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Symrise AG UV-filter court case: the end of the EU animal testing ban for cosmetics?

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[1] ChatGPT 4 DALL•E prompt: An abstract representation of the legal battle between Symrise AG and the European Chemicals Agency (ECHA) over UV filters in cosmetics within the context of the European Union, focusing on the interplay of chemical safety, ethical considerations, and EU policy frameworks. The image should depict the complexities of regulatory governance in the EU cosmetics industry, against evolving environmental and health standards. Include elements such as a gavel and legal documents representing the legal case, chemical structures or molecular models symbolizing the UV filter 2-ethylhexyl salicylate, icons for environmental protection and ethical research, images of cosmetic products like sunscreen bottles, symbols or documents representing EU policy frameworks, and references to the European Union like the EU flag or emblem. (OpenAI, 2023)

Abstract
The Symrise AG v. ECHA court case marks a pivotal moment in the European Union's regulatory landscape concerning animal testing for cosmetics. This comprehensive review dissects the legal, regulatory, and ethical dimensions stemming from the conflict between the EU's ban on animal testing for cosmetics under Regulation (EC) No 1223/2009 and the REACH regulation (EC) No 1907/2006 requirements for chemical safety assessments, which may necessitate animal testing. Through an analysis of the European General Court's rulings, stakeholder questionnaires, and comparative case studies, this review highlights the intricacies of navigating between consumer safety, workers' safety, environmental protection, and animal welfare. It highlights the court's stance that neither regulation holds primacy, necessitating a harmonised application to fulfil safety and ethical standards. The review also delves into the implications for future regulatory policies, emphasising the need for the development and regulatory acceptance of alternative testing methods. This case sets a precedent for reconciling scientific assessment with ethical considerations, steering the cosmetics industry, regulatory bodies, and scientific community towards a more ethically conscious and safety-oriented chemical testing and safety assessment approach.

Layman's summary

The court battle between Symrise AG, a large company producing ingredients for cosmetics, and the European Chemicals Agency (ECHA) has stirred a significant discussion across Europe. At the heart of this issue is whether companies can be forced to test chemicals on animals to ensure their safety for humans and the environment, even if those chemicals are used in cosmetics. For years, the European Union (EU) has been proud of its ban on animal testing for cosmetics, a rule that reflects a commitment to animal welfare and ethical science. However, this case has revealed a complicated situation where another set of rules, known as REACH regulations, could require animal testing for certain safety assessments.

This review takes a deep dive into the complexities of this legal battle, exploring the arguments from both sides, the court's decisions, and what this means for the future of cosmetics safety and animal welfare in the EU. It is a story of how laws that aim to protect consumers and animals can sometimes conflict and how courts must decide the best way forward.

The court concluded that the safety of chemicals, including those used in cosmetics, must be assured through the REACH regulations, even if it means conducting animal tests. This decision has raised concerns among animal welfare advocates and those in the cosmetics industry who strive for cruelty-free products. It highlights the challenging balance between ensuring product safety and maintaining ethical standards in scientific research.

This review also touches on the broader implications of this case for future regulations in the EU. It discusses the urgent need for developing and accepting alternative testing methods that do not involve animals. These alternatives could provide a way to ensure safety without compromising ethical standards.

The case between Symrise AG and ECHA is more than a legal dispute; it is a reflection of the ongoing debate about animal testing, consumer safety, and environmental protection. It calls for a coordinated effort from scientists, policymakers, and the industry to find innovative solutions that uphold both safety and ethical principles. As we move forward, this case will likely serve as a reference point for how we navigate these complex issues, striving for a future where effective and ethical testing methods become the norm in ensuring chemical safety.

In essence, this review encapsulates a pivotal moment in EU regulatory history, where the intersection of legal, ethical, and scientific considerations demands a nuanced approach to safeguarding human health, animal welfare, and environmental integrity. It's a call to action for all stakeholders to engage in the development and regulatory acceptance of non-animal testing methods, ensuring a harmonious balance between safety and ethics in the cosmetics industry and beyond.

Abbreviations

Abbreviation	Meaning
AG	Aktiengesellschaft (Joint-stock company)
BPR	Biocidal Products Regulation (in the EU)
CEFIC	European Chemical Industry Council
CFE	Cruelty Free Europe
CJEU	Court of Justice of the European Union
CLP	Classification, Labelling and Packaging (regulation in the EU)
DNT	Developmental neurotoxicity
DG GROW	European Commission Directorate-General Grow: Internal Market, Industry, Entrepreneurship and SMEs
EARA	European Animal Research Association
EC	European Commission
ECHA	European Chemicals Agency
ECI	European Citizens' Initiative
ECVAM	European Centre for the Validation of Alternative Methods
EFfCI	European Federation for Cosmetic Ingredients
EH salicylate	2-ethylhexyl salicylate
EPAA	European Partnership for Alternative Approaches to Animal Testing
EU	European Union
EURL ECVAM	European Union Reference Laboratory for Alternatives to Animal Testing
GRI	Global Reporting Initiative
IRAS	Institute for Risk Assessment Sciences (at Utrecht University)
NAM	New Approach Methodologies (in toxicology)
NGO	Non-governmental organisation
NWA	Dutch Research Agenda
OECD	Organisation for Economic Co-operation and Development
PETA UK	People for the Ethical Treatment of Animals UK
PIC	Prior Informed Consent (regulation under the Rotterdam Convention)
PNDT	Prenatal Diagnostic Techniques
PPE	Personal Protective Equipment
REACH	Registration, Evaluation, Authorisation, and Restriction of Chemicals
SAFE	Safety Assessment through Animal-Free Evolution
SONC	Statement of Non-Compliance
Three Rs	Replacement, Reduction, and Refinement
TSAR	Tracking System for Alternative methods towards Regulatory acceptance
UK	United Kingdom
UU	Utrecht University
UV	Ultraviolet
v.	Versus

1. Introduction

What started in 1938 as the mandatory testing of animals to ensure product safety has changed over the years towards animal-free testing. Initially, this shift started with programmes to research and validate alternative methods for testing and labelling cruelty-free products. It accelerated in 1998 when the United Kingdom (UK) banned all animal testing for cosmetics and their ingredients; measures intensified further when the European Union (EU) passed laws in 2004 that banned animal testing for cosmetics. From this point on, increasing numbers of countries such as Canada, Brazil, Switzerland, Turkey, nations within the European Union, and some states of the United States have started banning animal testing on cosmetics and the ingredients of these cosmetics (The Humane Society of the United States, n.d.). However, this finally led to court cases with discrepancies in regulations between Symrise AG and the European Chemicals Agency (Court of Justice of the European Union - General Court First Chamber, 2023-a).

As mentioned, since 11 September 2004, the EU has banned the use of animals on the end products of cosmetics. Since 11 March 2009, this ban has also applied to cosmetics ingredients (European Commission, 2009). The animal testing ban also specifies that it is prohibited to market cosmetic products in the EU when these were tested on animals, regardless of the location of testing. This ban affects the whole cosmetics industry as it applies not only to products such as makeup, sunscreen, and other beauty products but also to all toiletries such as shampoo, soap, shaving cream, and toothpaste (Grossman, 2013).
One producer of such products or ingredients is Symrise AG, a large company headquartered in Holzminden, Germany, specialising in flavour, fragrance, and care. Symrise's operations span across more than 100 locations in Europe, Africa, the Middle East, Asia, the United States, and Latin America, emphasising its global reach and impact on diverse consumer markets (Symrise AG., n.d.).

One of the ingredients that Symrise produces is 2-ethylhexyl salicylate (EH salicylate) (European Chemicals Agency (ECHA), 2023). This chemical is a commonly used Ultraviolet (UV) filter in sunscreen cosmetics, which is crucial in protecting skin from harmful UVB radiation. Structurally, it is an ester of salicylic acid and 2-ethylhexanol, offering effective UVB absorption capabilities (National Center for Biotechnology Information, 2023), which aids in preventing sunburns and skin damage and the ability to mitigate UV-induced carcinogenesis and premature ageing caused by UV exposure, likewise known as photoaging (Young et al., 2017). EH salicylate is valued in cosmetic applications for its stability and compatibility with other sunscreen ingredients, making it an integral component in broad-spectrum sunscreen products (Gaspar & Maia Campos, 2006), and it has favourable properties, including photostability and minimal skin irritation potential (Matta et al., 2019). However, it necessitates a thorough understanding of the toxicokinetics of the UV filter, its potential for bioaccumulation, and long-term ecological effects. Studies have indicated that while EH salicylate is generally considered safe at specific concentrations, its environmental persistence and potential bioaccumulation in aquatic ecosystems warrant further investigation (Krause et al., 2012; Balmer et al., 2005; Environmental Working Group, 2019).

However, Symrise actively works towards reducing its environmental footprint and promoting ethical sourcing practices, with a strong focus on ethical practices, including its approach to animal testing. In alignment with industry regulations and consumer expectations, Symrise adheres to strict policies that aim to minimise and replace animal testing wherever possible. While Symrise operates within the regulatory frameworks that sometimes require animal testing for safety evaluations, the company actively seeks and advocates for alternative methods. The company invests in alternative testing methods and technologies that can provide safe and efficacious data without using animals (Symrise AG., 2023). In line with Symrise's endeavour is the Three Rs principle (Replacement, Reduction, and Refinement), which remains a cornerstone in the ethical considerations of animal testing within scientific research. Initially proposed by Russell and Burch in their work "The Principles of Humane Experimental Technique" (1959), it advocates for methods that either replace the need for animal testing, reduce the number of animals used, or refine procedures to minimise suffering. The relevance of the Three Rs has been increasingly recognised in legislative and regulatory frameworks globally, notably within the European Union's Directive 2010/63/EU, which mandates their application in all animal-based research (European Parliament & European Council, 2010). This directive sets a commitment to animal welfare while ensuring the scientific integrity of research practices. The ultimate aim of the EU Directive 2010/63EU is to phase out animal testing altogether. Collectively, these developments underscore a paradigm shift in scientific research towards more ethical and responsible practices, anchored by the Three Rs principle.

Operating under European Union regulations often necessitates compliance with directives from bodies such as the European Chemicals Agency (ECHA). Established in 2007 after adopting the REACH Regulation (EC No 1907/2006), ECHA is crucial in the EU's chemical regulatory framework, focusing on the safe use of chemicals and safeguarding human health and the environment. ECHA's responsibilities extend beyond the implementation of REACH, encompassing (but not limited to) the Classification, Labelling and Packaging (CLP) Regulation, the Biocidal Products Regulation (BPR), and the Prior Informed Consent (PIC) Regulation, thereby consolidating its position as a central authority in the EU's chemical management landscape (European Parliament & European Council, 2006). The agency is instrumental in registering, evaluating, authorising, and restricting chemicals, facilitating communication between industry and regulatory bodies to ensure compliance with legal standards (European Chemicals Agency (ECHA), n.d.-a). ECHA's REACH regulation, which stands for Registration, Evaluation, Authorisation, and Restriction of Chemicals, is a foundational legislative framework within the European Union designed to protect human health and the environment from the risks that chemicals can pose. Implemented on 1 June 2007, under Regulation (EC) No 1907/2006, REACH imposes a "no data, no market" principle, requiring companies to assess and manage the risks associated with the chemicals they manufacture and market in the EU. This regulation mandates the registration of substances produced or imported into the EU in quantities of over one tonne per year, ensuring that comprehensive information on these chemicals' hazards and safe use is collected and shared (European Parliament & European Council, 2006; European Chemicals Agency (ECHA), n.d.-b). However,

sometimes, there is a clash between the cosmetics ban and REACH, which can lead to court cases.

In this review, the discussion of one such court case between Symrise and ECHA, from now on the Symrise v. ECHA case, where ECHA requested Symrise to perform animal testing under REACH while Symrise desired not to perform animal testing under the cosmetics regulation (Court of Justice of the European Union - General Court First Chamber, 2023-a), will look into the dimensions of the case and what the future might hold.

Antecedent to this court case, Symrise requested an appeal to ECHA, which was dismissed by the ECHA Board of Appeal (European Chemicals Agency (ECHA), 2022).

The court case represents a critical intersection between REACH and the Cosmetics Regulation. This legal confrontation brings into focus the complex regulatory landscape governing the use of chemical substances in consumer products, especially those with significant health, safety, and environmental implications. Central to this legal dispute is EH salicylate. The case emerged from ECHA's directive for Symrise to conduct additional toxicological testing to ascertain the comprehensive safety profile of EH salicylate, assessing workers' safety and environmental protection. These three additional tests are OECD No. 414 (OECD, 2018), prenatal developmental toxicity test, OECD No. 234 (OECD, 2011), Fish Sexual Development Test, or aquatic life study, and OECD No. 443 (OECD, 2018b), extended one-generation toxicity study, and can be found in Table 4. The REACH directive became a point of contention, considering the EU's stringent regulations on animal testing for cosmetic ingredients. This literature review aims to provide a comprehensive analysis of the Symrise AG v. ECHA court case and includes a questionnaire inventory among key stakeholders to:

1. Ascertain the legal and regulatory dimensions of the court case, particularly how the cosmetics ban intersects with REACH.
2. The implications of this case for future regulatory decisions and policies emphasising the integration of scientific assessment with ethical considerations in chemical testing.
3. Approved OECD test methods and (in progress) alternatives to animal testing in workers' safety and aquatic safety.
4. Reflect on the similarities and differences of a similar court case to learn why the outcomes differed where one case was won while the other lost.

2. Methodology

This analysis examines the court case between Symrise AG and the ECHA on 22 November 2023, emphasising its legal, regulatory, and ethical dimensions. The focus is on how the case intersects with the EU's REACH regulations, as well as the prohibition of animal testing in cosmetics under Regulation (EC) No 1223/2009.

Search strategy

The literature search was conducted using a comprehensive approach to ensure a thorough review of all relevant materials. Multiple databases and sources were utilised, including:

1. Legal Databases: LexisNexis, EUR-Lex, Overton, Policy Commons, and InfoCuria for legal documents, court rulings, and legislative texts.
2. Academic Databases: Google Scholar, EMBASE, PubMed, JSTOR, and PROSPERO for (peer-reviewed) articles, research papers, and (systematic) literature reviews for information on the UV filter and toxicological testing information.
3. Institutional websites: ECHA, the European Commission, Joint Research Centre, OECD, Tracking System for Alternative methods towards Regulatory acceptance (TSAR), European Partnership for Alternative Approaches to Animal Testing (EPAA), European Animal Research Association (EARA), and NGOs focussed on cosmetics chemical safety (European Federation for Cosmetics Ingredients (EFfCI), animal welfare and rights (Cruelty Free Europe (CFE), People for the Ethical Treatment of Animals (UK) (PETA (UK)), Eurogroup for animals, the Good Lobby), which are relevant to the case.
4. Corporate websites: Symrise AG and Unilever, as these corporations are involved in the court case as well as producing or using UV filters.
5. News Websites and Archives: ProQuest for reading news articles related to the court case.

Inclusion and Exclusion criteria

The inclusion criteria led to materials selected based on the following: their relevance to the Symrise AG v. ECHA case, their focus on REACH regulations and the EU cosmetics animal testing ban, their contribution to understanding the broader implications of the case, and information on the chemical 2-Ethylhexyl salicylate. Therefore, primary sources (court documents, legal texts, interviews, company statements) and secondary sources (academic papers, expert commentaries, news articles) were included. Exclusion criteria were non-peer-reviewed scientific literature articles, opinion pieces without substantial factual backing, and materials not directly related to the case, such as court cases on bans outside the EU or the key themes were excluded. The Court of Justice also ruled in the similar Symrise v. ECHA case regarding the UV-filter homosalate (Court of Justice of the European Union - General Court First Chamber, 2023-b) with similar reasoning; therefore, to gain a better understanding, the choice is made to focus on EH salicylate only. Therefore, the exclusion criteria also contain court cases on homosalate and information on the chemical homosalate.

Data extraction and analysis

Information was extracted by scanning, reading or summarising software (such as Apple summarise function) from each consulted source, including the author's credentials, publication date, and specific relevance to the Symrise AG v. ECHA case or supporting other statements. Furthermore, a thematic analysis was conducted, where the collected data was presented into divisions such as the legal and regulatory dimensions of the court case, the implications of this case for future regulatory policies, emphasising the integration of scientific assessment with ethical considerations in chemical testing, OECD tests and alternatives (approved or not approved), similar court cases. This approach facilitated a comprehensive understanding of the case and its broader context. AI tools have been used to optimise writing, grammatic, and spelling.

Questionnaire

A questionnaire was sent to legal specialists and well-informed scientists involved in or informed about the Symrise v. ECHA court case to understand the court case better and understand thought processes and involved laws, regulations, and policies. The inclusion of interviewees was based on involvement with the Symrise v. ECHA court case, lobbying organisations with the EU, information bodies within the EU, or indirect involvement or interest in the case. These recipients are noted in Table 1. The questionnaire can be found in Appendix A. A list of abbreviations is given after the abstract.

Table 1 Recipients of the questionnaire

Stakeholder	Reply	Pro (intervener) or Contra (defendant)
CEFIC	No	Neutral
CFE	No	Pro
ECHA	Filled in questionnaire	Contra
EFfCI	Cannot share any information	Pro
EPAA	No	Neutral
Eurogroup for Animals	Filled in the questionnaire	Pro
European Commission DG GROW	Yes, forwarded to court outcomes and ECHA/REACH protocols	Contra
PETA UK	Filled in the questionnaire	Pro
Symrise AG	Filled in questionnaire	Pro
The Good Lobby	No	Pro
Unilever	No	Pro
University of Zurich (Three Rs project)	Filled in questionnaire	Pro

Limitations

The review acknowledges potential limitations such as publication bias. Efforts were made to mitigate these by including a wide range of databases and contacting experts/specialists on the topic. Furthermore, the reviewer does not have in-depth knowledge of the legal field. The review is limited to a 5-week time constraint and could, therefore, not encompass every detail.

3. Case details and background

In 2018, ECHA requested Symrise to perform animal testing on EH-salicylate to evaluate risks associated with worker exposure and aquatic life. Symrise challenged this request, arguing that the safety of EH-salicylate for human health had already been evaluated under the EU Cosmetics Regulation and that ECHA's request conflicted with the EU's ban on animal testing for cosmetics. Symrise went to the General Court of the Court of Justice of the European Union to appeal this decision. On 22 November 2023, the EU General Court rejected Symrise's pleas. The Court declared that cosmetic ingredients could be tested on animals for REACH purposes, stating that no provisions establish the primacy of either REACH or the EU Cosmetics Regulation. Therefore, both must be interpreted and applied consistently and competently, where the court said filling the gaps of available date, noticed by a member of Eurogroup for Animals. Symrise was supported in its case by several organisations, including Cruelty-Free Europe, the European Federation for Cosmetic Ingredients, PETA International Science Consortium Ltd, PETA Science Consortium International, and Unilever (Court of Justice of the European Union - General Court First Chamber, 2023-a; COSlaw, 2023).

Table 2 Overview of pleas in Symrise AG v. ECHA case, with Court rulings

Plea	Symrise AG and Interveners' Arguments	ECHA's Counterarguments	Court ruling
1	Claimed that 2-ethylhexyl salicylate is **exclusively used in cosmetics** and already assessed for human health, thus not requiring REACH testing.	Stated that REACH mandates comprehensive safety data on chemicals, which **may include animal testing for worker safety and environmental protection.**	**Did not find exemptions for substances used in cosmetics from REACH's requirements**, emphasising the need for comprehensive safety assessments.
2	Claimed that ECHA's **request for animal testing violated the EU Cosmetics Regulation ban** on such practices for **cosmetic ingredients.**	Emphasised that the REACH regulation is not subject to the cosmetics ban and **applies to all substances**, **including those in cosmetics, to protect workers and the environment.**	Ruled that **REACH** and the **EU Cosmetics Regulation must be applied in a consistent manner, with no provision indicating a primacy** that exempts cosmetics from REACH requirements.
3	Claimed that the **substance's safety** had been **thoroughly evaluated** under the Cosmetics Regulation, making additional tests redundant.	Asserted that the safety assessments required by REACH **are broader and cover aspects beyond the scope of the Cosmetics Regulation.**	It was determined that the scope of safety assessments under REACH **extends beyond the Cosmetics Regulation,** justifying additional tests.
4	Claimed that ECHA's request **infringed on procedural rights and did not consider the company's right to comment on the draft decision.**	Highlighted that the procedural steps followed **were in accordance with REACH requirements** and that Symrise AG had opportunities to present its case.	The Court found procedural **compliance within REACH's framework**, suggesting that Symrise AG's rights to comment were considered.

4. Results, Discussion, and Conclusion

Dimensions of the Symrise AG v. ECHA Case

The Symrise v. ECHA case critically examined the legal and regulatory dimensions concerning the intersection of the cosmetics ban on animal testing regulation (EC) No 1223/2009 and the REACH regulation (EC) No 1907/2006. The central legal issue in the case was whether the EU Cosmetics Regulation's ban on animal testing for cosmetic ingredients could be reconciled with REACH's requirement for safety data, which may necessitate animal testing. The European General Court's ruling in November 2023 clarified several key points of this intersection, as seen in Table 2. The Court found that both regulatory frameworks operate with distinct objectives: the Cosmetics Regulation focuses on the safety of consumers and bans animal testing for cosmetic products, while REACH ensures the safety of chemicals throughout their lifecycle, including manufacturing and environmental impacts. The Court ruled that no legal provisions establish primacy between the two regulations, thus requiring them to be interpreted and applied consistently and reasonably. This interpretation is pivotal, as it confirms that the ban on animal testing under the Cosmetics Regulation does not exempt cosmetic ingredients from REACH's broader safety assessment requirements. According to a surveyed Symrise staff member, this was an important learning moment on how the Cosmetics Regulation and REACH are in relation.

The Court further distinguished between the types of risks each regulation addresses. While the Cosmetics Regulation ensures the safety of end-users and professionals using cosmetics under normal or reasonably foreseeable conditions, it does not cover other risks, such as worker exposure or environmental protection. Conversely, REACH encompasses a more comprehensive scope that includes occupational hazards and environmental risks, hence the requirement for animal testing if no alternative methods are available to assess these risks. However, based on a reply from ECHA, there is a publicly available factsheet (European Chemicals Agency, 2014), which states the following:

> "Registrants of substances that are exclusively used in cosmetics may not perform animal testing to meet the information requirements of the REACH human health endpoints. The exception is any testing required to assess the risks from exposure to workers [...] (Further) all registrants (whether or not they only use the substance for cosmetic purposes) are permitted to perform animal testing, as a last resort, for all environmental endpoints [...] This means that the Cosmetics Regulation does not restrict testing under REACH, if: this testing is required for environmental endpoints".

Besides this, as a reply to the questionnaire, a representative of EC DG GROW and ECHA provided a flowchart stating when to use animal testing and when not, as shown in Figure 1.

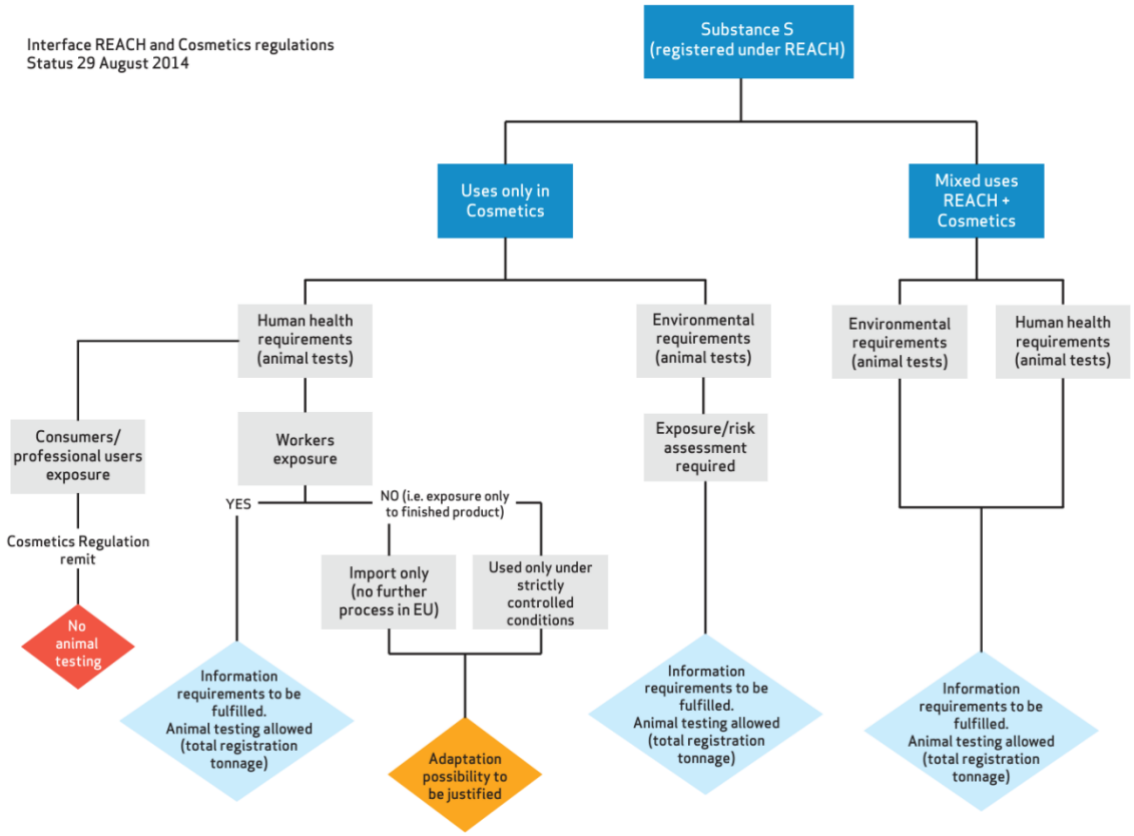

Figure 1 Flowchart provided by EC DC GROW and ECHA on when to divert to animal testing.

Following this reasoning and the flowchart in Figure 1 it is almost impossible to avoid animal testing, as workers' safety can be used as an argument for the use of animals in most situations. This is reflected in that 419 chemicals are registered under REACH that are ingredients of cosmetics use only of which 63 have been tested *in vivo* since the cosmetics ban (Knight et al., 2021).

Even though a robust regulatory intent exists to minimise animal testing in the EU, evidenced by the stringent ban under the Cosmetics Regulation, on the other hand, there is a need to ensure comprehensive safety for all potential chemical exposures as mandated by REACH, which reverts to animal testing. This creates a tension between ethical considerations and the pragmatic aspects of ensuring safety for all stakeholders, including workers and the environment. Future regulatory policies must continue navigating these complexities, fostering the development and validation of alternative testing methods that align with safety and ethical standards. As the regulatory landscape evolves, this case will likely serve as a reference point for how the cosmetics industry, regulatory bodies, and the scientific community navigate the ethical challenges associated with chemical testing and safety assessment. The ongoing development, regulatory validation, and acceptance of alternative testing methods will be crucial for advancing EU chemical safety legislation in alignment with ethical animal testing considerations. In the survey, the Swiss Three Rs project member mentioned that the Court ruled that Symrise AG can provide adaptations or alternatives to animal tests requested by ECHA to fulfil the REACH requirements; however, these methods still have to be validated, meaning while possible to submit alternatives, these alternative methods

still need to be accepted by ECHA. All in all, the Symrise case underscores the ethical, legal, and political complexity inherent in the EU's approach to chemical safety.

Implications for Future Regulatory Policies

The Symrise v. ECHA case has set a precedent with far-reaching implications for integrating scientific assessment with ethical considerations within the EU regulatory landscape. The decision by the European General Court has solidified the understanding that the REACH regulation's ((EC) No 1907/2006, 2006) comprehensive safety assessment requirements can necessitate animal testing, even for substances solely used in cosmetics. The Court's ruling emphasised the need for harmonisation between the REACH regulation and the EU Cosmetics Regulation (EC) No 1223/2009, clarifying that neither has primacy over the other. This interpretation mandates a cooperative approach to chemical safety and consumer protection. The decision impacts future regulatory policies by necessitating a balanced application of both regulations in a way that considers the full scope of human health and environmental safety concerns. Interestingly, as mentioned in the survey by a Swiss Three Rs project member: "Should there even be a distinction between the different categories of human health endpoints in the first place?".

In juxtaposition, the European Commission and ECHA could reflect on requirements stated in the REACH regulations, as Symrise mentioned in the court case, that intentional exposure by end-users, including vulnerable groups such as children and babies, is much higher than workers. Furthermore, workers wear Personal Protective Equipment (PPE), which, if used correctly, can protect the workers (Triebig et al., 2009). PPE includes, among other things, face masks, air filters, bodysuits, gloves, safety goggles, etcetera. It is of utmost importance to reflect on whether it is necessary, such as the flowchart in Figure 1 suggests, to distinguish between end-users and workers or that creating one group of human exposure is possible, thus eliminating the need for animal testing.
Furthermore, as mentioned by a representative of PETA UK in the survey, the EU could follow the UK in abolishing animal testing to fulfil REACH data requirements. For instance, the UK no longer accepts cosmetics where any animal testing was performed and offers workshops on New Approach Methods (NAM) for the industry, which was welcomed by the cosmetics industry in the UK (Zainzinger, 2024).

REACH EU Exemptions and Alternative Methods

A significant aspect of the ruling was acknowledging the ethical tension surrounding animal testing. The Court's decision allows for alternative methods to be proposed in place of animal testing if presented by Symrise, which aligns with REACH regulation (EC) No 1907/2006 Article 13 (1), which states:

> "Information on intrinsic properties of substances may be generated by means other than tests, provided that the conditions set out in Annex XI are met. In particular for human toxicity, information shall be generated whenever possible by means other than vertebrate animal tests, through the use of alternative methods, for example, in vitro methods or qualitative or quantitative structure-activity relationship models or from information from structurally related substances (grouping or read-across). Testing in accordance with Annex VIII,

> Sections 8.6 and 8.7, Annex IX and Annex X may be omitted where justified by information on exposure and implemented risk management measures as specified in Annex XI, section 3. (Article 13 (1))".

Where Annex XI describes the "General Rules for Adaptation of the Standard Testing Regime set out in Annexes VII to X". This facet of the decision encourages further investment and development in non-animal testing methodologies, such as *in vitro* techniques, computational models, and the use of existing data to predict outcomes (read-across approaches). However, ECHA and the Court suggest animal tests as the default option in this case, which encourages the industry to use animal studies to have their product accepted for market use. At the same time, the industry should prioritise developing and accepting scientifically valid alternative testing methods if possible. Furthermore, the Court's ruling in the case may also influence global regulatory policies, as the EU often leads global chemical regulation and consumer safety standards (EnHeSa, 2023). Future policies should continue to promote the use of such alternatives, gradually moving towards minimising animal testing in line with ethical expectations and the REACH regulations, stating that animal studies should only be done as a last resort. Through mechanisms like a European Citizens Initiative (ECI), European citizens have expressed their desire for alternatives to animal testing as reported to the European Citizens' Initiative in 2023, where more than 1,2 million EU inhabitants signed this petition. This sentiment was also supported by those who intervened in the Symrise v. ECHA court case, as stated by the Eurogroup for Animals (2022). The European Commission replied to the ECI: "The Commission acts to accelerate phasing out of animal testing in response to a European Citizens' Initiative" (European Commission, 2023).

In navigating the intricate landscape of chemical safety assessments, the EU endeavours to set a global benchmark by merging strict scientific research with deep ethical considerations. This approach aims not only to uphold the highest safety standards but also to foster an ethical framework for testing practices. The nuanced stance taken by the EU seeks to inspire other regions to strike a similar balance, thus promoting a paradigm where scientific integrity and ethical responsibilities are in harmony.

However, the implications of regulatory decisions, such as the one exemplified by the Symrise v. ECHA case, stresses the complexity of aligning these objectives. The ruling in question has sparked a broader debate on the ethical dimensions of safety assessments, particularly around the controversial topic of animal testing. Contrary to a simplistic interpretation of the ruling as a straightforward endorsement of current practices, it presents a multisided challenge. Industries dependent on chemical substances are now compelled to navigate a more rigorously defined regulatory landscape, where the expectation is not just compliance but proactive engagement with ethical scientific methodologies. This calls for a considerable investment in research and development to devise alternative testing methods that satisfy scientific, legal, and ethical criteria.

While the ruling possibly advocates for an increase in animal testing as a means to ensure product safety, it could also open the door for critical discussions and potential shifts in legislative frameworks within the EU. Policymakers should now be prompted to reflect on this case's ramifications, contemplating adjusting regulations that might better align with evolving scientific capabilities and ethical standards. The EC and ECHA should reflect on the need for separate groups of humans and look into alternatives for aquatic life safety

tests. The aftermath of the Court's decision could potentially catalyse enhanced support for exploring and accepting alternative testing methods. Anticipated increases in EU research grants, as highlighted by the European Commission in 2023, aim to stimulate scientific innovation in this domain. Such financial backing is crucial for expanding the scientific literature and databases, like the Tracking System for Alternative methods towards Regulatory acceptance (TSAR) Database, which catalogues validated non-animal testing methodologies (European Commission, 2024). As the EU moves forward, the challenge will be to refine regulatory frameworks to foster innovation while addressing ethical concerns related to animal testing. The ultimate goal is to create a regulatory environment that ensures public safety and respects the welfare of all beings involved in the testing process.

Similar Court Case

In seeing the Symrise v. ECHA case as the foundation of this review, it is vital to explore the nuanced dynamics of regulatory compliance under the REACH framework. By juxtaposing this with the Esso Raffinage v. ECHA case, the aim was to draw comparative insights. This comparative analysis is essential to comprehensively understand EU chemical law's legal complexities and evolving regulatory practices.

On 8 May 2018, Esso Raffinage sued ECHA for an annulment of a letter sent to the French Ministry of Ecology, Sustainable Development, Transport and Housing (Court of Justice of the European Union - General Court Fifth Chamber). This letter contained ECHA's Statement of Non-Compliance (SONC) following a Dossier Evaluation Decision under Regulation (EC) No 1907/2006, describing Esso Raffinage's failure to meet all the REACH required tests for a chemical, which is interestingly not further described. REACH rules described that the volume at which the chemical was being sold required prenatal developmental toxicity (PNDT) tests. PNDT studies, also known as embryo-foetal developmental studies, are seen as crucial in understanding the potential risks posed to the developing foetus. The process generally involves administering the test substance to pregnant animals to assess the effects of prenatal exposure on the pregnant test animal and the developing organism. This test is also known as test No 414 (OECD, 2018), which is the same test requested in the Symrise v. ECHA court case (Table 3). Esso Raffinage desired not to perform animal testing and countered this request by stating REACH regulation Article 13 (1) and Annex XI (Regulation (EC) No 1907/2006, 2006). The CJEU's decision, based on these arguments, annulled ECHA's directive, exempting Esso Raffinage from additional animal testing for their chemical approvals.

To remain on the Esso v. ECHA court case, on 21 January 2021, the Federal Republic of Germany, together with the French Republic and the Kingdom of the Netherlands, which were interveners for ECHA during the Court of Justice of the European Union - General Court Fifth Chamber (2018) court case, tried to appeal the decision by the CJEU. The appeal was primarily due to concerns about the interpretation and application of the REACH regulation, specifically concerning the roles and responsibilities of ECHA and national authorities. Ultimately, the Federal Republic of Germany was met with a rejected appeal. The Court upheld the General Court's decision, favouring Esso Raffinage, emphasising the need to carefully evaluate animal testing requirements and consider

alternative testing methods (Court of Justice of the European Union - General Court Third Chamber, 2021). Noteworthy in this situation is that member states of the EU went to Court to request annulment of the previous appeal, therefore requesting animal testing, while the Court requested not to use animals in testing. Furthermore, this is striking, as countries like the Netherlands in the EU have significant ambitions and missions to reduce animal testing in the national TPI program (Transitie Proefdiervrije Innovaties; Ministry of Agriculture, Nature and Food Quality et al., 2023).

Noteworthy, this court case resembles the Symrise v. ECHA court case; however, with the Esso case, there was a clear focus on the exploration and possibilities of adaptations and alternative methods. The similarities and differences are described in Table 3. Seeing that one of the extra tests requested by ECHA in the case with Symrise was the same as with the Esso case, it sparks the idea that it could be possible to use the Esso Raffinage v. ECHA as an example for not having to perform the animal testing within the REACH regulations.

Table 3 Overview of comparison of Symrise v ECHA with the similar Esso v. ECHA court case

	Symrise v. ECHA (T-655/20)	Esso Raffinage v. ECHA (T-283/15)
Basis	Argued against regulatory decisions made by ECHA under REACH regulations.	
Main issue	Focussed on the classification, labelling, and restriction of UV filters as cosmetics ingredients and the compliance with REACH requirements, which requires animal testing.	Involves substance evaluation processes, compliance with REACH requirements, and requesting animal testing.
Arguments by the Applicant	Symrise argued against ECHA's interpretation and application of REACH provisions in relation to the workers' safety and environmental protection, therefore requiring animal testing. Symrise stated that safety is assessed by voluntary use and falls under the cosmetics ban.	Esso contested ECHA's letter: Statement of Non-Compliance sent to the French ministry, requiring animal testing. Esso argued the Article 13 (1) and Annex XI in REACH as proof that no animal tests are needed.
ECHA's Position	ECHA defended its decisions by emphasising the scientific basis of its evaluations and the need to protect human health and the environment.	ECHA defended its decisions on the grounds of strict adherence to scientific evaluations and legal frameworks within REACH.
General Court's Decision	The outcome ruled the Court's interpretation of REACH regulations and that the cosmetics ban and REACH do not have primacy, making both valid.	The Court ruled that it is possible to deviate from animal testing if alternative methods are possible and allowed within Article 13 (1) and Annex XI.
Similarities	Involved disputes over the interpretation and application of REACH regulations, focusing on protecting human health and the environment. One of the tests is requested in both cases, OECD No 414.	
Differences	The Court ruled that workers' safety and environmental protection are not yet guaranteed within current safety data. The requirement of animal testing stays. If Symrise can show alternative testing methods, ECHA could deviate from animal testing.	The Court granted an annulment of the letter by ECHA, giving Esso space to deviate from animal testing and using alternative methods. The substance was not subjected to the cosmetics ban.

Alternative (non-validated) testing methods

In the Symrise AG v. ECHA court case (Court of Justice of the European Union - General Court First Chamber, 2023), ECHA requested three types of extra studies that Symrise AG needed to perform (Table 4). No alternative is available in the TSAR database for the OECD No 414 or the prenatal developmental toxicity test (European Commission, 2024). Nevertheless, looking back at the similar Esso case, OECD No 414 could be replaced with other available data, or Weight of Evidence (WoE). Replacing such a test would save many rats and rabbits. Furthermore, a test could potentially be split up into multiple tests with alternatives. For instance, for developmental neurotoxicity (DNT), an *in vitro* testing battery is being developed (Masjosthusmann et al., 2020) that has been included in the European Food Safety Authority (ESFA) Development of a Roadmap for Action on New Approach Methodologies in Risk Assessment (Escher et al., 2022). DNT is part of the development of a foetus and, therefore, is of interest. Moreover, developing organs on a chip could play a role in placenta testing (Luconi et al., 2022).

The OECD No 234, fish sexual development (FSDT) test, or aquatic life study, currently has no alternative on the TSAR database. However, there is a zebrafish embryo acute toxicity test for acute fish toxicity testing (European Commission, 2013), which could potentially be developed to assess fish sexual development instead of acute toxicity (96 hours) by prolonging the exposure in lesser concentrations if further tested. However, this is limited to 120 hours, as after this a zebrafish is seen as animal. If longer exposure is required, more research on alternatives is needed. With the OECD No 443, extended one-generation toxicity study (EOGRTS), there are currently no alternatives on the TSAR database or other databases. One test related to EOGT was stopped in the TSAR database (European Commission & EURL ECVAM TSAR, 2024). This means that for this study, more research on alternatives is needed if this study is required to approve chemicals.

Table 4 Overview of requested tests in the Symrise AG v. ECHA court case and proposed alternatives or remarks.

Test required by ECHA	Test name	TSAR Database alternatives available	Possible replacement or remark
OECD No 414 (2018)	Prenatal developmental toxicity (PNDT) test.	No alternatives for PNDT.	Similar to Esso's case, could be replaced with other available data (WoE), saving many rats and rabbits. Splitting test up might be possible: developmental neurotoxicity (DNT) *in vitro* testing battery. Organ on a chip placenta.
OECD No 234 (2011)	Fish sexual development test (FSDT).	No alternatives for FSD.	Zebrafish embryo acute toxicity test could potentially be developed for this purpose by prolonging exposure at lower concentrations.
OECD No 443 (2018b)	Extended one-generation toxicity study (EOGRTS).	No alternatives for EOGT.	One test related to EOGT was stopped in the TSAR database. More research on alternatives is needed.

Discussion and conclusion

The Symrise AG v. European Chemicals Agency case has ignited a comprehensive debate surrounding the EU's animal testing ban for cosmetics, juxtaposed against the requirements set forth by the REACH regulation. This landmark case highlights an essential moment in the chemical safety and animal welfare regulatory landscape within the European Union, presenting a complex relationship between legal mandates, ethical considerations, and scientific advancement.

The European General Court's decision in November 2023 not only addressed a legal contestation but also elucidated the nuanced relationship between the EU Cosmetics Regulation and the REACH regulation. The Court's ruling affirmed that neither regulation holds primacy over the other, thereby necessitating a harmonised approach to their implementation. This demonstrates that it is of the utmost importance that regulations are constantly evaluated and that outdated protocols are reshaped to maintain a future-proof framework applicable to humans, animals, and nature. Furthermore, this interpretation ensures that while the ban on animal testing for cosmetics remains a testament to the EU's commitment to animal welfare, it does not exempt chemical substances used in cosmetics from the comprehensive safety assessments required under REACH, potentially including animal testing, particularly for worker safety and environmental protection.

The Court's decision to require Symrise AG to conduct additional toxicological testing on EH salicylate under the framework of REACH sets a precedent for future regulatory policies. It highlights the ongoing need to balance ethical considerations with the imperative of ensuring chemical safety across all potential exposure scenarios. This ruling reinforces the importance of advancing and validating alternative testing methods that can provide reliable safety data without resorting to animal testing. The decision is a wake-up call to the scientific community and industry stakeholders to intensify efforts towards the development, especially the acceptance and regulatory incorporation of such alternatives by policymakers and ECHA.
Furthermore, the case serves as a critical reference point for the cosmetics industry, regulatory bodies, and the scientific community in navigating the ethical challenges associated with chemical testing and safety assessment. The ruling elucidates the regulatory expectation that safety assessments should encompass a wide array of potential risks, including those to workers and the environment, beyond the direct consumer use of cosmetics. Perhaps it is possible to assure workers' safety in a way the UK now does by stating that it is assessed the same way as end-users. This broadened perspective necessitates continuously evolving testing methodologies that align with safety and ethical standards, using scientific evidence to choose the most optimal methods while assuring that procedures are still relevant.

Drawing lessons from the Esso v. ECHA court case, it is evident that the journey towards fully integrating alternatives into regulatory frameworks is challenging but not impossible. The Esso case highlighted the potential for legal and regulatory systems to adapt and evolve, paving the way for more inclusive approaches that recognise scientific advancements. In the Symrise AG case, while ECHA's insistence on animal testing reflects

a cautious approach to chemical safety, it also reveals a gap in the current regulatory mindset, where room for alternative methodologies is limited.
In light of the Symrise AG v. ECHA case, the need for harmonisation in regulatory practices has never been more apparent. The symbolic representation of the ECHA flowchart, regarded as a roadmap for compliance, must encompass this progressive shift towards alternative methodologies, as it currently shows a significant focus on animal testing. This does mean that the European Commission must honour the promise: "The Commission acts to accelerate phasing out of animal testing in response to a European Citizens' Initiative" (European Commission, 2023). This could be by ensuring a roadmap to phase out animal testing in chemical safety assessments. Moreover, the European Commission should pass laws mandating animal-free testing in chemical safety assessments, such as what the UK has done regarding all cosmetics chemicals. Besides that, EC and ECHA could revise REACH on the part that assures workers' safety, as it might be outdated that there is a need for separate groups of humans. Workers work in controlled environments with personal protective equipment (PPE), while end-users, including vulnerable groups such as babies, children, and people with diseases, use these chemicals intentionally.

In conclusion, the Symrise AG v. ECHA case exemplifies the dynamic interplay between regulation, science, and ethics in the realm of chemical safety and animal welfare. The ruling stresses the EU's commitment to maintaining high safety standards while respecting animal welfare, guiding future regulatory directions towards a more harmonised and ethically conscious approach. As the EU and its member states forge ahead, the imperative to support and adopt non-animal testing alternatives will become increasingly of importance, shaping a future where scientific integrity and ethical responsibility merge in the pursuit of protecting human health and the environment.
Therefore, the Symrise v. ECHA case is a call to action – a reminder that while significant progress has been made, the journey towards a regulatory landscape where alternative testing methods are not just an option but a norm is still ongoing. Finally, at the time of writing, Symrise AG has full rights to appeal the Court's ruling, which could change outcomes with the newly obtained knowledge. It is a battle worth continuing, not only for the sake of advancing science but also for upholding ethical standards in the pursuit of protecting human health and the environment.

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7. Appendix

A. Questionnaire

General questions:

- What is your name:
- What is your occupation:
- Country of your occupation:
- If applicable, how is your occupation connected to the Symrise AG v. ECHA case T-655/20:

Court case-specific questions:

- What specific legal issues were addressed by the European General Court in the Symrise AG v. ECHA case T-655/20?
- What were the main arguments Symrise AG and its interveners presented regarding the exemption of 2-ethylhexyl salicylate from additional REACH regulation testing?
- On what grounds did ECHA argue that 2-ethylhexyl salicylate required further testing under the REACH regulation?
- How did the European General Court interpret the relationship between REACH regulation and the EU Cosmetics Regulation in its decision?
- Can you identify and summarise any precedents or similar cases that the Court considered when deliberating on the Symrise AG v. ECHA case or have followed a similar setup?

Other:

- Do you have any remarks, tips, or anything else you want me to look into, find out, check, or think about, feel free to write it down as well:

B. Questionnaire results

Answers to the questionnaire remain withheld from this document, per the request of some respondents. The answers to the questionnaire are known to the people responsible for this review.