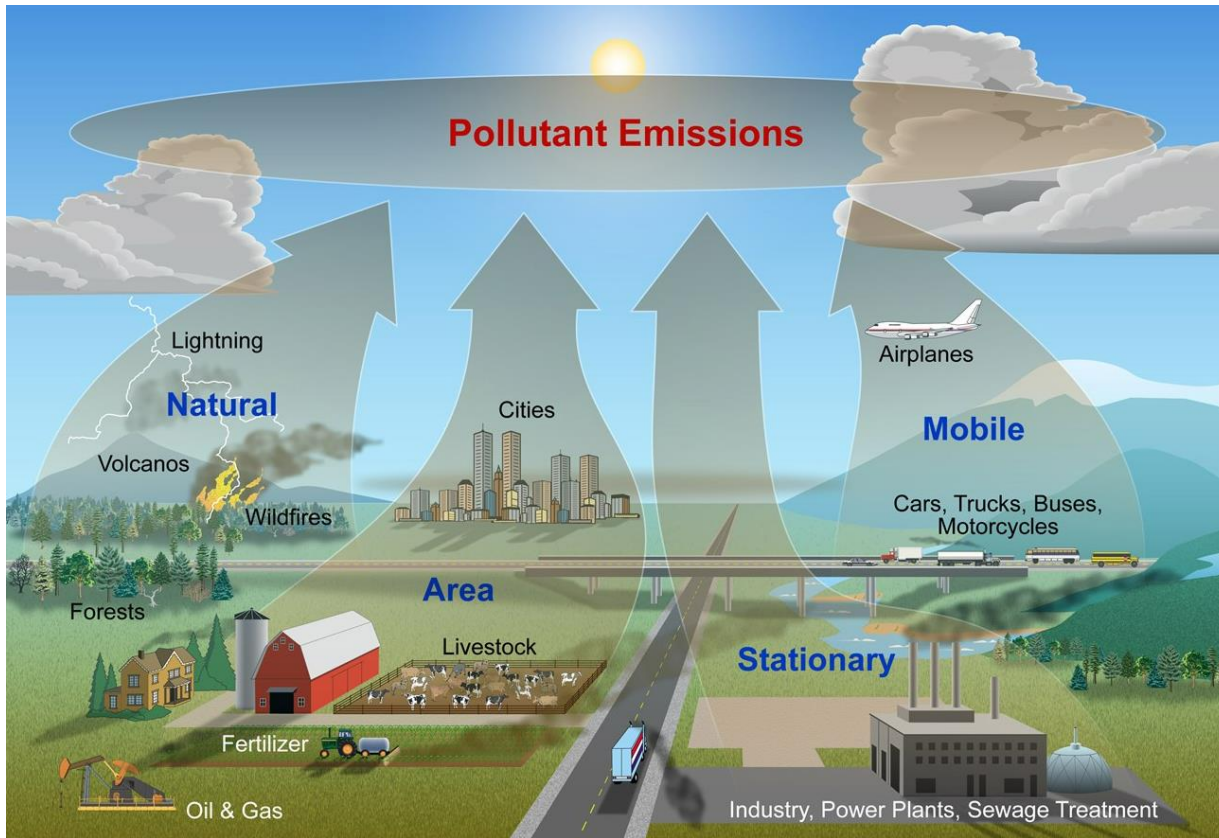
Based on Verhaar categories



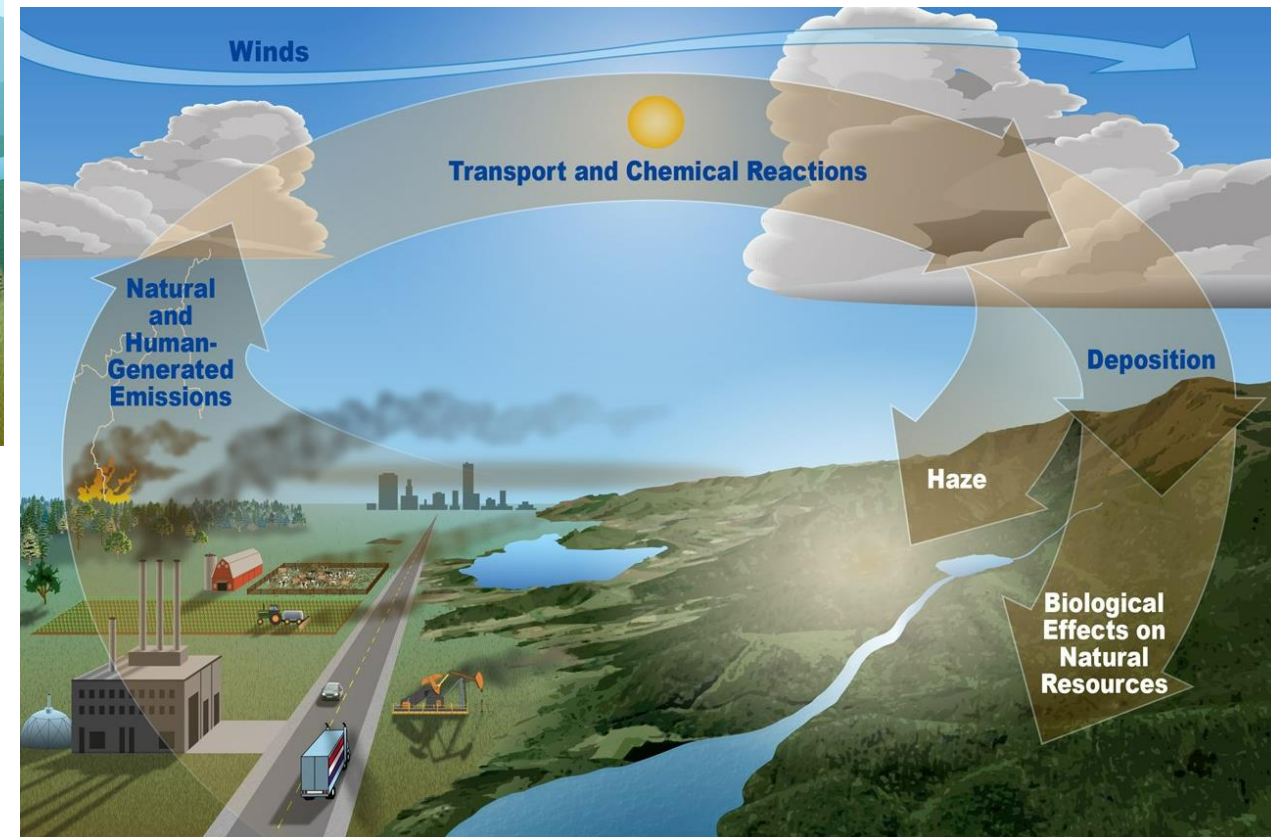
Zhou, Z. et al. *Environmental Toxicology and Chemistry*, **2022**, 41(9), 2305.

Verhaar, H. J. *et al.* Classifying environmental pollutants. *Chemosphere*, **1992**, 25, 471.

Biodegradation/(Bio)-Accumulation Score

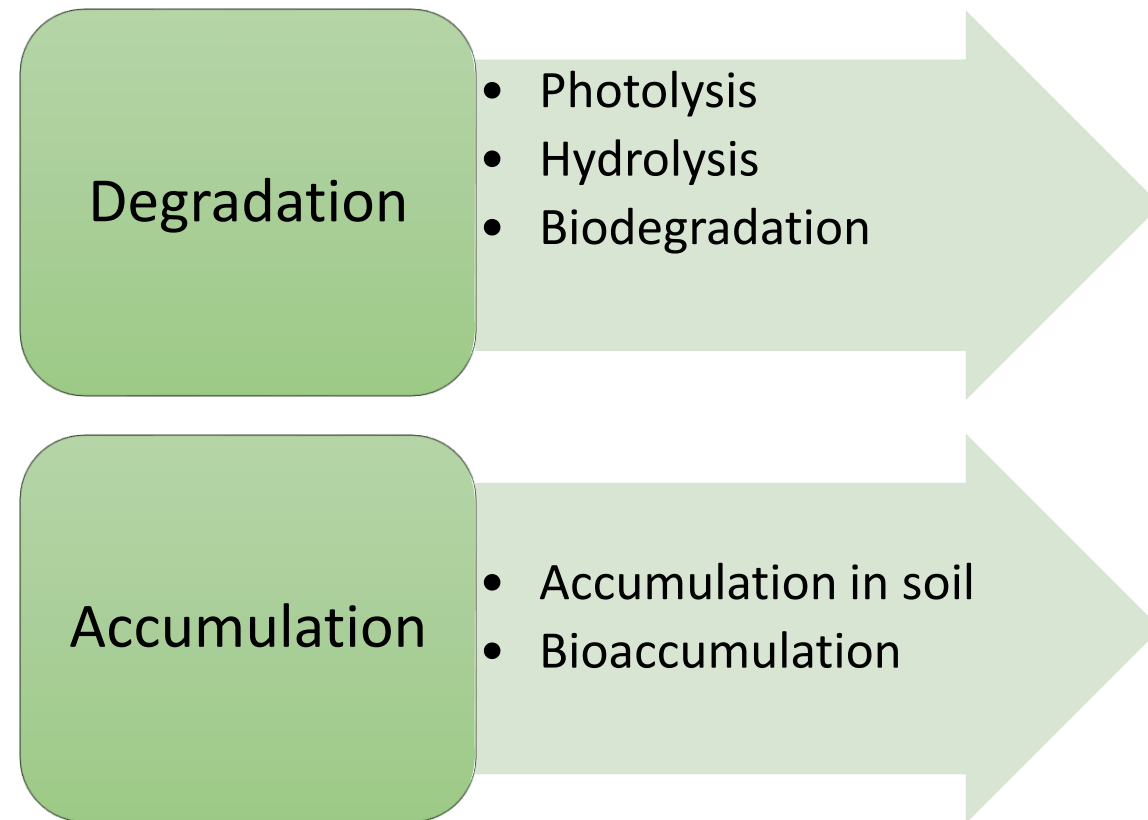


<https://www.nps.gov/subjects/air/sources.htm>



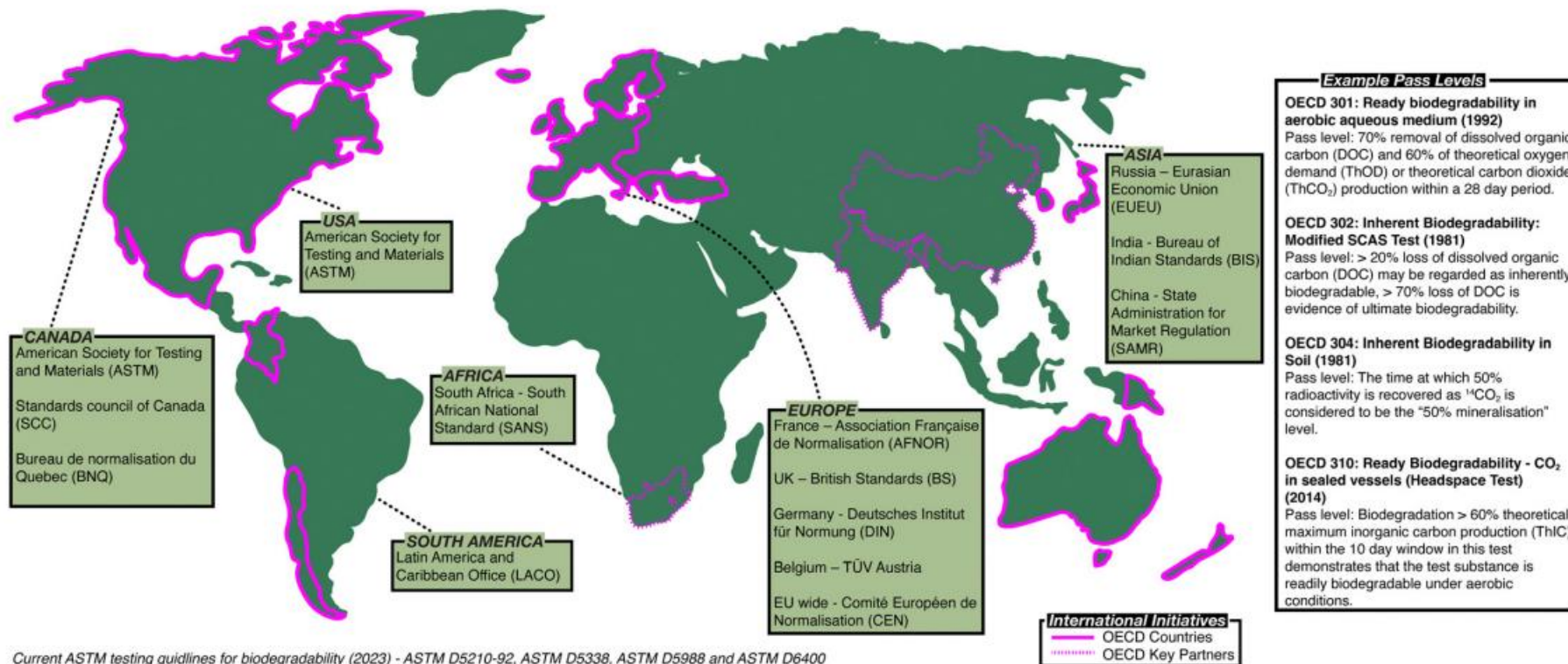
Biodegradation/(Bio)-Accumulation Score

Biodegradation/(Bio)-Accumulation Score



Biodegradation/(Bio)-Accumulation Score

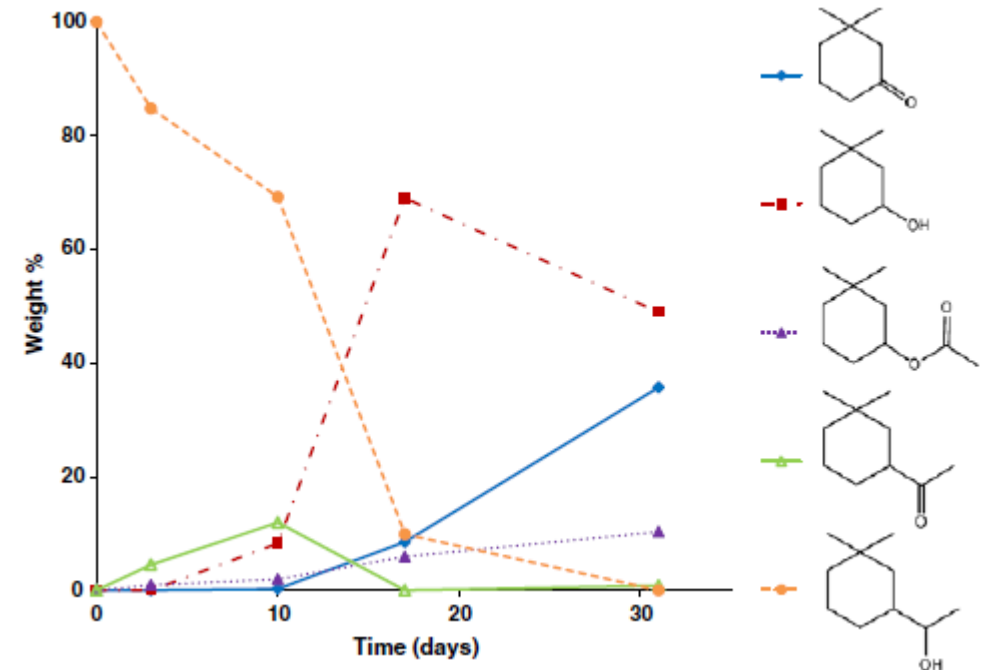
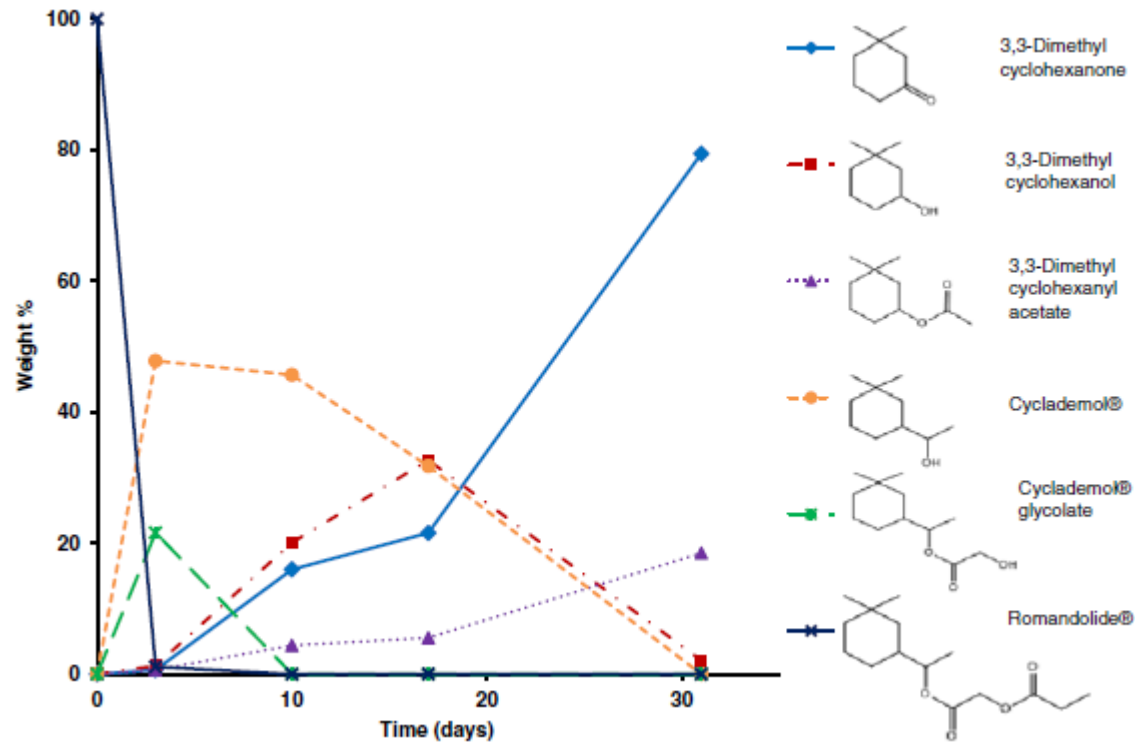
The global regulatory landscape for assessment of biodegradation



Biodegradation/Bioaccumulation Score

Example from Perfumery Industry:

Acyclic musk Romandolide in activated sludge; OECD Screening tests



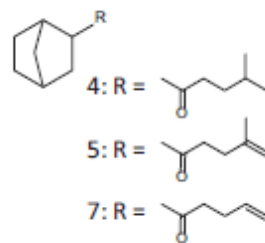
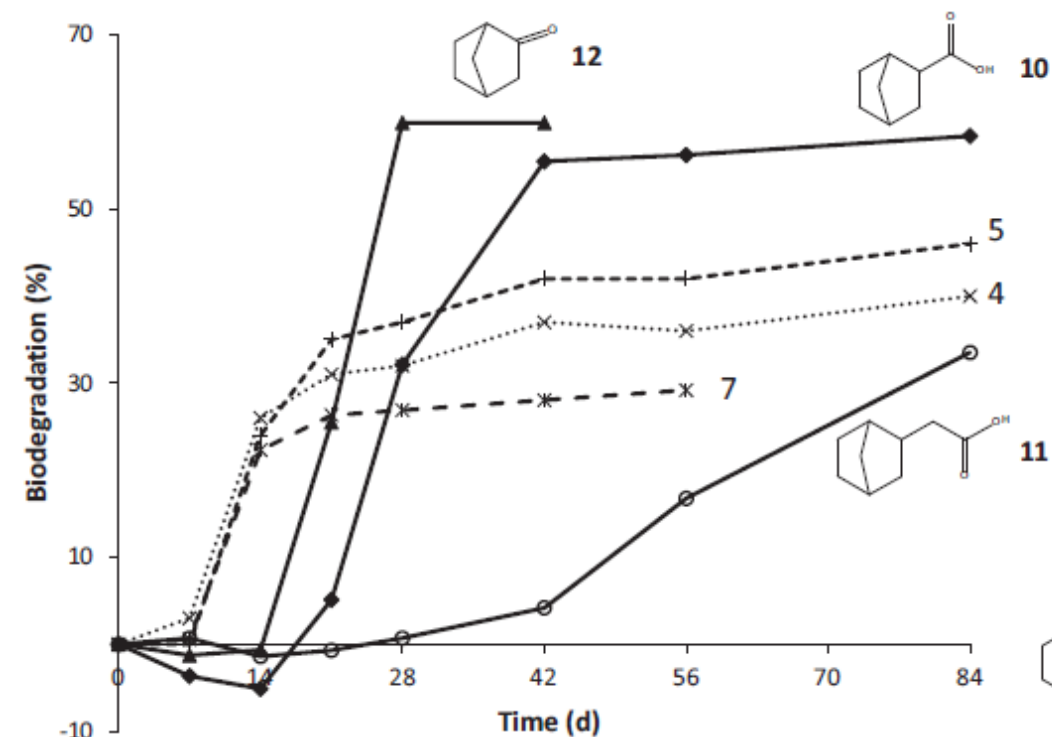
Persistence assessment of cyclohexyl- and norbornyl-derived ketones; OECD Screening tests



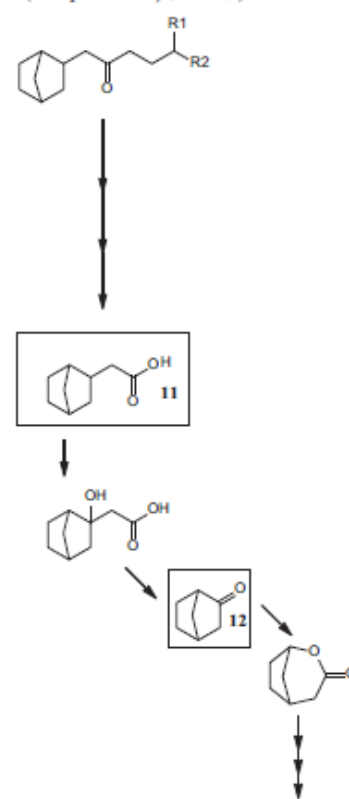
Biodegradation/Bioaccumulation Score

Example from Perfumery Industry:

Persistence assessment of cyclohexyl- and norbornyl-derived ketones; OECD Screening tests

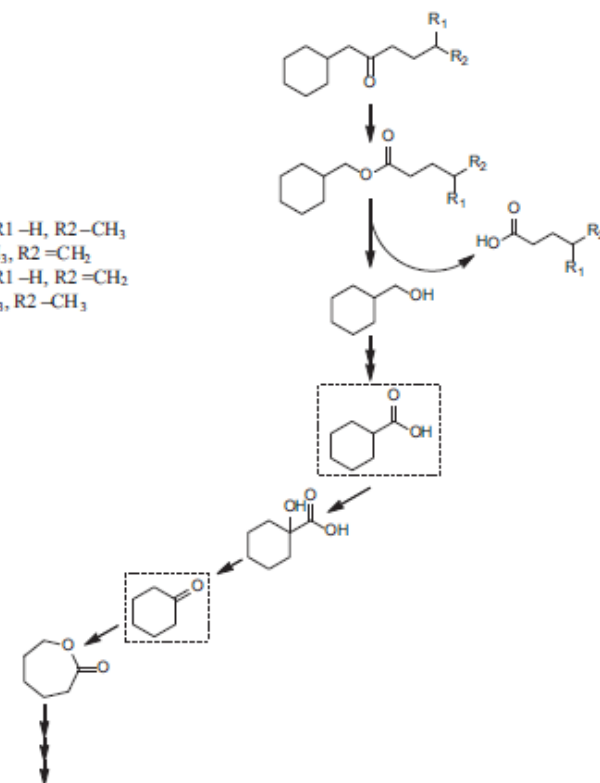


Norbornyl - derived ketones
(compounds 4, 6 and 7)



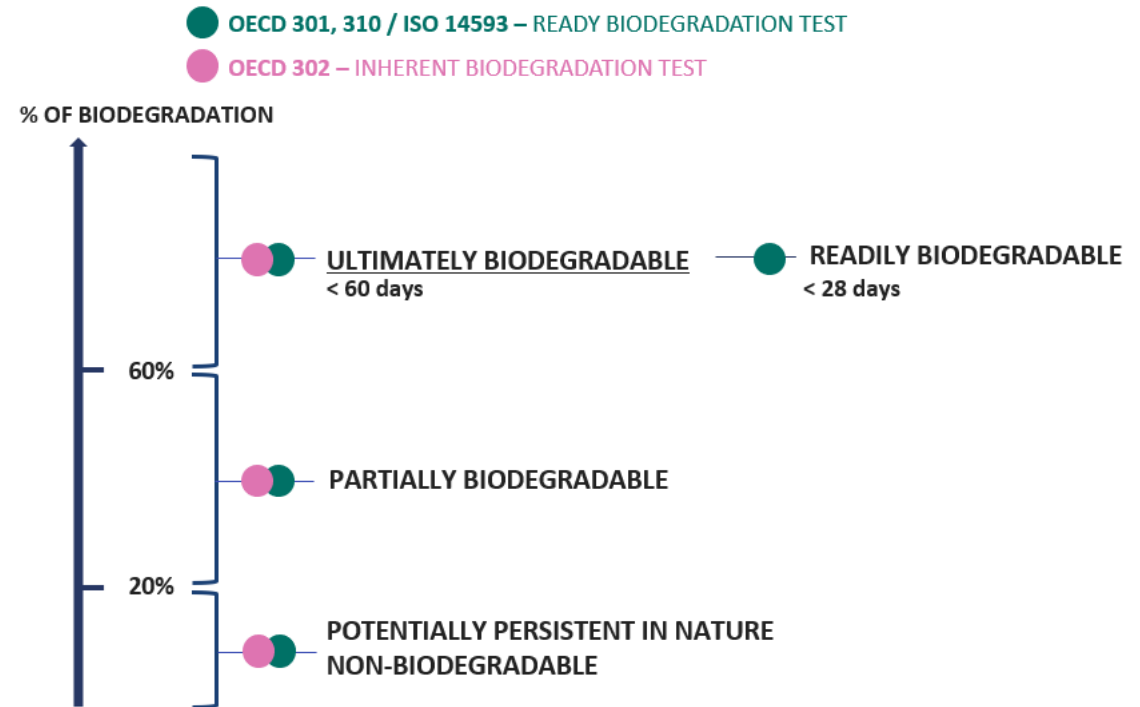
Cyclohexyl - derived ketones
(compounds 1, 2 and 3)

Compounds 1 and 6: R1 -H, R2 -CH₃
Compound 2: R1 -CH₃, R2 =CH₂
Compounds 3 and 7: R1 -H, R2 =CH₂
Compound 4: R1 -CH₃, R2 -CH₃



Biodegradation/Bioaccumulation Score

Example from Perfumery Industry: Biodegradation



Energy Metrics

Energy

2 major cases:

- Commodity chemicals, in contrast, energy consumption plays a prominent rôle and could be perfectly calculated
- Multipurpose production facilities, energy usage is often not allocated to particular processes.

Energy Metrics

Energy

Energy Intensity = (Energy consumed in the production process + energy consumed in overhead)/kg of Material Produced

Energy

$$\frac{\text{Total process energy (MJ)}}{\text{Mass of product (kg)}} \quad \text{MJ/kg}$$

M. Bernstein, K. Fonkych, S. Loeb, D. Loughran, State-Level Changes in Energy Intensity and Their National Implications, RAND, Santa Monica, **2003**.

https://www.rand.org/pubs/monograph_reports/MR1616.html

Energy Metrics

Energy for solvent recycling

Energy

$$\frac{\text{Total solvent recovery energy (MJ)}}{\text{Mass of product (kg)}} \quad \text{MJ/kg}$$

Energy Metrics

Energy

Production of Energy produces CO₂....as a waste often neglected during the E Factor calculation

Not in E-factor: heating, cooling, stirring, pumping, etc.

$$E^+ = \frac{\sum m(\text{wastes})}{m(\text{products})} \frac{\text{kg}}{\text{kg}} + \frac{W \times CI}{m(\text{product})} \left[\frac{\text{kWh} \times \frac{\text{kg}(\text{CO}_2)}{\text{kWh}}}{\text{kg}} \right]$$

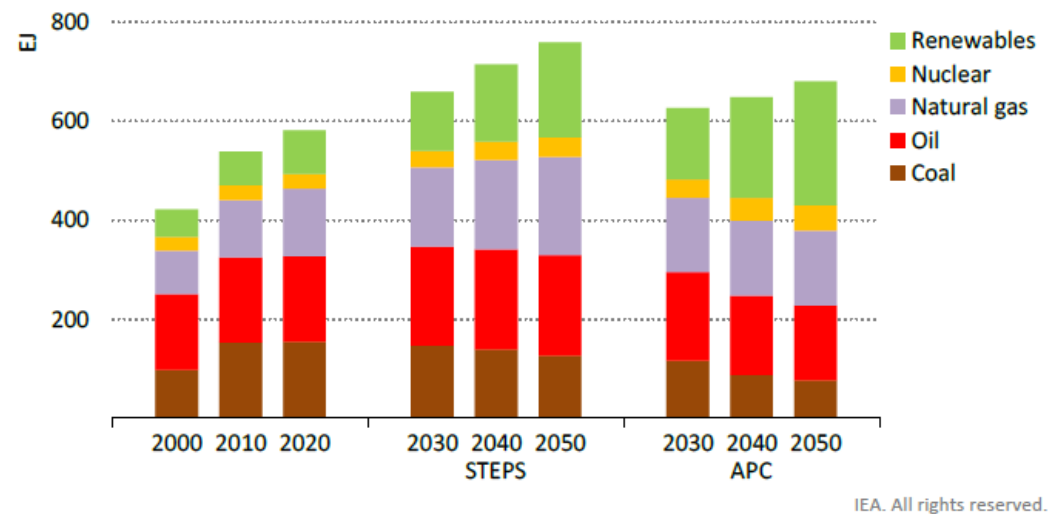
W = electrical power used

CI = carbon intensity, i.e. the local average CO₂ emissions caused for the generation of electricity.

But the world does not stand still

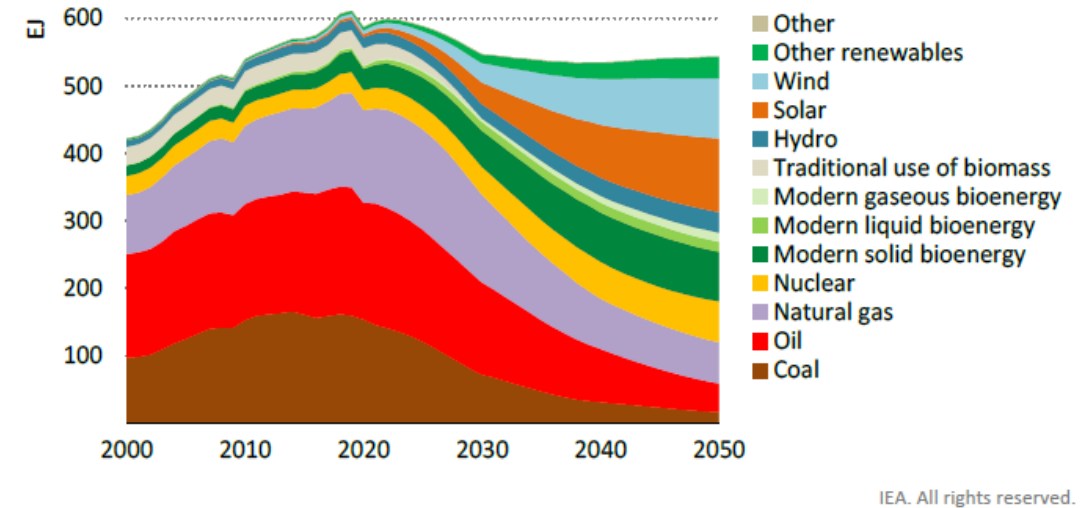
The energy transition will lead to shifts in energy sources ⇒ towards more renewable energy sources.

Figure 1.12 ▶ Total energy supply by source in STEPS and APC

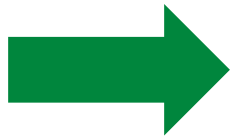


Announced net zero pledges lift renewables in the APC from 12% of total energy supply in 2020 to 35% in 2050, mainly at the expense of coal and oil

Figure 2.5 ▶ Total energy supply in the NZE



Renewables and nuclear power displace most fossil fuel use in the NZE, and the share of fossil fuels falls from 80% in 2020 to just over 20% in 2050



Will that make a difference to Carbon Footprints?
How to implement that transition into LCA-models?

Natural Extracts

Nagoya Protocole:

Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization
to the Convention on Biological Diversity

Adopted in 2010

Entered in force in 2014

In 2022, ratified by 137 states

Benefit-sharing obligations

Compliance obligations

<https://www.cbd.int/abs/doc/protocol/nagoya-protocol-fr.pdf>

Natural Extracts

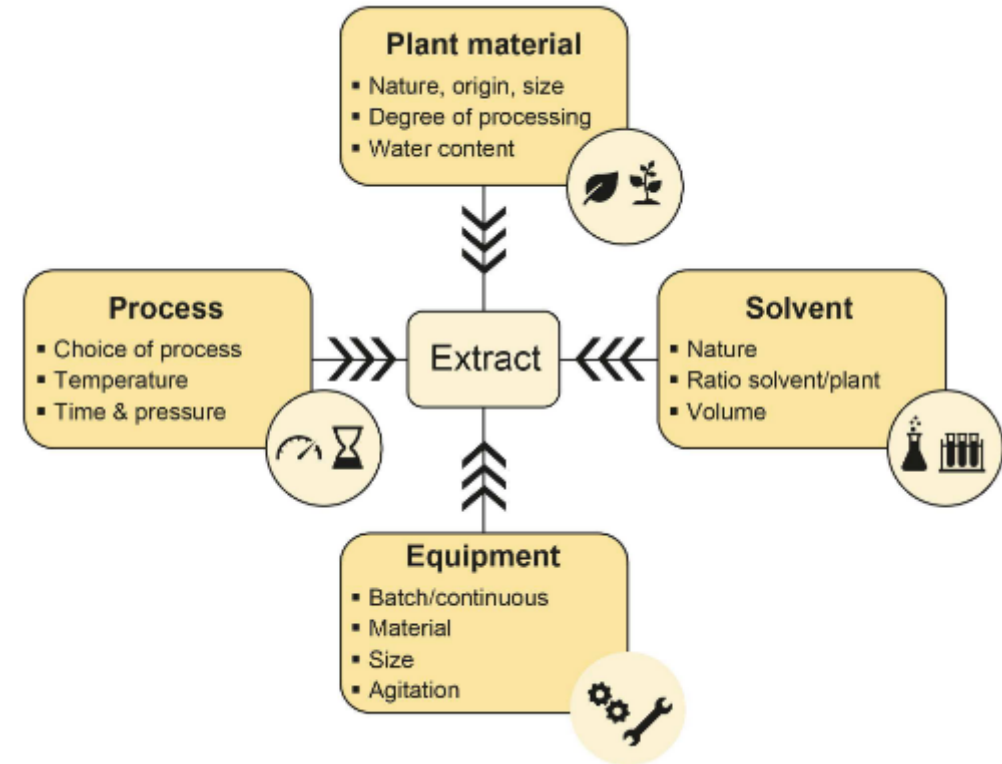
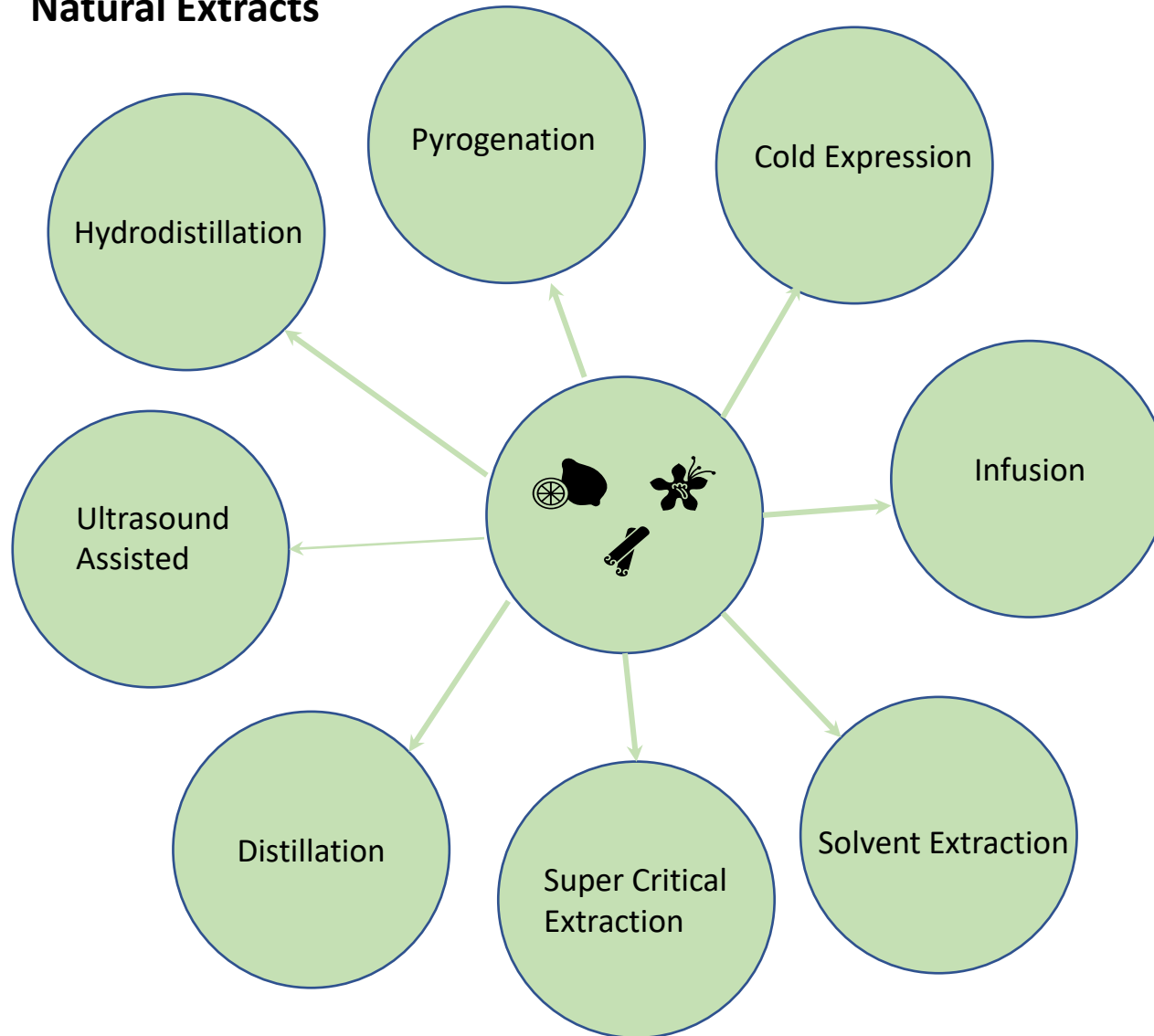
Natural Extracts

Category	Agrochemicals	Cosmetics	Aroma, Flavours and Nutrition	Pharma
Market volume	1 Billion USD	200 Billion USD	10 Billion USD	107 Billion USD (forecast 2017) [21]
Market growth	Double digit annual growth rate	Double digit annual growth rate	Double digit annual growth rate Market for nutrition additives decreases Market for aromas grows	Double digit annual growth rate Decline in prescription market Growth in over-the-counter market
Challenges	Market dominated by SMEs as well as global players Small volume/low cost products bulk High cost/low volume niche products	Significant amount of products with natural claims but up to 75% synthetic ingredients; No uniform and binding standards for natural, fair-trade, organic labels	Low cost products (in the order of 1–10 €/kg) Many products with small volumes (100–1000 kg/a)	Most products are OTC Only few blockbusters Restrictive regulatory hamstrung R&D
Medium-term research demands	Efficient total process design for SMEs; Integrate process intensification Methods for SMEs and scale-up of infrastructure to fully integrated manufacturers; Energy efficient and low waste processes for decentralised utilization of natural resources [21,22] *	Efficient ways of finding new natural ingredients [23,24]; * Ensuring sustainability of supply	Apply and adopt more often scCO ₂ , bio-based solvents *, PHWE Biomass valorization, e.g., carrot, broccoli, artichoke etc. do have 30–80% herbal raw material waste	Speed up of development of herbal raw cell fermentation by omics [25] * Process Analytical Technology for inline-analysis of extraction processes; Parametric defined release at manufacturing of herbal raw extracts; * Homogeneity at production of extracts in large-scale Lyophilisation instead of vacuum-belt drying; Fresh herbal raws instead of dried raw material; HGACP instead of GMP on field incl. extraction media and pomace to be deposited on field again
Long-term research demands	Development of new products	Shift from wild collection to greenhouse or field cultivation in Europe; Energy efficient and low waste processes for decentralised utilization of natural resources [21,22]	Energy efficient and low waste processes for decentralised utilization of natural resources [21,22]	Determination of distribution behaviour of herbal raw ingredients in “single pot model” with herbal raw cell membranes and a gastrointestinal membrane for fast prediction of bioavailable components; Efficacy studies for new herbal raws and products which enable IP protection to cover the costs via patents on the new processes

Uhlenbrock, L. *et al. Processes* **2018**, 6, 177.

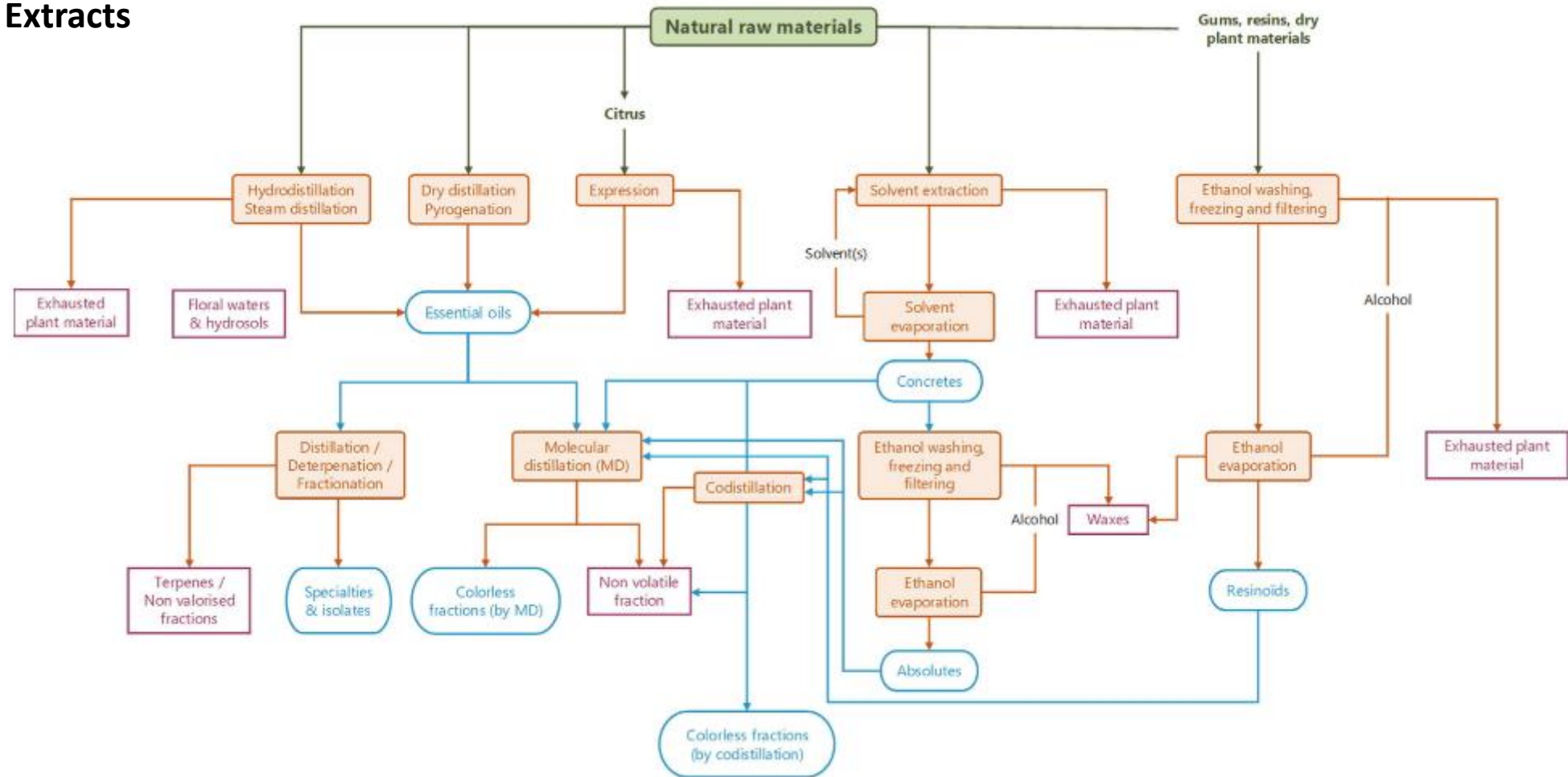
Natural Extracts

Natural Extracts



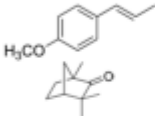
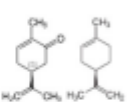
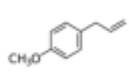
Natural Extracts

Natural Extracts



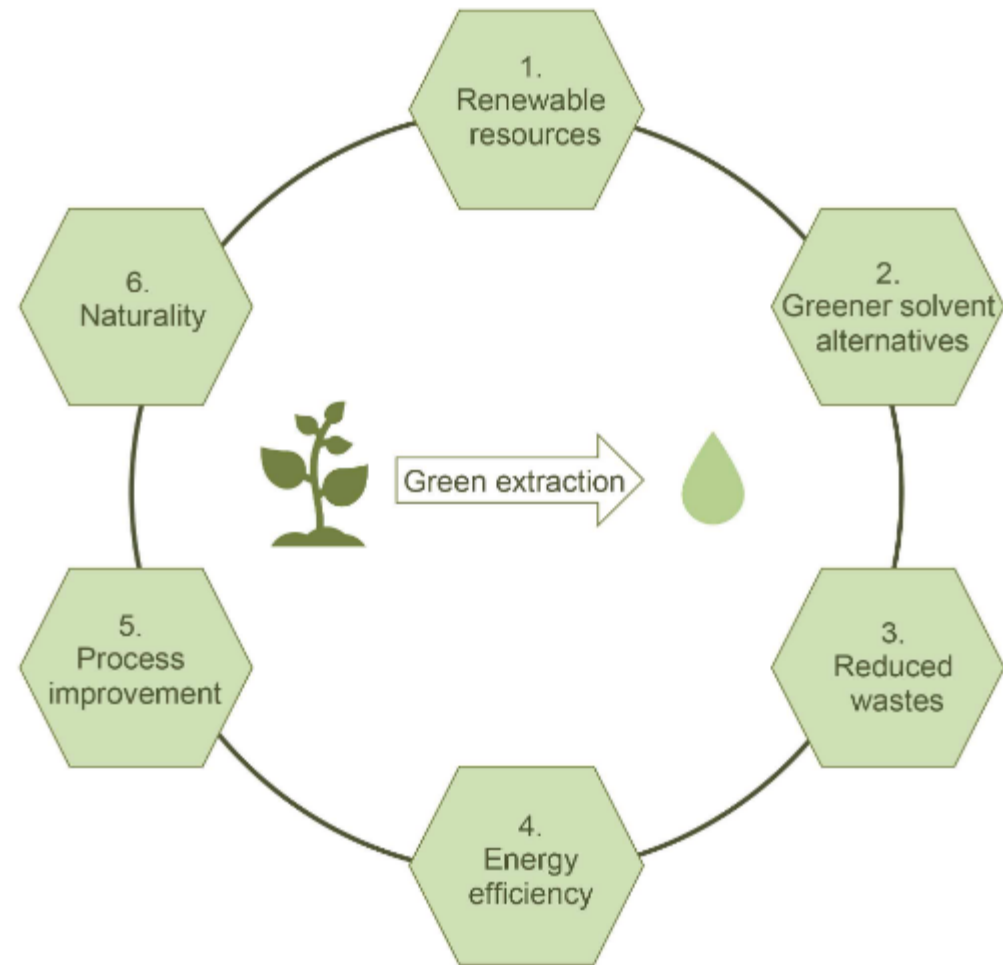
Natural Extracts

Natural Extracts

Category	<i>Foeniculum vulgare</i> L. Mill.	<i>Carum carvi</i> L.
Use	Aroma/fragrance	Aroma/fragrance
Target component	Anethole (5.3%), Fenchone (2.9%) essential oil (~8% w)	Carvone, Limonene essential oil (~2% w)
Molecular structure and weight	 148.2/152.23 Da	 150.22 Da
Side component	Estragole (0.2%)	
Molecular structure and weight	 148.2 Da	
Location	Fruit Oil channels	Fruit Oil channels
Solvent	Ethanol [60]	

Natural Extracts

Natural Extracts



Natural Extracts

Natural Extracts

Energy Intensity?

Land Impact & Societal Impact?

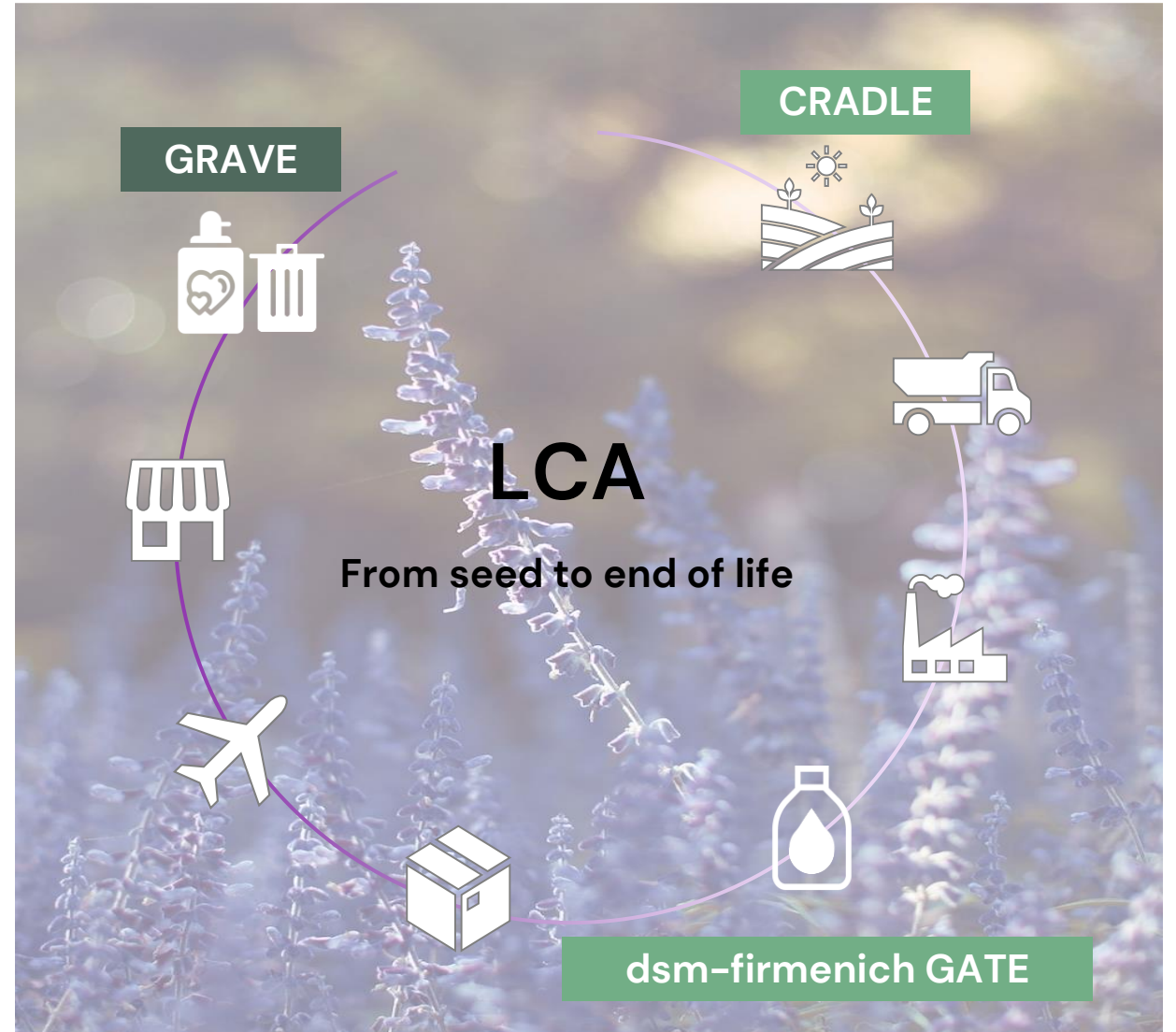
Extraction Yield? Recycling of Solvent or «Green» Solvent?

Ethical questions & Problems

Beyond Green Metrics & Sustainability Metrics

What's next?

Life cycle Analysis/Inventory
Carbon Footprint



Measure today To shape tomorrow

Precision through data



100% LCA Data on all ingredients in 2024

Global standards



Foster Carbon Emissions data access & exchange

Data-driven future



Track, inform & drive progress towards decarbonisation

LCA/LCI

Life cycle Analysis/Inventory Definition

LCA

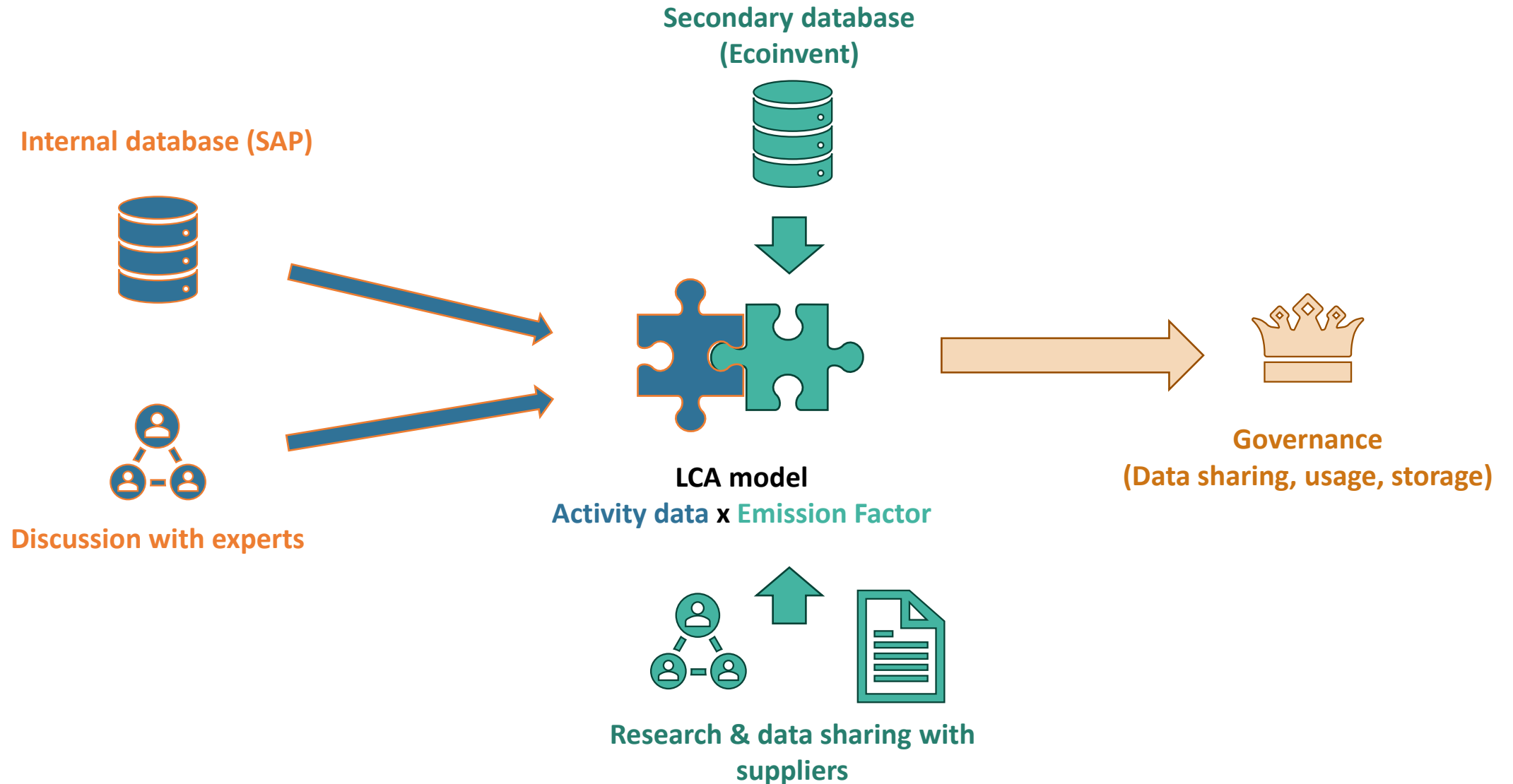
Life-cycle assessment (LCA) is a procedure for quantifying the total environmental impact of a product or service across its entire lifetime. This multi-step process includes goal and scope definition, inventory analysis, impact assessment, and interpretation. LCAs are iterative by nature as the plausibility, quality, and completeness of pertinent information changes over time.

LCI

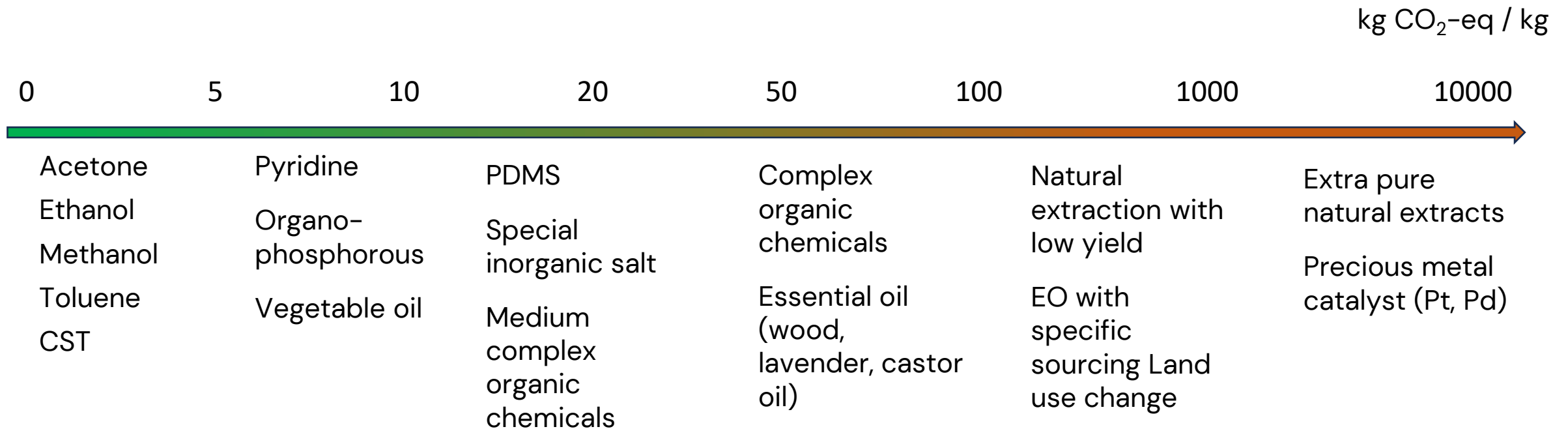
Life-cycle inventory (LCI) is the data-collection component of an LCA. Basically, an LCI endeavors to take an account of everything involved in the product or service. LCI considers the "system" at play by tracking all the inputs and outputs involved in making the product or service. The detailed accounting may include raw resources or materials, energy by type, water by source, and the various emissions to air, water, and/or land by substance. An LCI may be extremely complex, involving any number of individual unit processes contributing to relevant supply chains (e.g., the extraction of raw materials, various production processes, transportation, etc.) along with any/all constituent substances (for which there could be hundreds).

LCA is inherently uncertain, and communication of LCA results should therefore account for uncertainty.

LCA data management: Activity data – Emission factor – Governance



Carbon Footprint: Order of magnitude



1 kWh electricity
 0,5 kg CO₂-eq (EU mix)
 0,05 kg CO₂-eq (Solar PV)
 20 smartphone charge/discharge



1 day emission for an avg Swiss
 38 kg CO₂-eq / day

14t per year (scope 1/2/3)

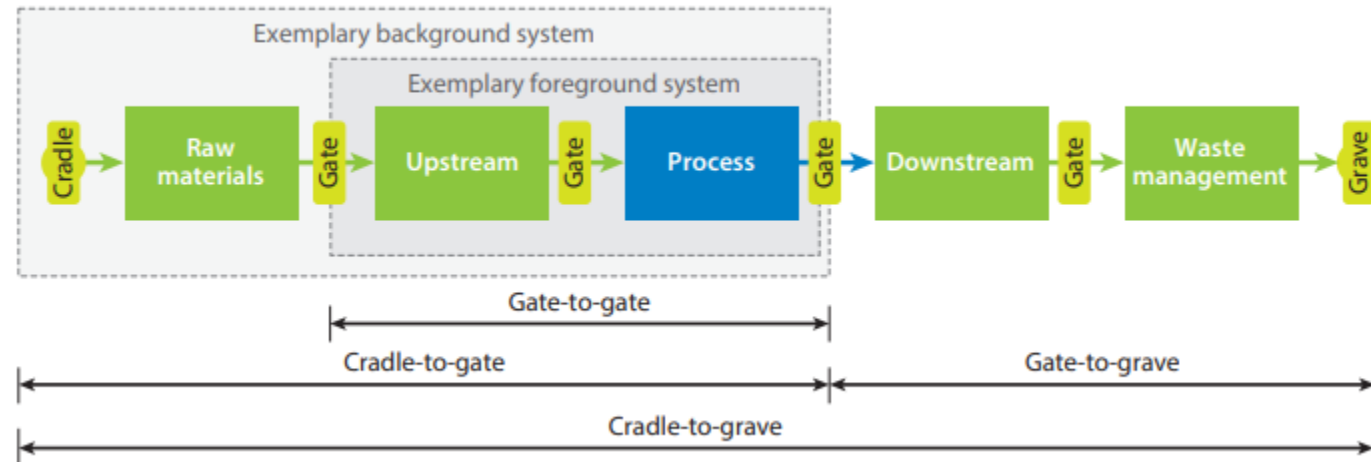


Zürich – Auckland in Economy
 3'700 kg CO₂-eq / travel

LCA/LCI

Boundary of the System:

Modular cradle-to-gate life cycle inventory/assessment methodologies enable one to see inputs and outputs each step of the journey from raw material extraction through each processing step



System boundaries in life cycle assessment. Ideally, all processes are included in a so-called cradle-to-grave boundary. The system boundary can further be divided into foreground and background systems. The foreground system is here defined as the part that is “under control,” i.e., within the design space.

LCA/LCI

An impact category makes it possible to come to a single metric for climate change

15 environmental impact categories:

Impact category / Indicator	Unit	Description
Climate change – total, fossil, biogenic and land use	kg CO ₂ -eq	Indicator of potential global warming due to emissions of greenhouse gases to the air. Divided into 3 subcategories based on the emission source: (1) fossil resources, (2) bio-based resources and (3) land use change.
Ozone depletion	kg CFC-11-eq	Indicator of emissions to air that causes the destruction of the stratospheric ozone layer
Acidification	kg mol H ⁺	Indicator of the potential acidification of soils and water due to the release of gases such as nitrogen oxides and sulphur oxides

LCA/LCI

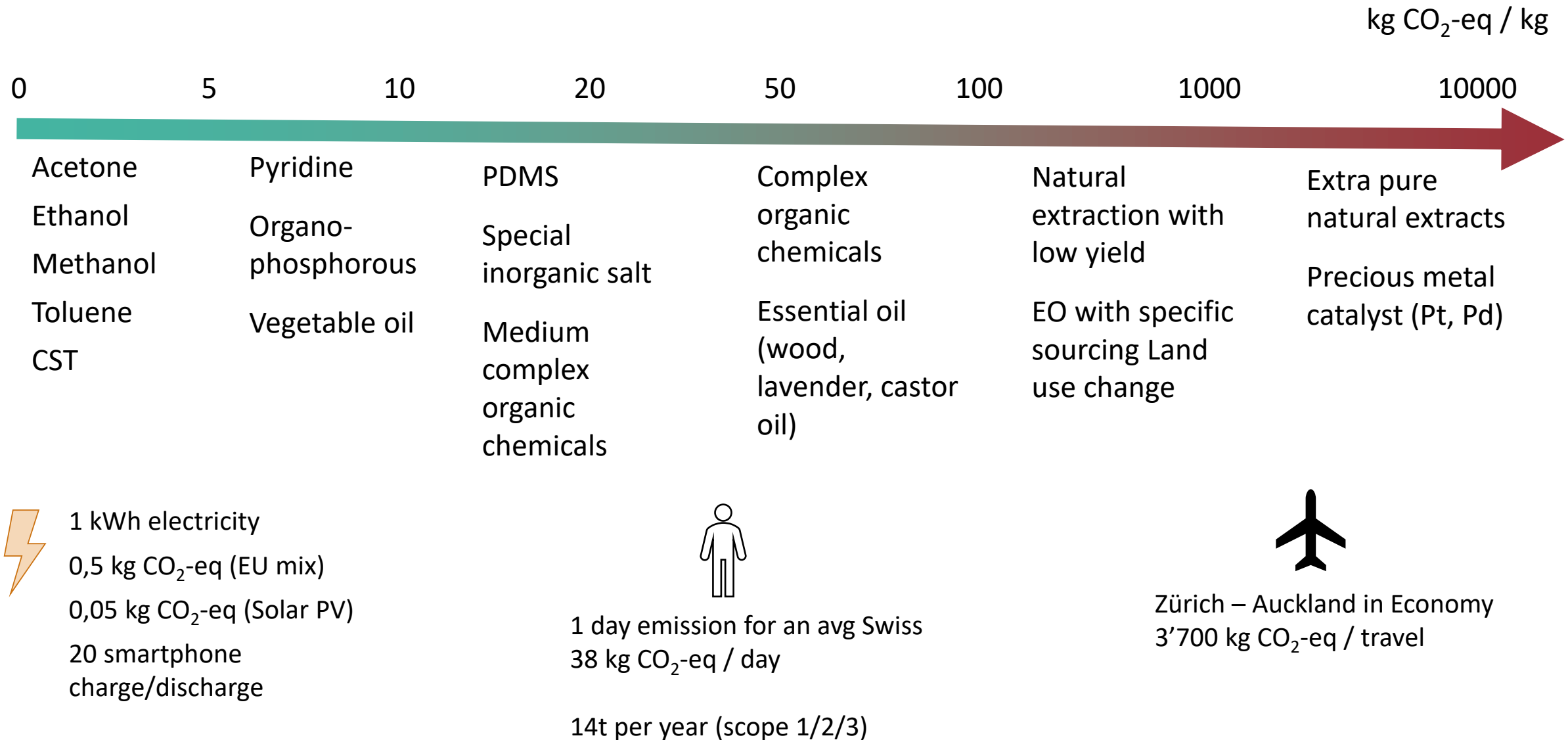
15 environmental impact categories:

Different emissions that cause the same impact are converted into one unit that translates into one impact category.
For example: CO₂, CH₄, N₂O, HFC, PCF, etc.

An impact category makes it possible to come to a single metric for climate change

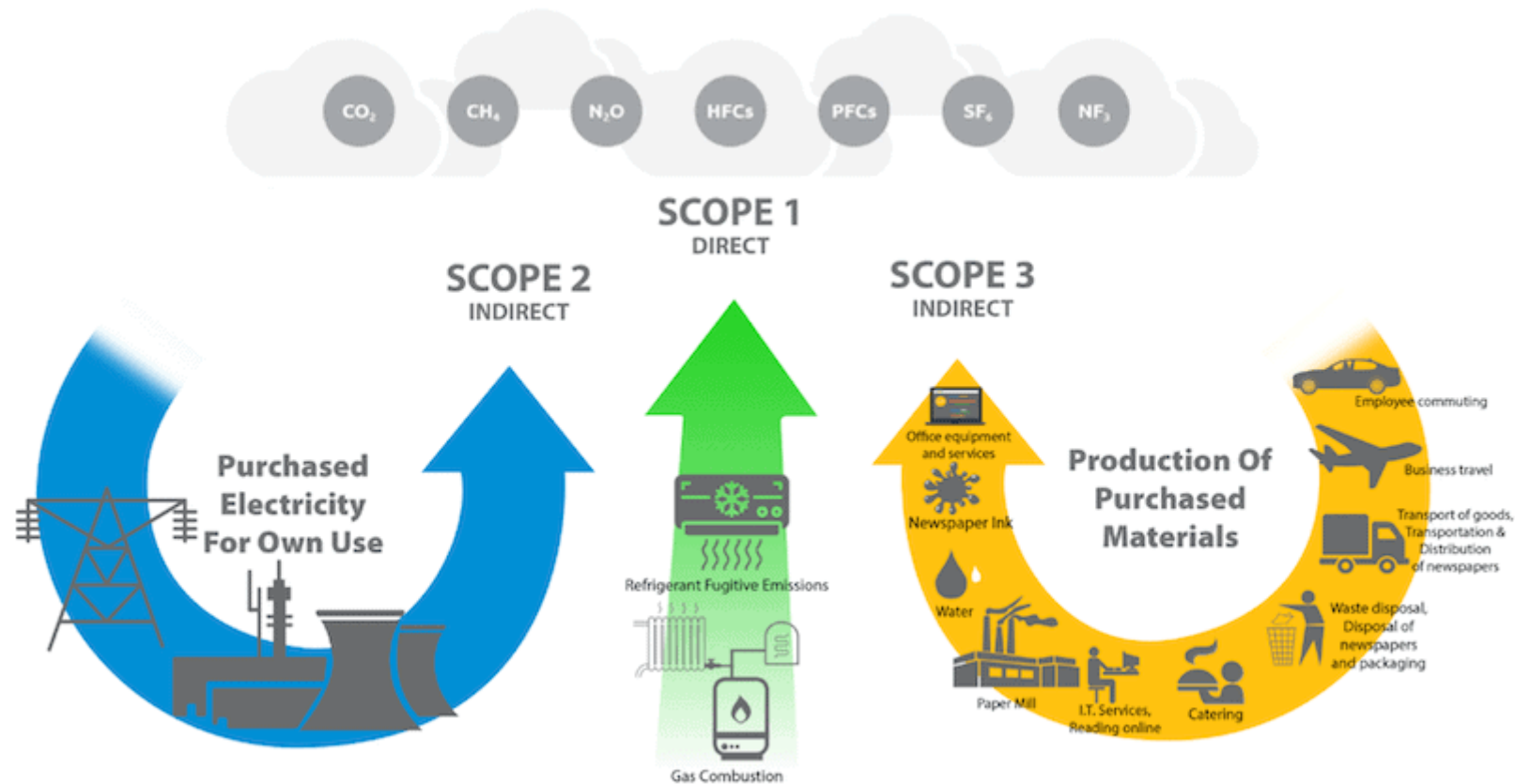
Greenhouse gas (GHG)	Equivalent in kg CO ₂ -eq of the release of 1 kg of the GHG
CO ₂ from fossil source	1
CO ₂ from renewable carbon	0
CH ₄	28
N ₂ O	273
PF ₆	25'200
HFC-23	14'600

Carbon Footprint: Order of magnitude



LCA Analysis

Carbon emission Impact



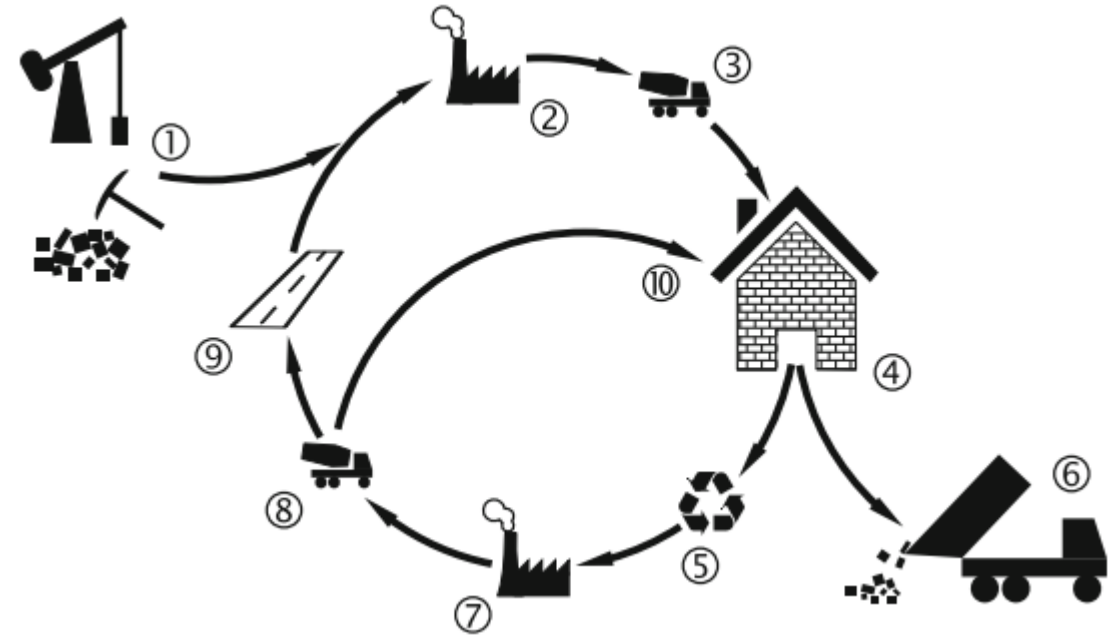
Green Metrics: Real-Life Tools

Sustainable Chemistry

LCA: Life Cycle Assessment.

Life cycle of non-renewable materials:

1. Extraction of raw material
2. Manufacturing
3. Processing
4. Use phase
5. Recycling
6. Landfilling/waste production
7. Secondary manufacturing
8. Secondary processing for reuse
9. Second use phase
10. Second reuse phase



[Open Access: Biomaterials for Building Skins | SpringerLink](#)

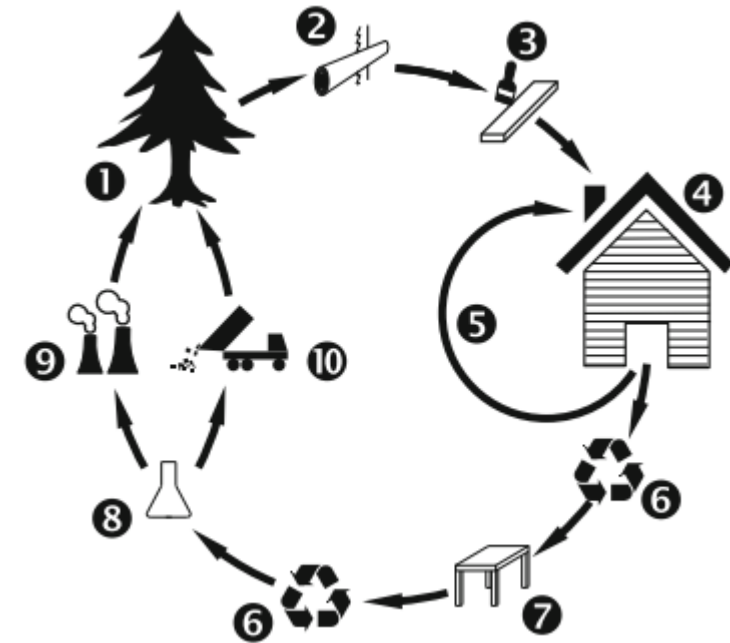
Green Metrics: Real-Life Tools

Sustainable Chemistry

LCA: Life Cycle Assessment.

Life cycle of renewable materials:

1. Harvesting
2. Primary processing
3. Secondary processing
4. Use phase
5. Reuse
6. Recycling
7. Second use phase
8. Cascading to tertiary use
9. Energy generation
10. Landfilling, closing the biological and technical metabolism

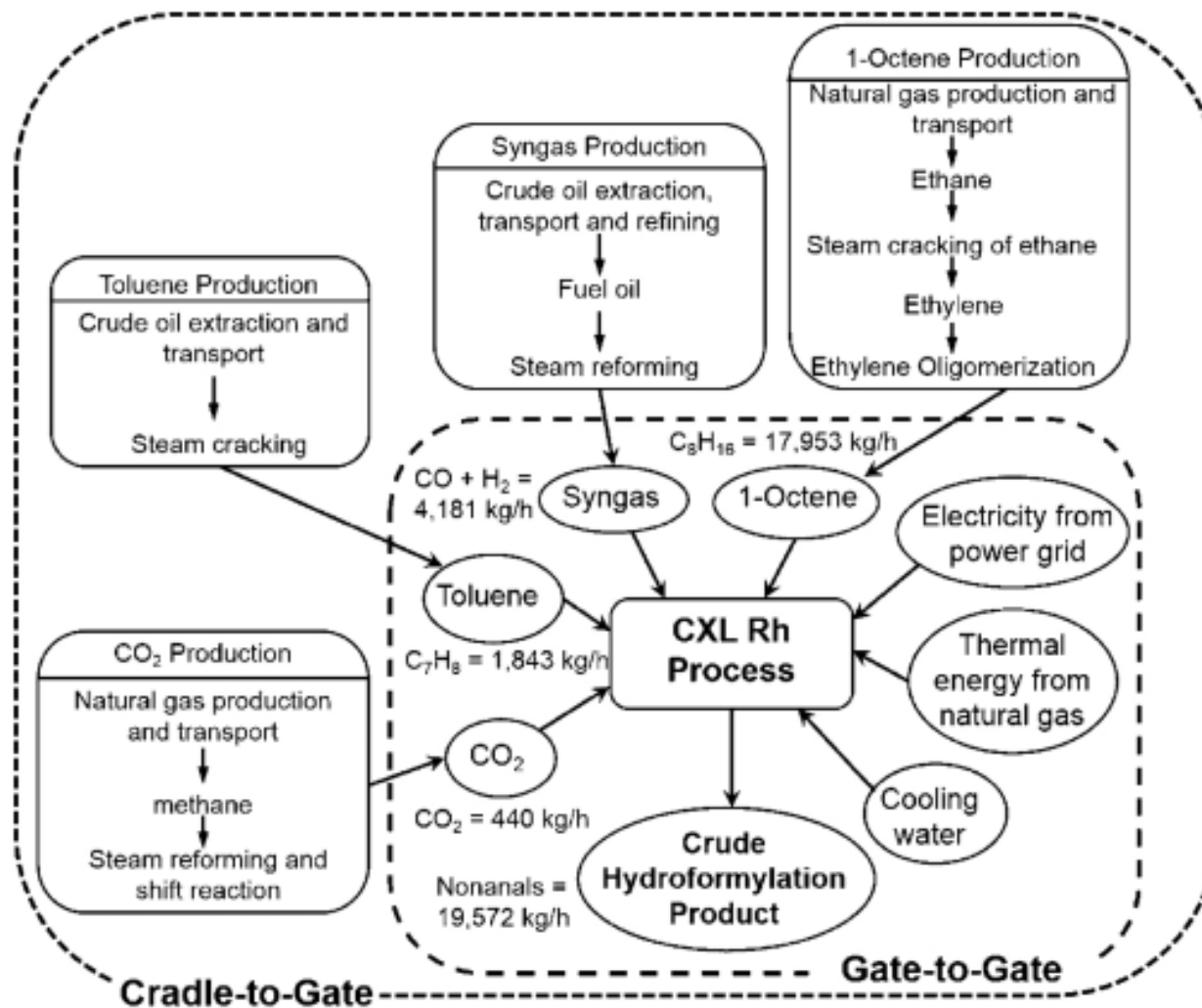


[Open Access: Biomaterials for Building Skins | SpringerLink](#)

LCA Analysis

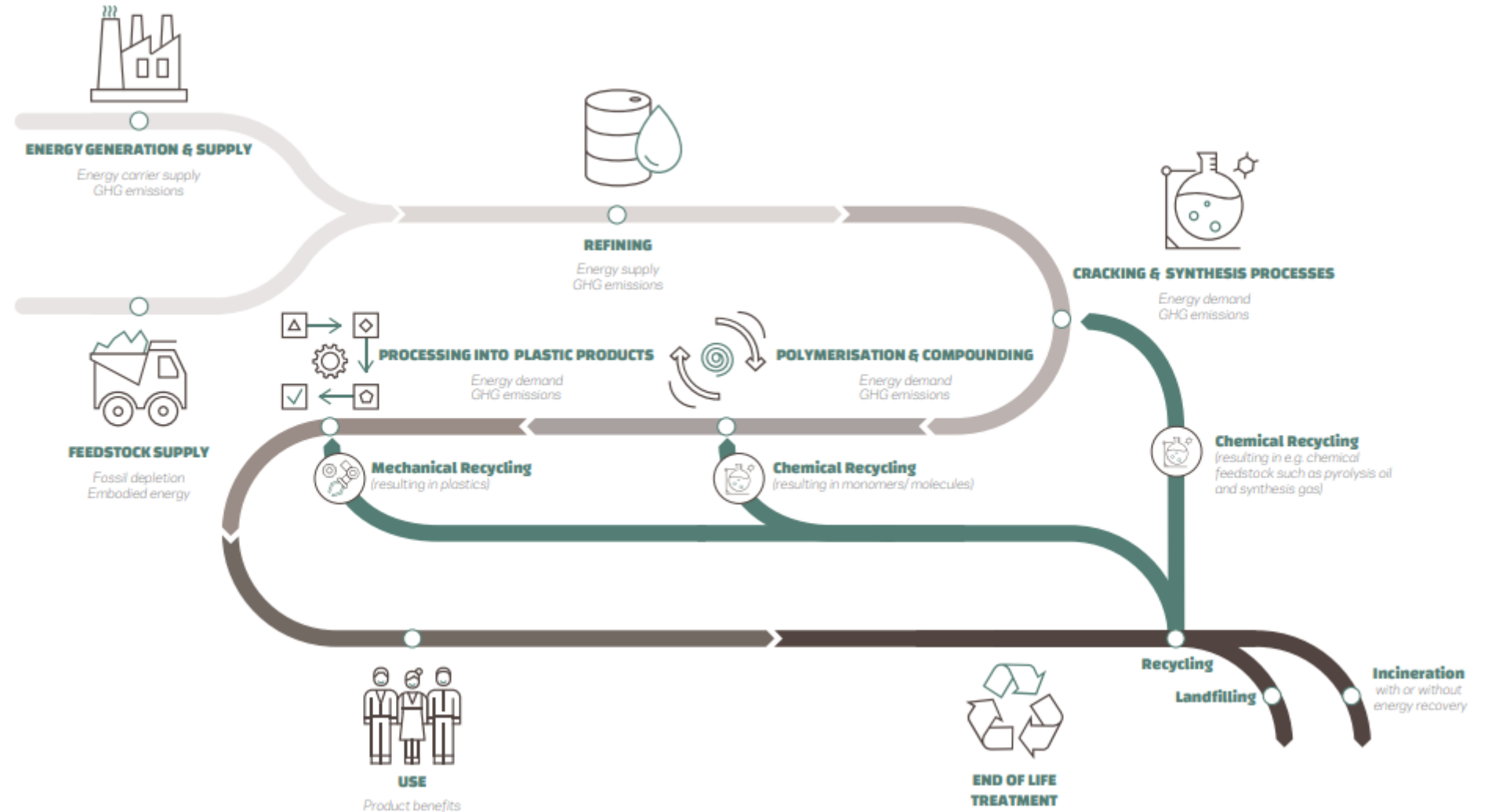
Analysis

Hydroformylation of Olefin



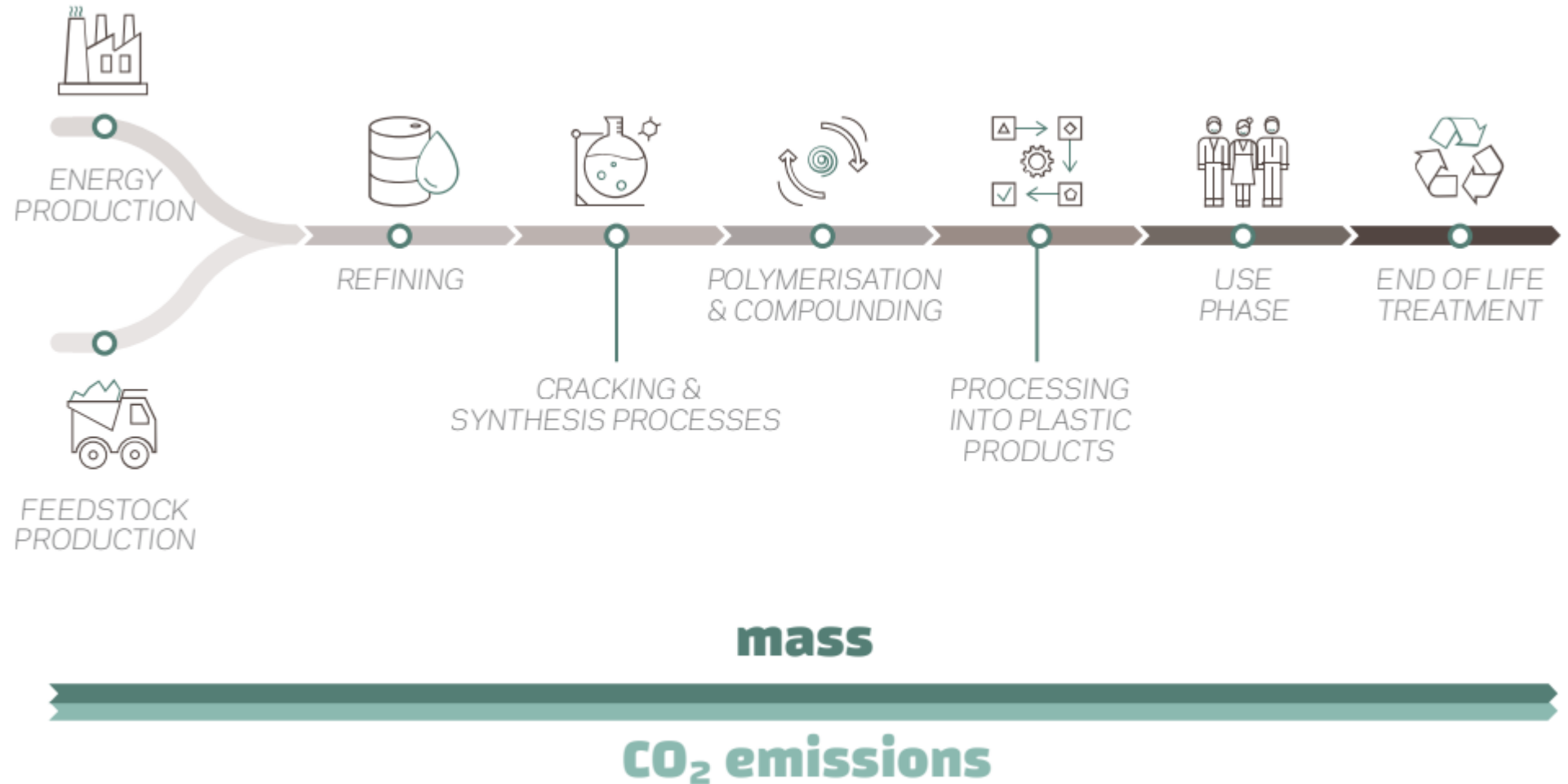
Circular Economy-Recycling

Value chain in polymers: Mechanical & Chemical recycling

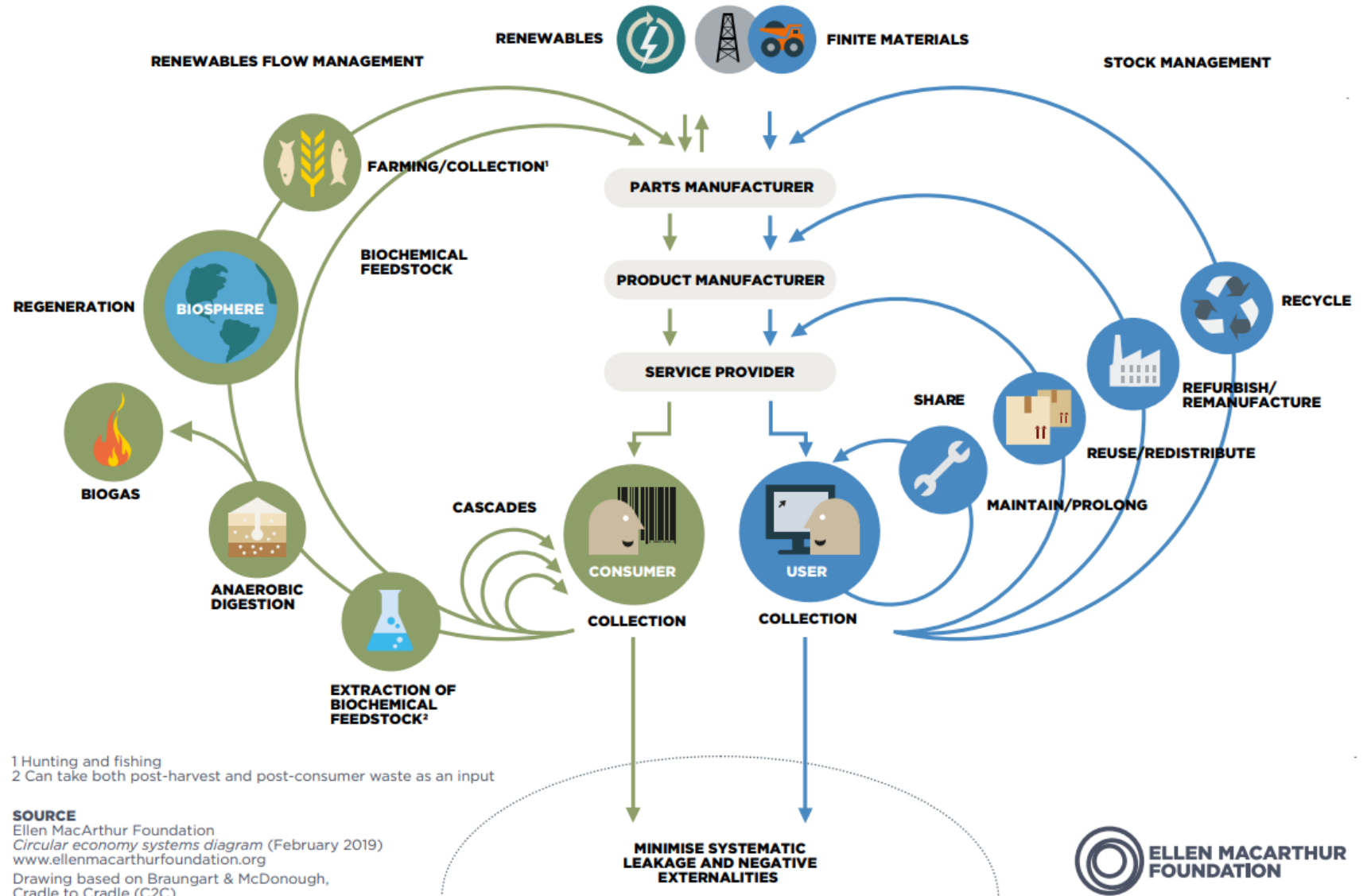


Circular Economy-Recycling

Material Flow Analysis



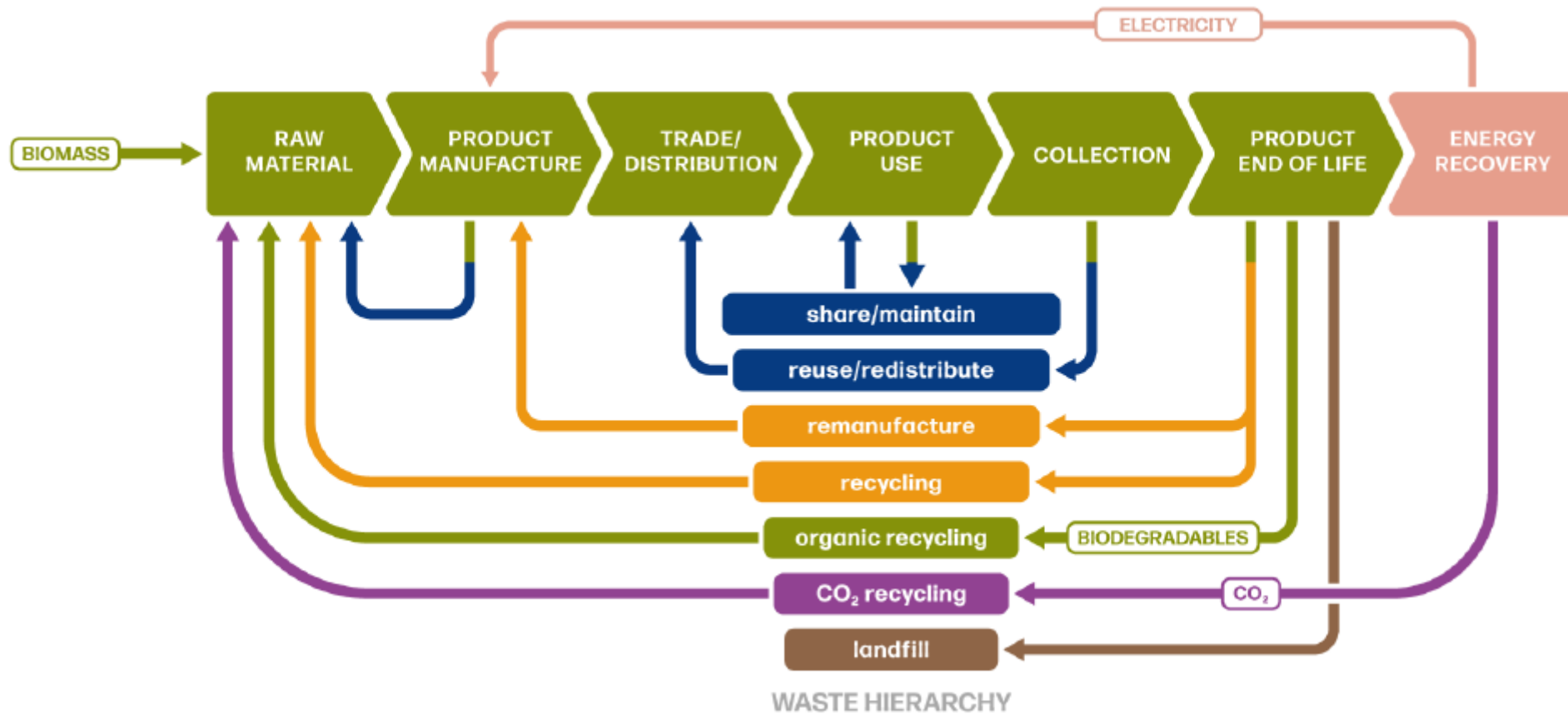
Circular Bioeconomy



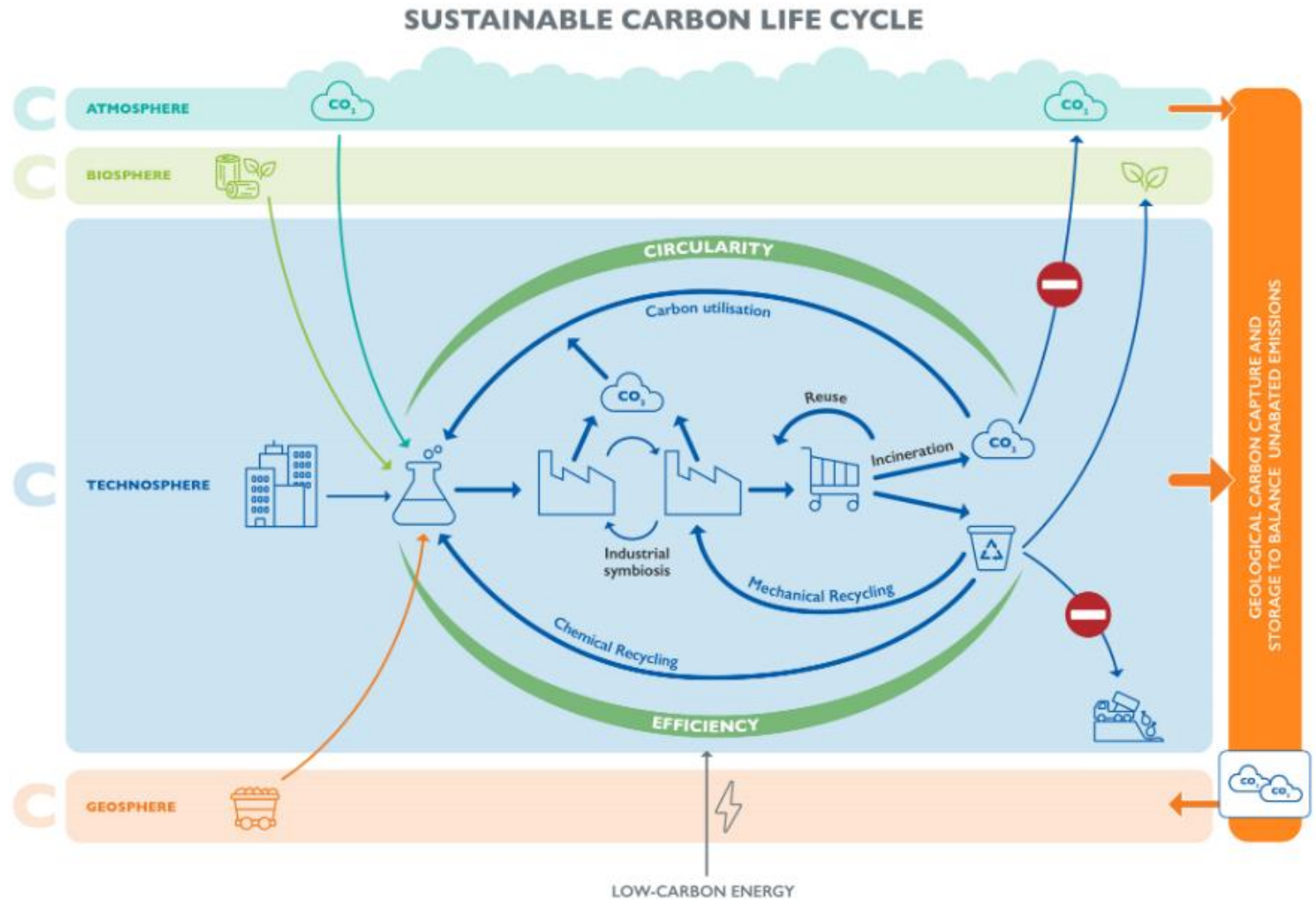
[The Butterfly Diagram: Visualising the Circular Economy \(ellenmacarthurfoundation.org\)](http://ellenmacarthurfoundation.org)
<https://renewable-carbon.eu/graphics>

Circular Bioeconomy

Value chain in polymers: Mechanical & Chemical recycling



Sustainable Carbon Cycles



Critical Review:
Dees, J. P. et al. *Green Chem.*, **2023**, 25, 2930.

<https://cefic.org/>

Green Metrics & Sustainability

Global overview:

Green metrics:

Tools to compare different processes but no absolute values

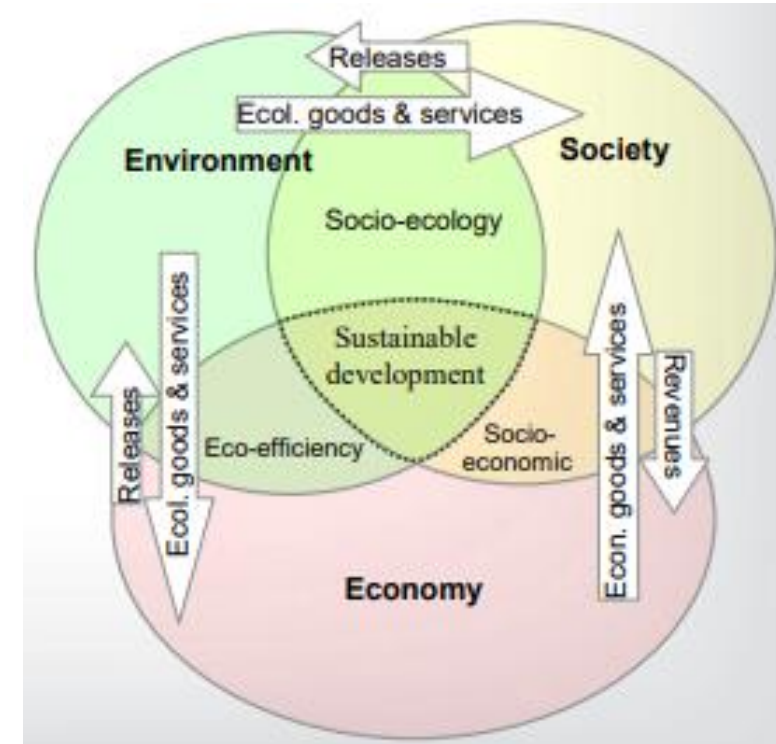
Not possible to conclude that a process is green !

Still a lot of work to be done: harmonize all the metrics, rules to use them

What about Societal Impact, Justice, Intergenerational Justice, Boundaries, etc

What are the values to prioritize to include/exclude?

After CO₂: Water,...



https://cfpub.epa.gov/si/si_public_file_download.cfm?p_download_id=542328&Lab=CESER

(accessed August 23, 2023).

Sheldon, R. A. *ACS Sustainable Chem. Eng.* **2018**, 6, 32–48.

Diverse values of nature for sustainability, *Nature* **2023**, 620, 813.

Kunming-Montreal Global Diversity Network: <https://www.cbd.int/gbf/>

Green Metrics & Sustainability: Future ?

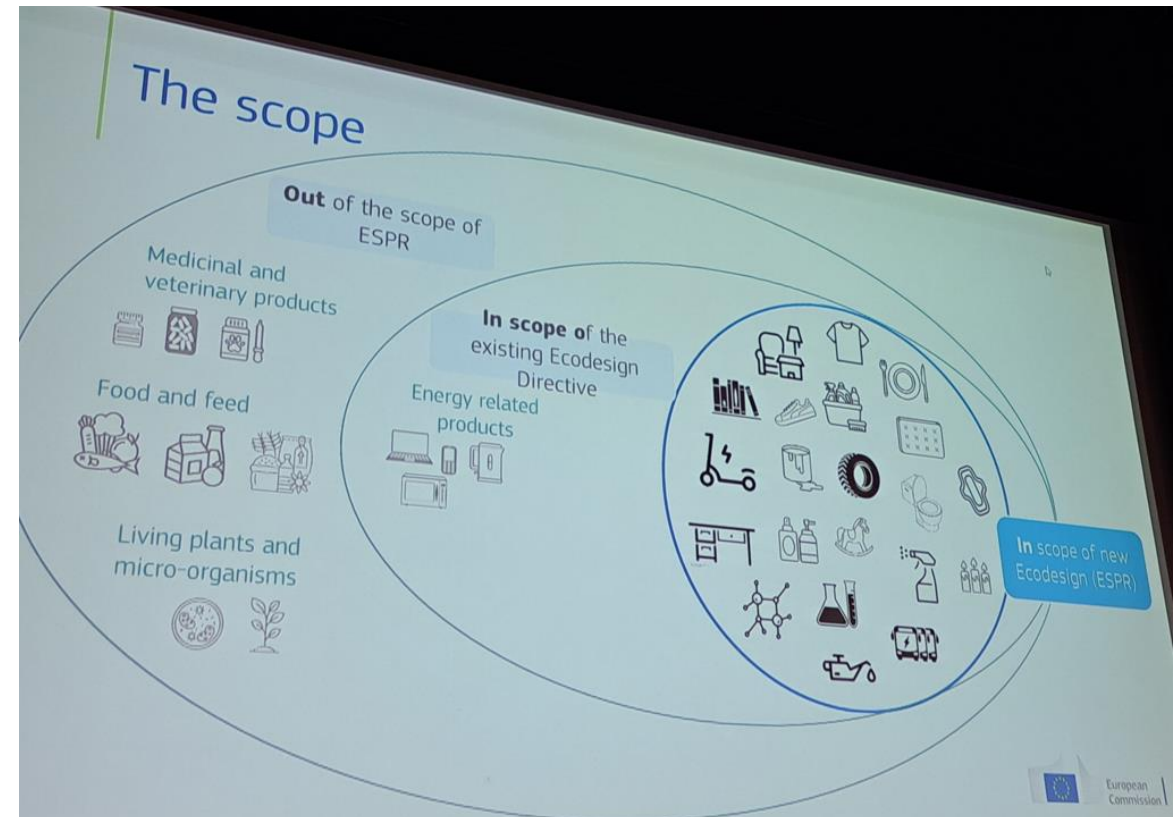
For example: Europe

NEW Ecodesign framework: ESPR (replace the Ecodesign) in force 2025 based on 2024 numbers.

And **CBAM:** **C**ross **B**order **A**adjustment **M**echanism cement, iron & steel, aluminum, fertilizers (ammonia, urea, nitric acid, ammonium nitrate) and electricity.

January 2030: Evaluation if chemicals and polymers.

https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/sustainable-products/ecodesign-sustainable-products-regulation_en
<https://www.reachlaw.fi/the-ecodesign-for-sustainable-products-regulation-espr/>



Green Metrics & Sustainability: Future ?

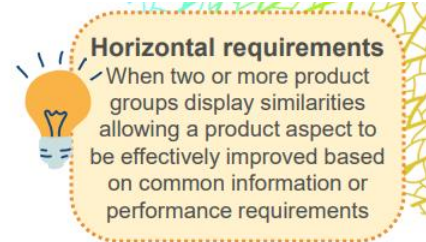
For example: Europe/NEW Ecodesign framework:

[Link to EU presentation-slides deck](#)

[Cosmetics - European Commission \(europa.eu\)](#)

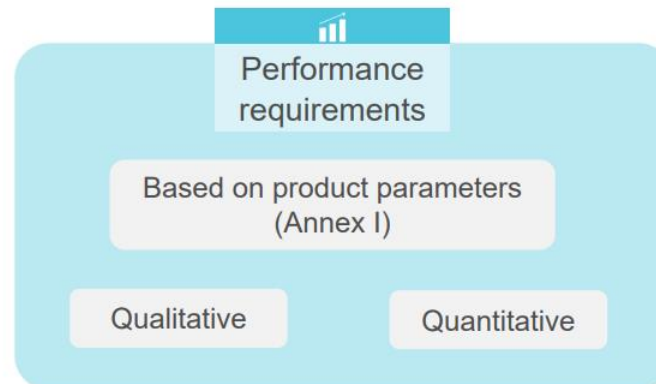
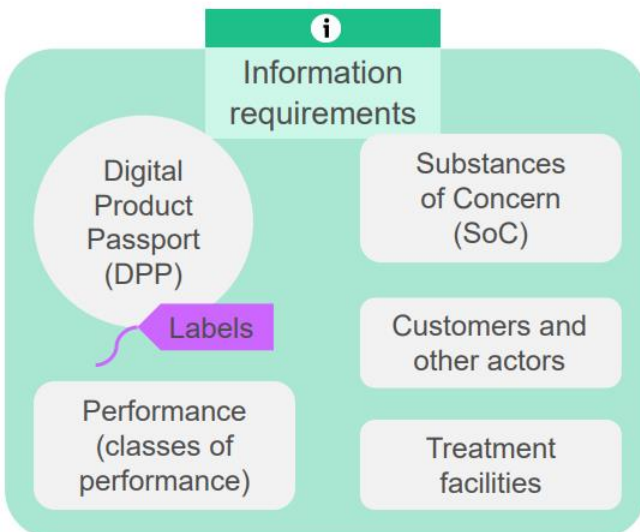
Key product aspects under ESPR

Article 5 – Ecodesign requirements



Ecodesign requirements

Product specific or horizontal



Green Metrics & Sustainability: Future ?

Using prospective LCA models: IAM-LCA coupling flow [Integrated **A**ssessment **M**odels]
Future scenarios such as the socioeconomic pathways are used as inputs together with e.g. ecoinvent

Step 1: Ecoinvent data are connected to Integrated Assessment models (IAMs) by creation of a superstructure database.

Step 2: connection between ecoinvent and additional inventories, that represent emerging and future technologies.

Step 3: Export of the database into a common LCA software (Simapro, Brightway2)

Step 4 and 5: Producing LCA resource and environmental indicators (and feeding back into IAM).

Green Metrics & Sustainability: Future ?

For example: Europe

Digital Product Passport (DPP):



https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/sustainable-products/ecodesign-sustainable-products-regulation_en

https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/sustainable-products/about-sustainable-products_en

Green Metrics & Sustainability: Future ?

For example: Europe

Digital Product Passport (DPP):



- The new “Digital Product Passport” will provide information about products’ environmental sustainability.
- This information will be easily accessible by scanning a data carrier.
- It will include attributes such as the durability and reparability,
the recycled content
the availability of spare parts of a product.
- It should help consumers and businesses make informed choices when purchasing products,
facilitate repairs and recycling and
improve transparency about products’ life cycle impacts on the environment.
- The product passport should also help public authorities to better perform checks and controls.