Overview of Product Safety Assessment of Consumer Products

Presentation to WA DoE

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Unilever Safety & Environmental Assurance Centre, UK

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People trust our Brands to use every day in their homes to safeguard their familyôs health

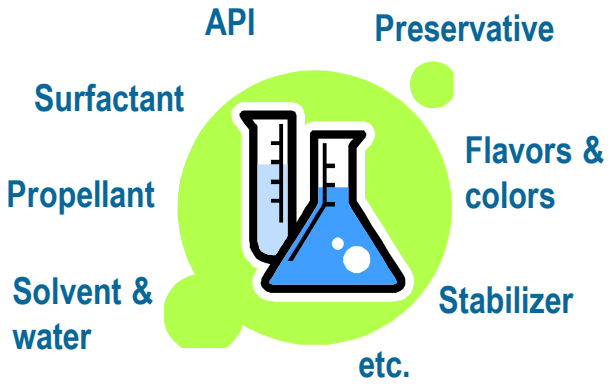
We take very seriously our responsibility
to meet their needs safely

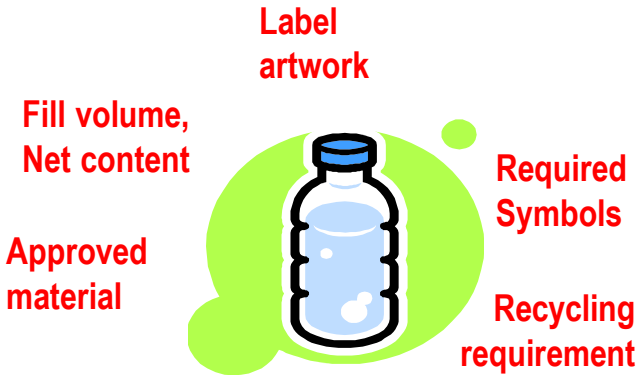
We follow rigorous safety & regulatory assessments to ensure that all products we place on the market are safe for use and compliant

Regulatory & Safety Assessment

Includes, but is not limited to, assessing:

- Ingredients
- Formulation
- Packaging
- Manufacturing
- Mandatory labelling requirements
- Product Classification
- Claims compliance with regulations
- Artwork approval
- Regulatory strategy to market
- Identification of Potential Issues to address, etc.





Social and Consumer Care

In a unique position to understand the relationships between nutrition, hygiene and personal care

Seek to understand and manage our social, environmental and economic impacts, working in partnership

Safety is our No. 1 priority –

Safety & Environmental Assurance Centre (SEAC), Colworth, UK

SEACôs Role in Unilever

Responsible for safety assessments of Ingredients and Products globally

Provide authoritative scientific evidence and guidance so that Unilever can identify and manage:

- Risks for consumers, workers and environment
- Environmental impacts

Safe, Sustainable Products & Processes by Design

SEACôs Wide-ranging Expertise

Deploying & developing capability in:

- **Hazard characterization**
- **Exposure assessment**
- **Risk & impact assessment**

for

<u>Consumer Safety</u>
- **Microbiology, Toxicology, Physical Hazards**

<u>Occupational Safety</u> (Safety at Work)
- **Process Safety, Occupation Hygiene**

<u>Environmental Safety</u>
- **Ecotoxicity**

<u>Sustainability</u>
- **Eco-design, Life Cycle Assessment, Environmental Sustainability**

SEAC has subject matter experts in these fields

A Risk-Based Approach Facilitates Safe Innovation

We use scientific evidence-based risk assessment methodologies to ensure that the risk of adverse health and/or environmental effects from exposure to chemicals used in our products is acceptably low

Hazard-based

- Check-list compliance
- Unnecessary testing
- Doesn't consider how product is used
- Yes / no decisions
- Overly conservative

Risk-based

- Expertise- & evidence-driven
- Essential testing only
- Product use / exposure determines outcome
- Options to manage risks
- Uncertainties explicit

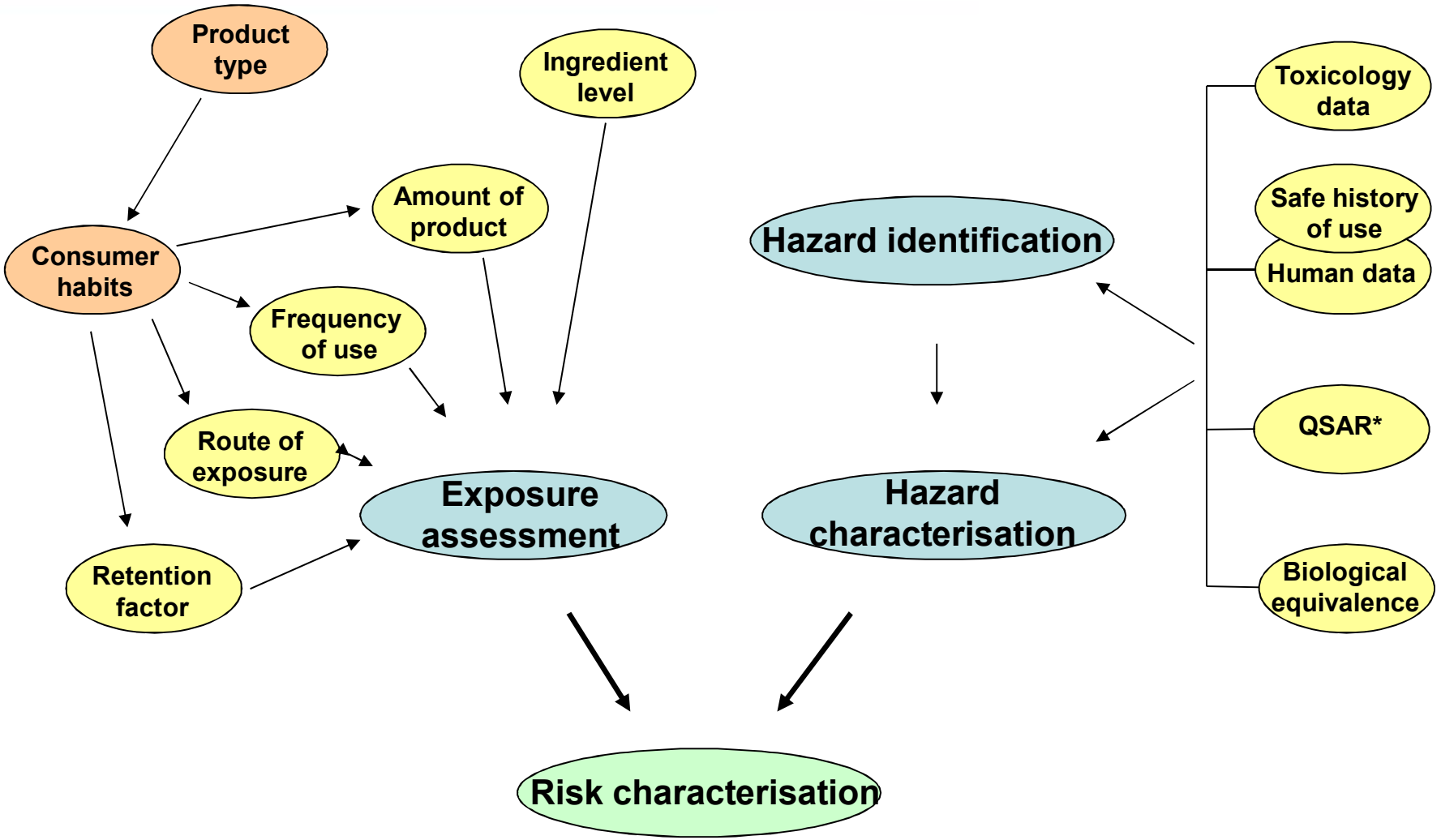
Outline

- Consumer Safety
  - Toxicology Risk Assessment
  - Microbiology Risk Assessment
- Environmental Safety
  - Environmental Risk Assessment
- Occupational Safety
- Sustainability
  - Environmental Impact Assessment

When does Unilever conduct safety assessments of products and ingredients

- Toxicological product safety assessments are conducted to support human consumer trials and marketing products where:
  - A novel ingredient is to be used in an existing product type
  - An existing ingredient is used in a new product type/format
  - Levels of ingredients are modified in an existing formulation
- Safety assessment may also be conducted in the case of product incidents (e.g. contamination, manufacturing error)

Risk based approach for evaluating consumer safety of ingredients and products



* Quantitative Structure-Activity Relationship

Safety Evaluations of Products

- Initial step is to evaluate ingredients in each specific product type
  - Relevant toxicological endpoints are considered
- In many cases consumer safety of the product is evaluated based on its similarity to other marketed products (Safe History of Use)
- In some cases evaluation of the irritation potential of the product will be benchmarked by conducting:
  - In vitro tests e.g. Rabbit enucleated eye, Episkin
  - Human studies e.g. covered patch test, arm immersion studies
- Individual ingredients are evaluated for relevant toxicological endpoints based on consumer exposure

Toxicological hazard endpoints considered

As with all toxicological safety assessments, relevant hazard endpoints are considered, dependent on the potential route of exposure:

- **Acute toxicity**
- **Irritation (skin and eye)**
- **Skin sensitization (type IV allergy)**
- **Allergy (type I)**
- **Phototoxicity**
- **Systemic toxicity**
- **Reproductive toxicology including teratogenicity**
- **Genotoxicity**
- **Carcinogenicity**
- **Inhalation toxicity**

Identifying and Characterising Toxicological Hazards

- For the majority of ingredients, toxicological data already exist
- For some ingredients toxicological evaluations will also have been conducted by external experts; e.g. EU SCCS, CIR, PCPC, RIFM, FEMA, GRAS, ECHA (REACH)
- Wherever possible, existing data are used in safety assessments for ingredients
- In all cases, published/manufacturer data, and published toxicological evaluations are scrutinised and their robustness established

Identifying and Characterising Toxicological Hazards

- QSAR evaluation, including read across to similar chemicals, may be used for an initial evaluation
- Other considerations such as safe history of use or human clinical data can be used in a weight of evidence approach
- Where data do not exist, or are not considered to be fit for purpose, toxicological testing may be conducted to identify and characterise the toxicological hazard
- Unilever does not test its products on animals for the purposes of assessing consumer safety, unless required by law
- Alternatives to animal testing are employed when possible

Risk Assessment Based on Understanding Consumer Exposure

- Establishing the extent to which consumers are exposed when using a product is fundamental to the risk assessment
- Risk to consumers is dependent on:
  - Route of exposure
  - Amount of exposure

- Mode of use has a big impact on how much product the consumer is exposed to. For example:
  - Use of most personal care products leads to direct exposure
  - Standard use of toilet cleaner leads to minimal exposure

Estimating Amount of Consumer Use of Products

- **Informed estimate of typical use (e.g., a consumer will use 10mL shampoo once a day)**
  - May be based on personal habits
  - May be based on pack instructions
  - Often worst case
- **Often obtained from marketing company**
  - Best estimate of how much product is used
  - Marketing data
  - Consumer trial data
  - Consumer habits surveys
- **Published surveys**
  - COLIPA Study (Europe)
  - PCPC Studies (US)
- **Internal databases**

Dermal Exposure

- Retention
  - Where a product is left on the skin (e.g. skin cream), potentially all is available to be absorbed to give a systemic exposure
  - It is assumed that in most rinse-off situations (e.g. shower gel) 1% of the product remains on the skin after rinsing → 0.01 retention factor in exposure assessment

- Skin penetration
  - For risk assessment of systemic toxicity endpoints an evaluation is required of the amount of ingredient penetrating the skin
  - In most cases 100% skin penetration is assumed in an initial risk assessment. If acceptable (i.e. sufficient safety margin) then further quantification of skin penetration may not be required
  - In some cases, experimental estimation of skin penetration of ingredient from the formulation is required this is generally conducted using an ex vivo skin model (pig or human skin)

Measuring Inhalation Exposure

- Where inhalation of a product may occur, studies can be conducted to measure this
- Usually concerned with aerosol or pump spray products. Other products can be tested under simulated use conditions
- Can measure inhalation of volatile and non-volatile components

- Can also measure secondary exposure

Respirable Dose (RDose) is an estimation of the weight of non-volatile respirable material (<7μm) that has the potential to be deposited in the bronchial, bronchiolar and alveolar regions of the human lung if inhaled under simulated use conditions.

Estimating Ingestion of Products

- Some products will potentially be ingested during normal use
- These include toothpaste, mouthwash and lipstick/lip balm
- Also includes dishwash products which may remain on crockery/pans after washing
- In these cases an estimation of the amount ingested in use is made; e.g. a child may ingest 0.5g toothpaste whilst brushing their teeth
- Amount swallowed is taken to represent systemic exposure in the risk assessment (i.e. gut penetration = 100%)

Other Exposure Considerations

- Aggregate exposure - to the same chemical from different sources
  - Some ingredients are used in many product types
  - Exposure assessment takes into account product type(s), application amount, and level of ingredient in the product(s) in order to account for multiple exposures
  - Conservative assumptions are used to ensure that even the highest applications are safe to the consumer
- Cumulative exposure – to the same chemical over time
  - Safety assessments take long-term exposure into account
  - The type of exposure – whether rinse-off or leave-on application, frequency and duration of exposure – are important parts of the assessment
- Combined exposure – to multiple chemicals
  - Is addressed where chemicals are known to act by the same mechanism of action
  - Not possible, or necessary where chemicals have independent mechanisms of action

Conclusion: Safety Assessments of Ingredients & Products

- The requirements of the risk assessment are driven by the amount and route of exposure, which in turn is driven by the product type
- For each ingredient/product, the critical endpoint needs to be determined that is relevant to both the exposure conditions and the relevant toxicology hazard data
- Where exposure is very low (e.g. little consumer contact with product, insignificant skin penetration) it may be possible to use exposure based waiving based on the concept of the threshold of toxicological concern, (TTC)
- Where standard toxicology data are available, a standard risk assessment approach is taken:
  - Margin of safety for systemic toxicity effects
  - Quantitative Risk Assessment for sensitisation
- In some cases the safety assessment will be based on a weight of evidence approach; e.g. using history of use, QSAR approaches

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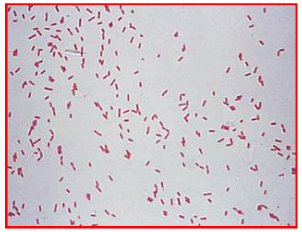
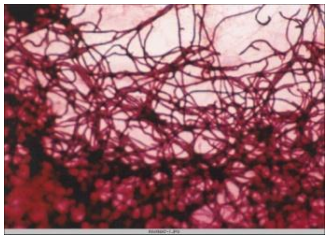
Microbiological Risk Assessment ï HPC products

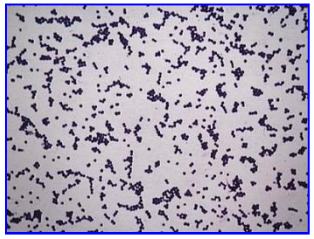
Å Microrganisms in HPC products can cause both spoilage and safety risks



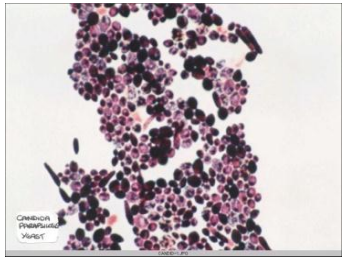
Gram negative bacteria e.g. Burkholderia, Pseudomonas, Klebsiella, Enterobacter



Moulds e.g. Aspergillus



Gram positive bacteria e.g. Staphylococcus, Bacillus



Yeasts e.g. Candida

Hygiene Risk Assessment

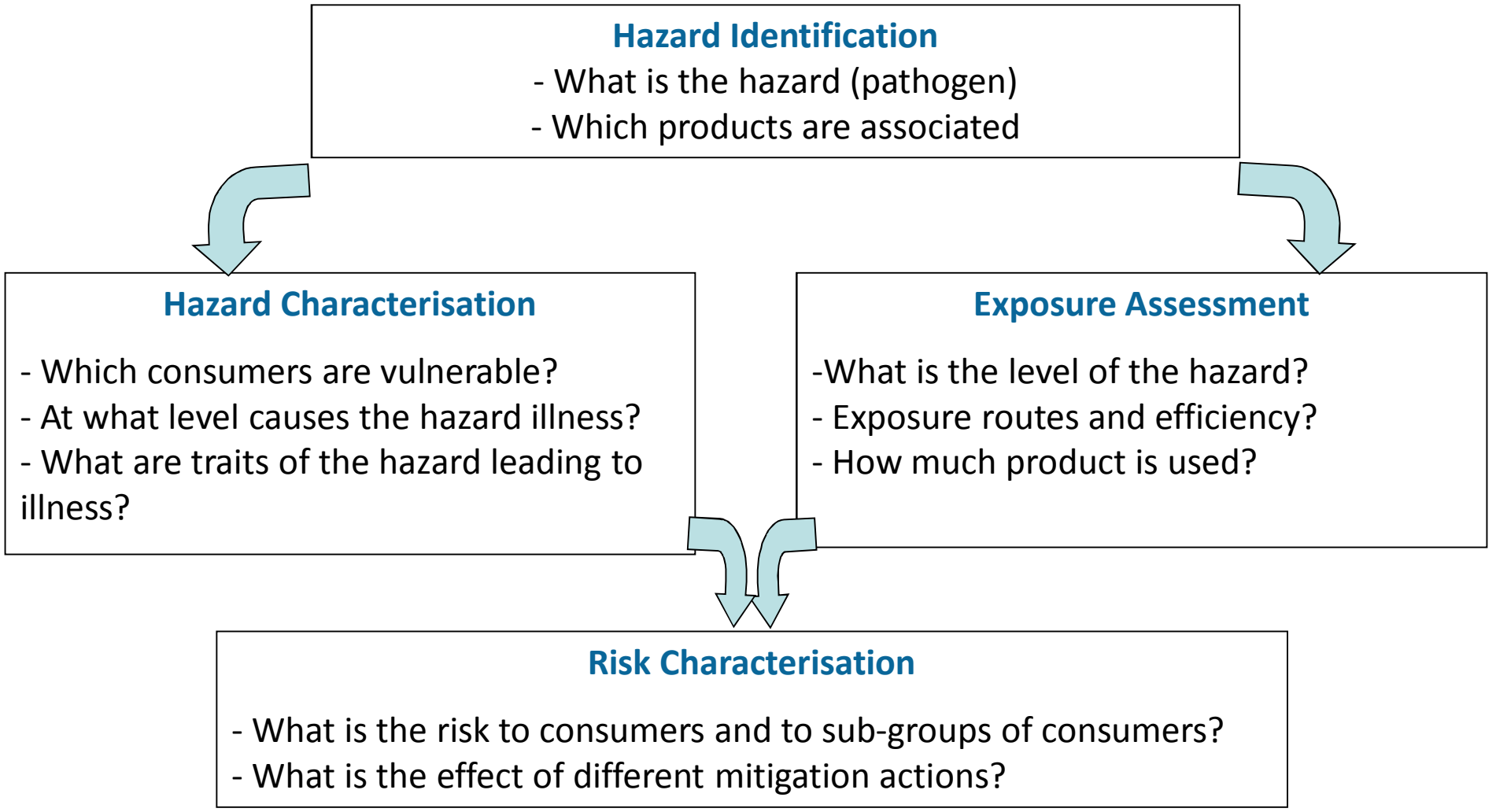
- Does the formulation require a preservative?

- Consider the degree of self preservation of product:
  - pH
  - Water Activity
  - Negative Ingredients (help the organisms survive)
  - Positive Ingredients (help to kill/ control the organisms)

- Consider the packaging
  - Consumer contact and in use risks
  - Material e.g. paper / card

- Challenge testing is carried out on HPC liquids considered to have a hygiene risk.
  - Preserved & unpreserved formulations are tested against bacteria, yeast and mould

Safety Risk Assessment: Steps



Microbiological Risk Assessment ï outcomes

Hygiene Risk Assessment

Assess hygiene risks in HPC innovation formulations to ensure that the formulations are adequately preserved to meet the demands of their life span

Safety Risk Assessment

Using a Microbiological Risk Assessment framework to assess - Hazard ID, Hazard Characterisation, Exposure Assessment and Risk Characterisation

Safe and Stable by Design

ÅOrganisms controlled to acceptable limits for spoilage and safety
ÅOften relies on preservatives
Å**Preservative replacement or reduction can impact growth of microorganisms and therefore safety and stability of HPC products**

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Why are ecotoxicology and risk assessment important?

ÅUnilever uses high volumes of surfactants (EU figures):

400 000 tpa of LAS*	(3g/person/day)
290 000 tpa AE*	(2g/person/day)
700 000 tpa fatty acids	(5g/person/day)
30 000 tpa CAPB*	(0.27g/person/day)

Use of mass market products results in continuous & widespread discharge into the environment, mostly via “down the drain” disposal

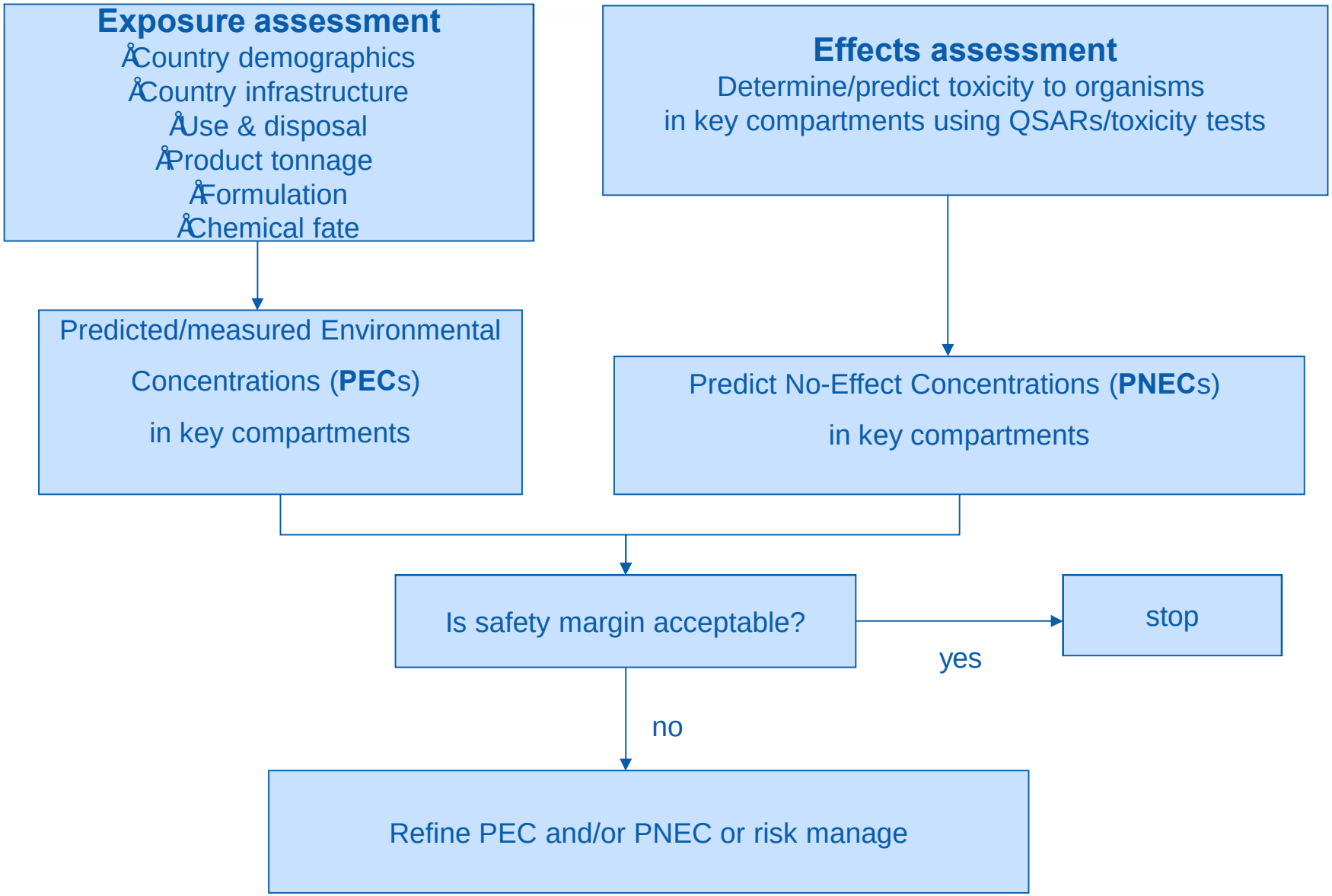
* Linear Alkylbenzene Sulphonates
Alcohol Ethoxylates
Cocamidopropylbetaine

Chemicals in consumer products *can* be hazardous

Chemical	Function	Environmental Half life	Acute aquatic toxicity (mg/L)
A	surfactant	days	5
B	surfactant	hours-days	1
C	surfactant	weeks-months	0.3
D	Hair conditioner	months-years	0.01
E	antidandruff	days-months	0.003
F	preservative	days	0.001
G	antioxidant	days-months	5
H	UV sunscreen	weeks-months	2
I	Moisturiser/ lubricant	months-years	Non-toxic

All of the above ingredients are include in products to give a definate benefit

Environmental Risk Assessment



Information required

nematodes

earthworms

Degradation properties of ingredient

Tonnage

Sediment toxicity

Soil toxicity

PECs **V** **PNECs**

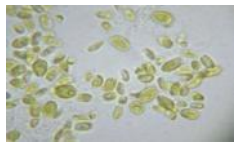
Disposal pathways & receiving environment

Demographic information on markets

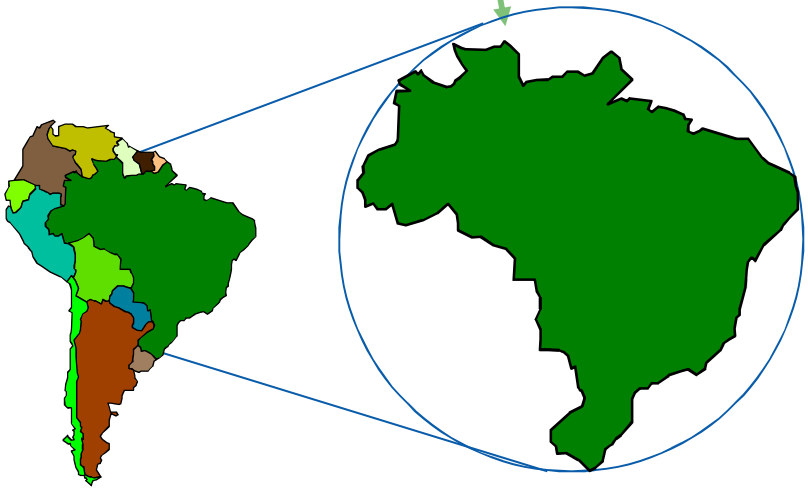
Aquatic toxicity

Daphnia

Fish
(if essential)



Unicellular algae

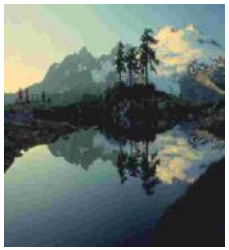


PEC estimation

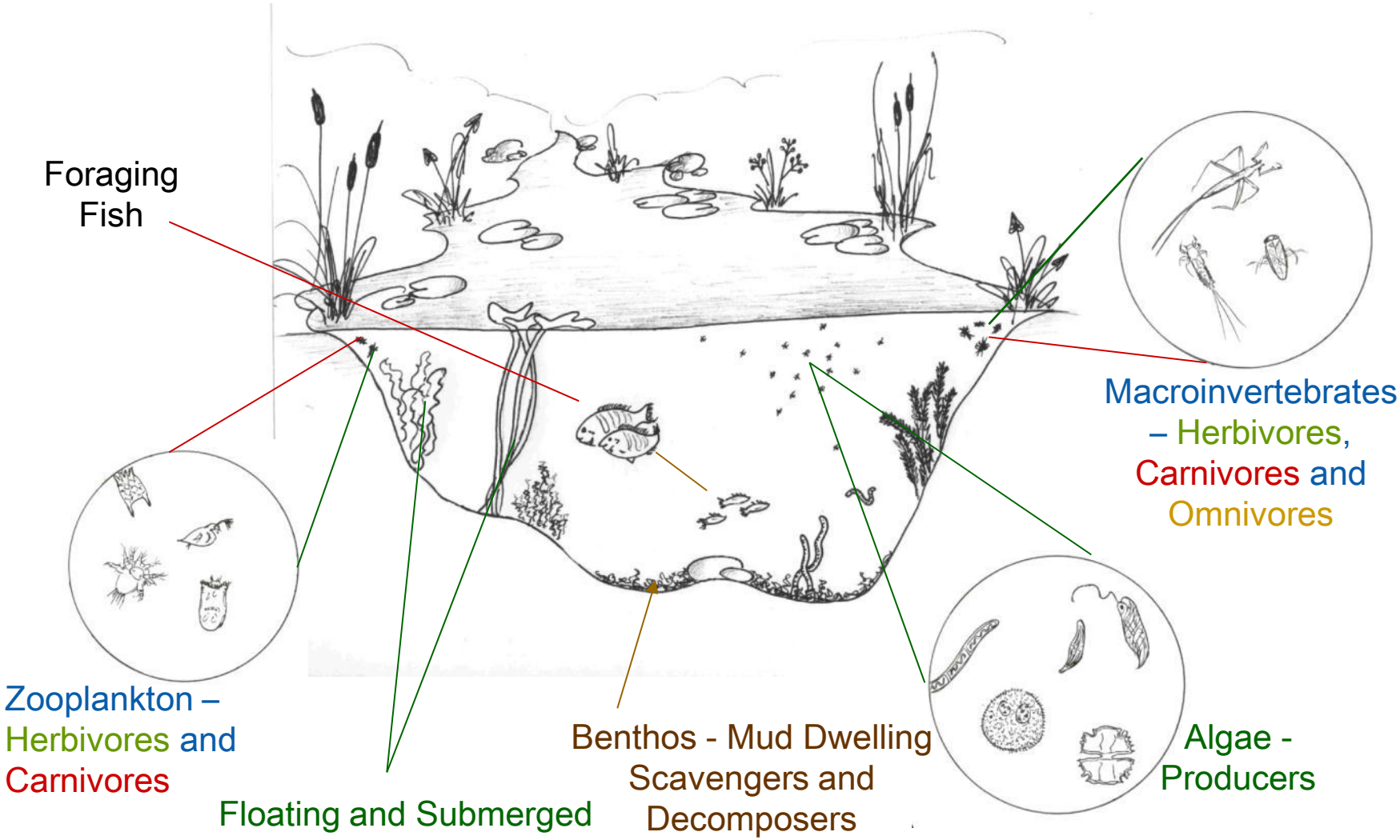
Sewage Treatment

Terrestrial Risk Assessment

Aquatic & Sediment Risk Assessment



Aquatic Communities - how can we assess the most sensitive species?



Derivation of PNECs - Effects assessment

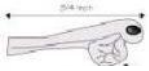
- **There are 2 approaches for estimating a PNEC:**
- *Use of application factors - deterministic approach:*
  - 3 acute (algae, Daphnia, fish) - Lowest EC50 ÷1000
  - 3 chronic (algae, Daphnia, fish) - Lowest NOEC ÷ 10
- *Use of statistical extrapolation – Species Sensitivity Distribution*
- If at least 10 NOECs on different spp (8 taxonomic groups) are available it may be appropriate to use a statistical extrapolation approach.

Tiered Approach to ERA

QSARs & Read-across

Acute ecotoxicity (L/EC_{50})

Chronic ecotoxicity (NOEC)



Mesocosms (artificial ecosystems)

Tier 1
PEC/PNEC <1

No

Tier 2
PEC/PNEC <1

No

Tier 3
PEC/PNEC <1

QSBRs/QSPRs & Read-across

Ready Biodegradation

Inherent Biodegradation

Simulation Tests

Monitoring

Conclusions

- We need to ensure our products have adequate environmental safety profiles while performing their function to the high standards dictated by consumers
- Use of consumer products results in large tonnages of many chemicals that are disposed to waste systems
  - high potential for environmental exposure - need to assess environmental safety.
- Wide range of aquatic toxicity tests available
  - Ecological relevance needs careful attention
- Environmental risk assessment
  - most appropriate method for assessing acceptability
- Risk assessment methodology is simplistic in comparison to the complexity of the environment
  - need many advances in understanding
  - Higher tier refinement is best done in consultation with regulators

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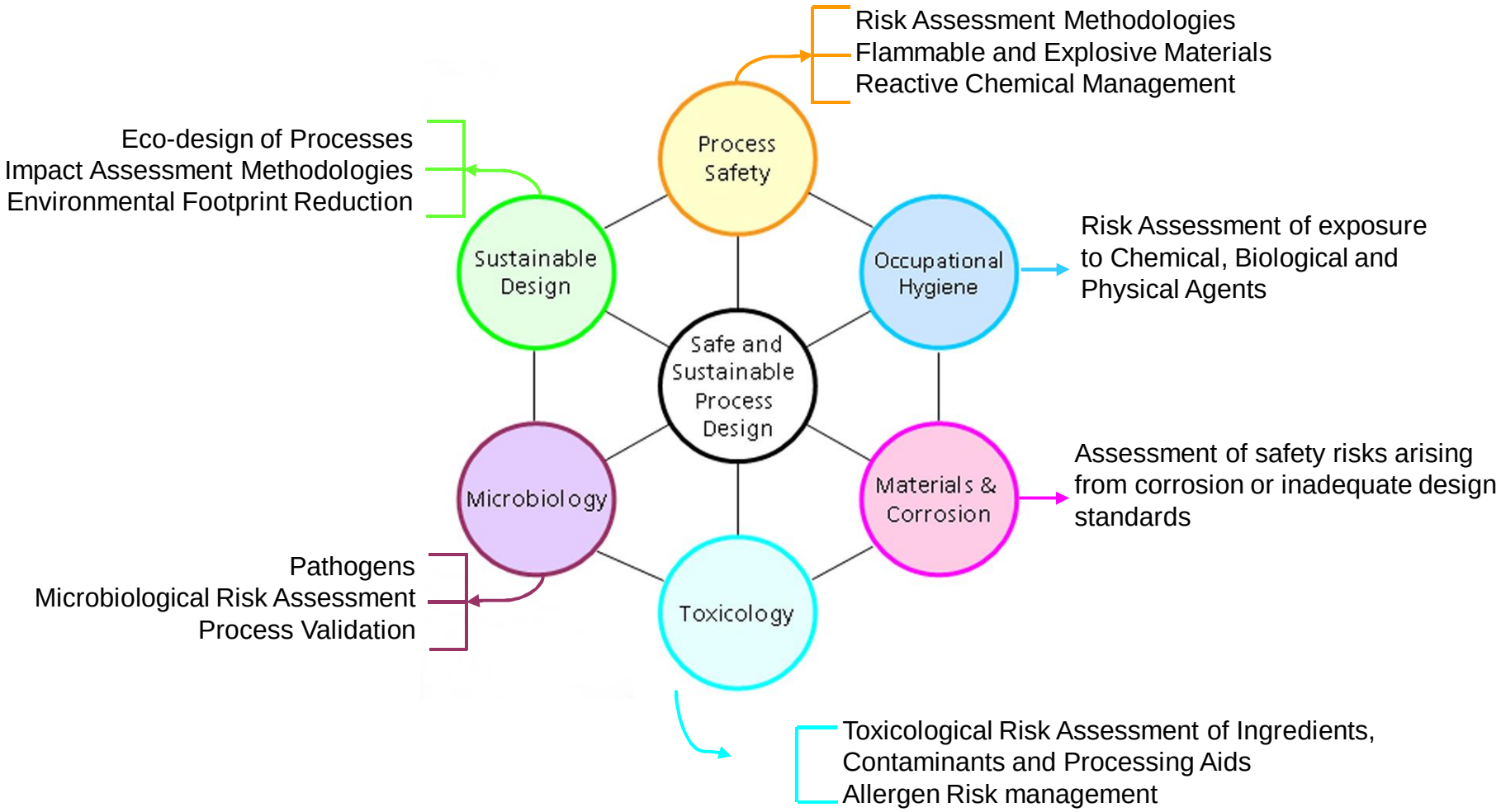
What do we mean by Occupational Safety

- Managing Hazards and Risks that arise across the Source - Make - Deliver continuum for protection of Employees, Members of the Public and Plant. Considering:
  - Ingredients
  - Formulation
  - Process Conditions
  - Equipment / Technologies
  - Packaging
  - Local Factors (e.g. scale, climate, resource / manning) etc.

SEAC Safety and Sustainability Capability



SEAC Occupational Safety Areas

Specialist Technical Areas

- Fire and Explosion Hazards
  - Flammable Gases / Liquids
  - Combustible Dusts
- Chemical Reaction Hazards
  - Thermal Stability
  - Self Heating
- Transport of Dangerous Goods
- Occupational Hygiene
  - Exposure to Hazardous Chemicals
  - Handling of Toxics and very Toxics
  - Respiratory and Skin Sensitisers
  - Allergens (e.g. enzymes)
- Noise Management
- Materials of Construction and Equipment Reliability

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UNILEVER SUSTAINABLE LIVING PLAN

Small Actions. Big Difference.

We have ambitious plans to grow our business, reaching more people with products and brands that improve their quality of life. But growth at any cost is not viable.

Launched November 15th 2010

What makes it different?

- **Broad:** life cycle approach, decouple economic growth from our environmental impact
- **Deep:** 50 time bound public goals
- **Scale:** across the whole business
- **Triple bottom line**
- **Scientific rigour**
- **Track record**
- **We want to work with partners**

Unilever Product Metrics

1. Greenhouse gases per consumer use

CO_2 equivalents across the product lifecycle (grams)

2. Water per consumer use in water-scarce countries

Water added to the product plus the water used by consumers in water-scarce countries (litres)

3. Waste per consumer use

Packaging and product leftovers that have not been re-used, recycled or recovered (grams).

4. Sustainable sourcing per weight of material

Raw or packaging material being sourced from verifiable sustainable renewable sources or made from recycled materials (% by weight)

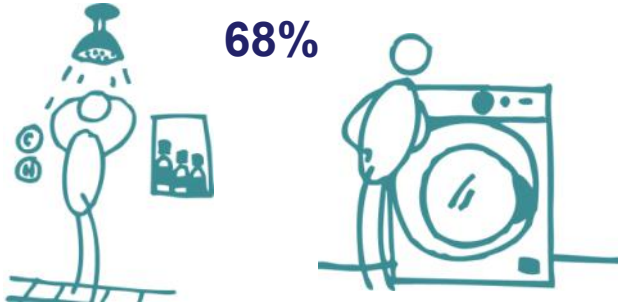
Why four environmental metrics?

- Representative of the key environmental impacts of our product portfolio
- Stakeholder views
- Measurable
- Inform management decisions

UNILEVER'S GREENHOUSE GAS FOOTPRINT
FULL VALUE CHAIN

Raw materials	Manufacture	Distrib. / retail	Consumer use	Disposal
26%	3%	2%	68%	1%




Social and Economic Impacts that Unilever considers

Our global economic footprint

Growing our business and increasing the benefits of economic development.

Sustainable Living Plan targets

Improving livelihoods for thousands of small-scale farmers and distributors.

Supporting smallholder farmers

Working with smallholder farmers to improve agricultural practices.

Supporting micro-enterprise

Many small businesses and farmers supply us with their products.

Making our products more affordable

People everywhere, whatever their income level, aspire to use high-quality and innovative products.

Understanding our economic impacts

Our business impacts in Indonesia, South Africa and Vietnam.

Summary

- Safety assessments are often bespoke – there is no “one size fits all” approach
- Safety of ingredients, products and processes is designed in from the start of the innovation process
- Substitution of an ingredient, or inclusion of a new ingredient in a consumer product needs to be considered at many levels
  - Risk-based approaches to all aspects of consumer, occupational and environmental safety are used
  - The environmental impact across the value chain needs to be considered
    - A variety of metrics are necessary to ensure that an improvement in one metric is not at the expense of another
  - The function of the ingredient in the product e.g. preservative
- To fully assess the risks and impact of a new ingredient or product it is necessary to cover a wide breadth of scientific domains

References

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