Deliverable 3.3: Sector specific briefs

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Introduction

The RECIPES project has given rise to the vision that implementation of the precautionary principle should ensure a high level of proactive protection of human health and the environment and stimulate societally desired innovation. Outcomes of the RECIPES project include case studies on the Precautionary Principle (PP) in specific technologies (such as plant protection products, GMOs, CRISPR-CAS9, artificial intelligence, nanotechnologies, etc..), and a guidance document on the application of the precautionary principle in the EU, advising on how to deal responsibly with uncertain risks[1] in the development and implementation of technologies. This sector-specific brief serves to complement the comprehensive main guidance, elaborating on what the lessons would mean for two **policy sectors** in the European Union (EU) (comprising of legal frameworks, policies and governing institutions such as directorates and departments) where the PP (in a double role- as a compass and a safeguard)[2] is relevant. The two policy sectors are:

- **Chemicals**, referring to both chemicals regulated by REACH, and specific groups of chemicals, such as biocides, pesticides, pharmaceuticals or cosmetics which are covered by their own legislation. The European Commission (EC) chemicals strategy for sustainability (2020) which is part of the EU's zero pollution ambition and a key commitment of the European Green Deal, aims to ensure that "*chemicals are produced and used in a way that maximises their contribution to society while avoiding harm to the planet and to current and future generations"* (EC, 2020, p 3).[3] The PP is central in several of the EC regulations relevant for the management of chemicals.
- **Gene technology**, referring here to technologies for modifying (GMOs) and editing (e.g. CRISPR Cas9) genes of non-human organisms, including gene-drives. These technologies are covered by the European GMO legislation, but discussions on the policies, regulations and the precautionary principle are ongoing especially in light of the recent Farm2Fork strategy of the EC.

[1] 'Uncertain risks' are understood in the RECIPES guidance as threats for which it is not possible to confidently quantify the magnitude of a defined and agreed range of outcomes or the probabilities of these outcomes.

[2] RECIPES (2022) *Policy Brief*, pp1: "*The precautionary principle works best in a dual role: as a safeguard and a compass. As a legal principle and safeguard, it can justify early policy or regulatory action to manage uncertain risks. As such, it ensures that the rights of current and future EU citizens are protected. As a compass and policy principle in research and innovation, the precautionary principle can trigger upstream debates and research about the potential impacts of emerging technologies and related innovation pathways, and can lead to adjustments in innovation development and stimulate responsible innovation*." https://recipes-project.eu/sites/default/files/2022-04/Recipes_PolicyBrief_03_Revised_220426.pdf

[3] Europeann Commission (2020). *Chemicals Strategy for Sustainability Towards a Toxic-Free Environment*. https://ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf

1. Chemicals

Public and scientific awareness on the growing global problem of chemical pollution[4] is increasing. This is coupled with an intensified focus on the management and regulation of chemicals, both in Europe with the EC Chemicals Strategy (2020)[5] and the Farm to Fork strategy (which is part of EUs Green Deal),[6] and globally with the agreement at the 5th UN Environment Assembly (early 2022) to start negotiations to establish an intergovernmental science policy panel to advise on chemical pollution and waste.[7] Chemical manufacturing is the fourth largest industry in the EU, and Global sales of chemicals were 3347 billion Euro in 2018.[8] In the EU governance system, chemicals are dealt with in policy areas such as Environment and Food Safety, and are especially relevant in the EC departments DG SANTE Health and food safety, DG GROW (Internal Market, Industry, Entrepreneurship and SMEs (where chemicals are a subsector) and DG ENV (Environment). **The PP is specifically mentioned as underpinning the guiding EC regulations for these policy areas**:

- PP underpins the 2007 Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).[9]
- PP underpins Regulation 1107/2009 for the marketing of Plant Protection Products (PPP).[10]
- PP is mentioned in Regulation (EU) No 528/2012 Concerning the making available on the market and use of biocidal products.[11]
- PP underpins Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products.[12]

Overarching lesson on the PP in the chemical sector: While the PP underpins the regulations mentioned above, there is criticism that the principle is not consequently or sufficiently applied, as indicated in is some of RECIPES' case studies[13] and other studies.[14] Below, some lessons on how to increase the relevance of the PP for balancing precaution and innovation of chemicals in the EU, are provided.

A) PP as a compass – steering research and innovation of chemicals

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[4] Landrigan, P.J., R. Fuller, N.J.R. Acosta, O. Adeyi, R. Arnold, N.N. Basu, A.B. Baldé, R. Bertollini, et al. (2018). The Lancet Commission on pollution and health. *The Lancet* 391: 462–512.
See also UNEP (2019). *Global chemicals outlook: From legacies to innovative solutions: Implementing the 2030 Agenda for sustainable development*. United Nations Environment Programme.

[5] EC (2020) Chemicals Strategy for Sustainability. Towards a Toxic-Free Environment. COM(2020) 667 final. https://ec.europa.eu/environment/pdf/chemicals/2020/10/Strategy.pdf.

[6] EC (2019) Communication on Green Deal (COM/2019/640 final) https://eur-lex.europa.eu/resource.html?uri=cellar:b828d165-1c22-11ea-8c1f-01aa75ed71a1.0002.02/DOC_1&format=PDF.

[7] https://www.unep.org/news-and-stories/press-release/un-environment-assembly-concludes-14-resolutions-curb-pollution and https://www.chemistryworld.com/news/world-agrees-to-sign-up-to-a-treaty-to-control-plastic-and-chemical-pollution/4015327.article.

[8] EC 2020 Chemicals Strategy for Sustainability Towards a Toxic-Free Environment Strategy.pdf (europa.eu)

[9] See Article 1 (3): *This Regulation is based on the principle that it is for manufacturers, importers and downstream users to ensure that they manufacture, place on the market or use such substances that do not adversely affect human health or the environment. Its provisions are underpinned by the precautionary principle. See* the 2022 consolidated version, https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02006R1907-20220501.

[10] SeeArticle 1 (4): *The provisions of this Regulation are underpinned by the precautionary principle in order to ensure that active substances or products placed on the market do not adversely affect human or animal health or the environment. In particular, Member States shall not be prevented from applying the precautionary principle where there is scientific uncertainty as to the risks with regard to human or animal health or the environment posed by the plant protection products to be authorised in their territory.* See the 2022 consolidated version, https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02009R1107-20210327.

[11] See Article 1 (1) : […] *The provisions of this Regulation are underpinned by the precautionary principle, the aim of which is to safeguard the health of humans, the health of animals and the environment. […]. See* the 2022 consolidated version, https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02012R0528-20220415;

[12] See consideration **Fout! De hyperlinkverwijzing is ongeldig.**36 of the preamble: Action by the Commission and Member States relating to the protection of human health should be based on the precautionary principle, and Article 19 (d): *particular precautions to be observed in use, and at least those listed in Annexes III to VI and any special precautionary information on cosmetic products for professional use.* See the 2022 consolidated version https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02009R1223-20220301.

[13] RECIPES case studies on neonicotinoids, glyphosate and endocrine disruptors, https://recipes-project.eu/results.

[14] EEA (European Environment Agency) (2013). *Late lessons from early warnings: Science, precaution, innovation*. Publications Office of the European Union. https://www.eea.europa.eu/publications/late-lessons-2.

Using the precautionary principle as a compass and policy principle can help policy makers and industry guide innovation towards more societally acceptable directions. It also implies that lock-in on particular technologies should be avoided. Precautionary steering of research and innovation of chemicals includes:

- **Promoting green chemistry[15] and safe and sustainable-by-design,** in line with EC chemical strategy (2020, p.4). It entails assessing product performance against requirements for safety and sustainability at the design stage of product development, rather than after a product has been designed and is on the market[16]. Broadening the anticipation phase, including considering possible substitutes (alternatives assessment)[17] could help avoiding regrettable substitution.[18] The case of Bisphenol A (BPA) is illustrative here where a chemical with a similar design replaced BPA instead of changing the design[19]. However, even safe-by-design products should be open for reconsideration if new knowledge emerges.
- **Enabling transparency and public discussions** of 'what innovative chemicals society actually needs and wants' and allowing such discussions to inform the regulation of chemicals, in line with the aims of Responsible Research and Innovation (RRI). The EC Chemicals Strategy states that "*Chemicals should be produced/used in a way that maximises their benefits to society while avoiding harm to planet & people*"[20], and thus the broader society should be engaged in determining what benefits society. Challenges here include avoiding that engagement and responsibility are not reduced to the ticking of boxes in research and innovation projects, and promoting RRI in research that is not publicly funded[21].
- **Investing in a diversification of technologies** and promoting innovation of alternatives.[22] The RECIPES case study on Neonicotinoids illustrates that restrictions imposed did not hinder innovation, but created different innovation pathways for pest management, such as new plant protection technologies and innovations of non-chemical alternatives.[23] Similarly, it is argued that applying the precautionary principle to all Endocrine Disrupting Chemicals can boost eco-innovation in finding sustainable and safer substitutes.[24]

B) PP as a safeguard: Managing and regulating chemicals on the market

While improving chemical regulation is mentioned in the United Nation's sustainability goals 3.9 and 12.4, and in the EU green deal[25] regulatory approaches and frameworks have not enabled adequate and timely action on most hazardous chemicals.[26] Precautionary considerations when managing and regulating chemicals for the market would imply:

- **Acknowledging the inherent uncertainties in risk assessments.** Accepting scientific uncertainty is at the core of the PP. There are significant scientific uncertainties on how different chemicals accumulate and affect living organisms and the environment, and on the cocktail effects of different chemicals on health and environment. However, it is found that

[15] RECIPES Case Study 3 on Endrocrine disruptors, p 23. See also: Tickner, J. A., Simon, R. V., Jacobs, M., Pollard, L. D., & van Bergen, S. K. (2021). The nexus between alternatives assessment and green chemistry: supporting the development and adoption of safer chemicals. *Green Chemistry Letters and Reviews*, *14*(1), 23-44.

[16] EEA (2021) Designing safe and sustainable products requires a new approach for chemicals. https://www.eea.europa.eu/publications/designing-safe-and-sustainable-products-1/delivering-products-that-are-safe For furhter guidance, see also OECD (2021) Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternatives https://sdg.iisd.org/news/oecd-releases-guidance-on-selecting-safer-chemical-alternatives/

[17] Tickner, J., Jacobs, M. M., & Mack, N. B. (2019). Alternatives assessment and informed substitution: A global landscape assessment of drivers, methods, policies and needs. *Sustainable Chemistry and Pharmacy*, *13*, 100161

[18] RECIPES Guidance on the application of the precautionary principle in the EU, p. 80**.**

[19] RECIPES Guidance on the application of the precautionary principle in the EU, p. 78, box 6.

[20] EC (2020) Chemicals Strategy for Sustainability Towards a Toxic-Free Environment Strategy.pdf (europa.eu)

[21] RECIPES Guidance on the application of the precautionary principle in the EU, p. 79.

[22] RECIPES Guidance on the application of the precautionary principle in the EU, p. 45.

[23] Case study on Neonicotinoids, pp. 33-35.

[24] Case study on Endocrine disruptors, p 23

[25] EC (2019) communicaiton on the European Green deal, pp 15: "*the regulatory framework will need to rapidly reflect scientific evidence on the risk posed by endocrine disruptors, hazardous chemicals in products including imports, combination effects of different chemicals and very persistent chemicals*". https://ec.europa.eu/info/sites/default/files/european-green-deal-communication_en.pdf

[26] UNEP (2019). *Global chemicals outlook: From legacies to innovative solutions: Implementing the 2030 Agenda for sustainable development*. United Nations Environment Programme. https://wedocs.unep.org/20.500.11822/27651.

current assessment regimes, such as in the BPA controversy, discount relevant uncertainties and rather emphasise the features of given problems that are most amenable to standardisation, protocolisation and quantification.[27]

- **Understanding what scientific uncertainty implies in relation to applying the PP.** The court cases on the bans of 3 neonics illustrate some different perceptions on this.[28] The need for some kind of plausibility of proof of a threat of harm does not require conclusive evidence, as it would be with the prevention principle. In assessing the situation, the decision on whether precautionary action is justified needs to take into consideration the 'knowledge condition', such as reasonable grounds for concern, and choose which interests are given the benefit of the doubt, such as environmental protection or national economy. These are political decisions that must be made, considering risk assessment, wider social and economic factors, legal requirements and policy imperatives.[29]
- **Acknowledging that the use of cost-benefit analysis is of limited value in cases that require the precautionary principle.** Not only the risks assessment of new products and technologies can be plagued by inconclusive evidence and uncertainties, the proclaimed benefits are often also poorly known. One cannot weigh fundamentally unknown costs against fundamentally unknown benefits without making highly speculative assumptions.[30]
- **Including a broader range of science advice for policy** such as peer-reviewed academic studies and local and experience-based knowledges, and be continuous open to including new (or previously overlooked) end-points for risk assessment – and/or new non-target organisms – for assuring a high level of protection.[31] As noted in the RECPES guidance, ***actionable knowledge for the precautionary principle*** *is knowledge on the severity and nature of potential adverse effects, the nature of the uncertainties on the risks and on the proclaimed benefits, explicit articulation of knowledge gaps regarding risks and benefits, and knowledge on possible alternatives to the risky technology, or product under scrutiny*.[32] Embracing non-standard knowledge may enhance inherent ambiguities and controversies over what constitutes valid, reliable and relevant research, but it is necessary to ensure that the most relevant research is considered.[33]
- **Enhancing public participation and transparency,** with awareness to risk governance arrangements, situational and institutional factors, the objective of stakeholder engagement, transparency of the participatory process as well as power asymmetries amongst stakeholders.[34] The case of Glyphosate illustrates some of the challenges of upholding transparency, and how the lack of transparency in both risk assessment and risk management processes was central in public controversies.[35] Transparency is more than access to information; it must be an active demonstration of timely and deliberative effort to include and inform relevant interested and affected groups and the wider public. In line with the Aarhus convention on Access to Information, Public Participation in Decision-Making and Access to Justice in Environmental Matters[36], the public needs open and unhindered access to data on what chemicals (including pesticides and biocides) are used where, when and in what quantities. Today, the EU's legal framework to warrant such access is weak and as a result, Eurostat receives incomplete data from Member States on the use of pesticides and only publishes very vague aggregated datasets.[37]
- **Increase learning and information sharing across regulatory domains and move towards a holistic approach to chemical authorization and regulation.**[38]

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[27] Lemus, D., & Kovacic Z. (2021). Precise yet uncertain: Broadening understandings of uncertainty and policy in the BPA controversy. *Risk Analysis*. https://doi.org/10.1111/risa.13860
[28] RECIPES Case study neonicotinoids
[29] RECIPES Guidance on the application of the precautionary principle in the EU, p. 46.
[30] RECIPES Guidance on the application of the precautionary principle in the EU, p. 48.
[31] RECIPES Guidance on the application of the precautionary principle in the EU, pp. 58, 70-77.
[32] RECIPES Guidance on the application of the precautionary principle in the EU, p. 15.
[33] RECIPES Guidance on the application of the precautionary principle in the EU, pp. 70-77.
[34] RECIPES Guidance on the application of the precautionary principle in the EU, pp. 116-118.
[35] Case study on Glyphosate, pp 31-3.
[36] https://ec.europa.eu/environment/aarhus/
[37] Client earth (2022). Time to fill the data gap on the use of pesticides - Analysis of the Council position on the reform of pesticides statistics. https://www.clientearth.org/latest/documents/time-to-fill-the-data-gap-on-the-use-of-pesticides/
[38] RECIPES Guidance on the application of the precautionary principle in the EU, p. 77.

Neonicotinoids represent a case of a substance that is recognized to be harmful in one regulatory domain and tolerable in others: some neonics are no longer authorized for use as pesticides but they can still be used as biocides and in veterinary medicine.[39] Another example is PFAS, where a substance-by-substance risk assessment and management approach is not adequate to efficiently prevent risk to the environment and human health from a single PFAS or mixtures of them.[40] The Green Deal 'one chemical one assessment' (OS-OA) is an important move in the direction of more holistic assessments.[41]

- A**cknowledging the limitations of regional safeguarding**, and work towards international chemicals management on both chemicals generally[42], and on more specific plant protection products.[43]
- **Enabling swifter reactions to early warnings, new knowledges or risks connected to already approved chemicals.** This implies improving and the system-uptake of emerging knowledges of risks. In the Commission 2000 Communication on the precautionary principle, it is stated that measures should be periodically reviewed in the light of scientific progress, and amended as necessary. There are processes and practises within EUs risk assessment procedures that address this[44] but it needs to be backed up and expanded.[45] In the case of neonics, early warnings were ignored because they came from beekeepers and explorative academic studies, and this hampered the timely application of the precautionary principle.[46]

[39] RECIPES neonicotionoids case study.
[40] EEA (2019) Emerging chemical risks in Europe – PFAS. See aslo Grandjean, P. (2018). Delayed discovery, dissemination, and decisions on intervention in environmental health: A case study on immunotoxicity of perfluorinated alkylate substances. Environmental Health, 17(62). https://doi.org/10.1186/s12940-018-0405-y .
[41] ECHA and EFSA (2020) In support of the EU chemicals strategy for sustainability: One substance – one assessment https://echa.europa.eu/documents/10162/21877836/efsa-echa-position-paper-osoa_en.pdf/74b1ae31-290b-a608-85e9-05b340840b34
[42] Wang, Z., Altenburger, R., Backhaus, T., Covaci, A., Diamond, M. L., Grimalt, J. O., ... & Suzuki, N. (2021). We need a global science-policy body on chemicals and waste. *Science*, *371*(6531), 774-776. https://doi.org/10.5281/zenodo.2559189
Wang, Z., Summerson, I., Lai, A., Boucher, J. M., & Scheringer, M. (2019). Strengthening the science-policy interface in international chemicals governance: A mapping and gap analysis. *Zenodo*.
[43] Drivdal, L., & van der Sluijs, J. P. (2021). Pollinator conservation requires a stronger and broader application of the precautionary principle. *Current opinion in insect science*, *46*, 95-105.
[44] See eg EFSA Scientific Committee publication: Hardy, A., Benford, D., Halldorsson, T., Jeger, M. J., Knutsen, H. K., More, S., Naegeli, H., Noteborn, H., Ockleford, C., Ricci, A., Rychen, G., Schlatter, J. R., Silano, V., Solecki, R., Turck, D. & Younes, M. (2017). Guidance on the use of the weight of evidence approach in scientific assessments. EFSA Journal, 15(8), 4971. https://doi.org/10.2903/j.efsa.2017.4971
[45] RECIPES Guidance on the application of the precautionary principle in the EU, pp. 70-77.
[46] Case study, p. 38, RECIPES Guidance on the application of the precautionary principle in the EU, pp. 71-72.

2. Gene technology in agriculture

Biotechnology is a topic in several EC departments, including DG GROW (Internal Market, Industry, Entrepreneurship and SMEs), DG RTD (Research and innovation) and DG agriculture and DG for Health and Consumers.[47] According to the ECs DG GROW**,** biotechnology contributes to the modernisation of European industry, and is used in a variety of industrial sectors such as healthcare and pharmaceuticals, animal health, textiles, chemicals, plastic, paper, fuel, food, and feed processing.[48] Here we focus on genetically modified organisms (GMOs) and new genomic techniques (NGT, such as CRISPR-Cas9) in agriculture. To date, EU has granted approval for the import of over 80 genetically modified (GM) food and feed varieties, but only one GM crop is currently commercially grown in the EU.[49] As part of a precautionary approach, the developer of a GMO has to apply for authorization under the Deliberate Release Directive. The Court considered NGTs to be subject to the EU GMO – Directive. NGT-products are GMOs in the legislation. There is an ongoing controversy around regulations of NGTs, which has intensified after the EC published a study in 2021 regarding the status of NGTs under Union law.[50] In the discussion around the European Green Deal and the Farm to Fork strategy, the role of NTGs is also subject of debate.

The two main EU legislations that regulate GMOs (including NGTs) (Directive 2001/18/EC and Regulation 1829/2003) specifically mention the Precautionary principle:

- Article 1 Directive 2001/18 provides that its provisions apply in accordance with the precautionary principle, and Article 4 provides a general obligation for Member States to ensure that all appropriate measures are taken to avoid adverse effects on human health and the environment 'in accordance with the precautionary principle.
- The principles for the Environmental Risk Assessment (ERA) of GMO's are described in Annex II of the Directive on Deliberate Release. Here, reference is made to the precautionary principle as underlying a number of general principles that should be followed when performing the ERA.
- In addition, the PP is central in the Cartagena Protocol on Biosafety which is ratified by all UN member states (except the United States). This binding agreement aims to protect biodiversity and human health and sets international rules to ensure the safe handling and transportation of GMOs.

Overarching lesson on the PP in the gene technology sector: Similar to the chemical sector, the PP is mentioned in regulations, but its actual role compared to other principles and considerations is uncertain and ambiguous. The PP is sometimes referred to in public controversies, where different stakeholders have very different interpretations of its role, meaning and significance.

A) PP as a compass – steering gene technology research and innovation

The main RECIPES guidance document supports the idea that there is no inherent contradiction between precaution and innovation, and that the precautionary principle can help steering innovation into societally beneficial directions. Thus, the precautionary principle as a compass requires to direct innovation processes towards inherently safe, clean and sustainable production, and guides innovation towards more societally acceptable directions.[51] Lessons from the RECIPES case studies and the guidance document consultations point out that steering innovations with precaution could imply:

- **Accommodating public discussions around future gene technological innovations.** Since gene technology may lead to major societal changes, the general public should be involved in the governance of these innovations. It is crucial to engage a broad group of stakeholders and citizens from early research phases, including before

[47] https://ec.europa.eu/food/plants/genetically-modified-organisms_en.
[48] https://ec.europa.eu/growth/sectors/biotechnology_en.
[49] Find details here: https://webgate.ec.europa.eu/dyna/gm_register/index_en.cfm.
[50] EC (2021) Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16. https://ec.europa.eu/food/plants/genetically-modified-organisms/new-techniques-biotechnology/ec-study-new-genomic-techniques_en.
https://www.europarl.europa.eu/RegData/etudes/BRIE/2021/698760/EPRS_BRI(2021)698760_EN.pdf.
[51] RECIPES Guidance on the application of the precautionary principle in the EU, p. 29.

research agenda setting[52]. How to do this in practice is however challenging, as societal implications in early phases are not yet clear, and societal commitment is lacking (the Collingridge dilemma)[53]. This means that such an anticipatory approach requires considerable effort and careful preparation. Different scenario approaches using creative tools enable discussions with citizens and stakeholders about desirable futures and the implications of uncertain developments.

- **Promoting the PP in research.** The PP can be seen as an ethical issue in GMO (including NGT) research, that is ideally incorporated in the research by highlighting and discussing scientific uncertainties and possible risks generated from the research[54]. However, we must keep in mind that researchers have a specific interest and perspective in this and must be guided and stimulated in this process by research programmers and policy makers[55]. Challenges include avoiding that ethics and anticipation are reduced to the ticking of boxes in research and innovation projects, and promoting RRI in research that is not publicly funded.[56]
- **Allowing for (moving to) alternative research pathways within research funding**.[57] It should be financially possible to broaden up the research agenda to alternative solutions - including social innovation.
- **Promoting safety-by-design, taking the environment and human health into account in the design phase of new technology.**[58] Examples are intrinsic biocontainment using genetic safeguards, or genetic reversal drives that can undo the unintended consequences of gene drives.[54] Safety-by-design requires a new kind of safety awareness and a different mind-set from researchers, their managers and investors. This can be promoted in their training, and there are also examples of tools that stimulate safety in the design practice.[59] While safety-by-design is promoted by some as central for balancing innovation and precaution,[60] it should be noted that it can also be problematic if the Safe-by-Design approach moves the bulk of the responsibility for safety to the actors in the research and development phase. Also, it assumes that safety can be defined and understood by all stakeholders in the same way.[61]

B) PP as safeguarding: Managing and regulating GM-crops for the EU market

While few GM-crops are approved for cultivation in the EU, discussions of reconsidering regulations (especially of NGT such as CRISPR Cas9) are ongoing.[62] The EC is for instance considering amending the GMO-Directive to treat small changes in the genome (targeted mutagenesis) differently from other GMOs. Considering the PP as a safeguard in current and in possible future regulations for GMOs (including NGT) would imply:

- **Explicit and transparent problem scoping:** policymakers, scientific experts, and, depending on the case, also relevant stakeholders should engage in a dialogue in order to define the risks and scientific uncertainties that need to be addressed in risk

[52] RECIPES CRISPR CAS9 Case study, abstract.
[53] Collingridge, D. (1980) The Social Control of Technology, New York: St. Martin's Press.
See also Genus, A., & Stirling, A. (2018). Collingridge and the dilemma of control: Towards responsible and accountable innovation. *Research policy*, *47*(1), 61-69.
[54] See eg the Norwegian National Committee for Research Ethics in Science and Technology (2016), guideline number 8 and 9. www.forskningsetikk.no/en/guidelines/science-and-technology/guidelines-for-research-ethics-in-science-and-technology/ . See also Strand, R., & Oughton, D. (2009). *Risk and uncertainty as a research ethics challenge*. National Committees for Research Ethics in Norway. https://www.forskningsetikk.no/ressurser/publikasjoner/risk-and-uncertainty-as-a-research-ethics-challenge/
[55] RECIPES CRISPR CAS9 Case study, p. 23.
[56] RECIPES Guidance on the application of the precautionary principle in the EU, p. 79.
[57] RECIPES CRISPR CAS9 Case study, p. 26.
[58] RECIPES Guidance on the application of the precautionary principle in the EU, p. 52.
[59] https://www.rathenau.nl/en/biotechnology-and-safety
[60] van Gelder, P., Klaassen, P., Taebi, B., Walhout, B., van Ommen, R., van de Poel, I., ... & Jung, D. (2021). Safe-by-design in engineering: An overview and comparative analysis of engineering disciplines. *International Journal of Environmental Research and Public Health*, *18*(12), 6329.
[61] Asin-Garcia, E., Kallergi, A., Landeweerd, L., & Dos Santos, V. A. M. (2020). Genetic safeguards for safety-by-design: so close yet so far. *Trends in Biotechnology*, *38*(12), 1308-1312.
Robaey, Z., Spruit, S. L., & van de Poel, I. (2018). The food warden: An exploration of issues in distributing responsibilities for safe-by-design synthetic biology applications. *Science and Engineering Ethics*, *24*(6), 1673-1696.
[62] Legislation for plants produced by certain new genomic techniques (europa.eu)

assessments.[63]

- **Broadening the risk assessment**[64] to capture all potential genomic irregularities arising from genome editing and suggest additional tools to assist the risk assessment of genome-edited plants and animals for the environment and food/animal feed in the EU.[65]
- **Addressing conflicts that concern values, knowledge and interests in decision making about applying the precautionary principle**. Participatory deliberations can contribute to research mission orientation/ problem scoping and help to identify decision alternatives.[66] An example of such a process is the societal incubator.[67] Social science literature has highlighted the lack of formal consideration of socio-economic or ethical considerations in assessment processes as a contributing factor of the nineties GMO-controversy.[68] An appeal to scientific evidence to convince society on the public value of GMOs has been shown to be insufficient, because scientific evidence on harms does not exhaust the issues society deems to be important.
- **Acknowledging the limitations of regional safeguarding**, and working towards international management and regulations. In the past twenty years we have seen that current EU regulations have led to a *de facto* moratorium on the cultivation of GMOs in Europe. However, in other countries this has not been the case. International regulations should be re-aligned with technologies on the horizon such as gene-drives that raise questions on **transboundary movement and transboundary harm** (Redford et al, 2019).[69]
- **Moving beyond the use of cost-benefit analysis.** This type of analysis would require the comparison of the overall cost to the EU of action and lack of action, in both the short and long term, including non-economic considerations.[70] It has early on been argued that precautionary approaches to GMOs underline the multidimensional nature of environmental qualities and risks, such as irreplaceability, irreversibility, uncertainty and complexity.[71] In practice, this is not feasible. Rather, cost-benefit analyses tend to discount future interests and needs and focus mostly on short terms benefits,[72] failing to take into account fundamental issues like poverty or climate change.[73]
- **Pluralization of expert knowledge and transdisciplinary approaches**[74] **is a cornerstone in responsible innovation.** Ambiguity with regard to for example the value of nature implies the need to emphasize mutual learning across academic, regulatory and other civil society communities.[75] The inclusion of other perspectives tends to provide a more holistic comprehension of the costs and benefits of a choice of action.[76]
- Stakeholders (such as developers of a new technology and the future generations) are affected in different ways by gene technology, and differ in terms of ability to defend their rights.[77] Gene technology can strongly affect inter alia nature and future generations, but their stake is always indirectly voiced.[78] **It is important that the power asymmetry is made explicit in participatory processes aiming at power transparency**.[79]

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[63] RECIPES Guidance on the application of the precautionary principle in the EU, p. 66.
[64] RECIPES Guidance on the application of the precautionary principle in the EU, pp. 69-70.
[65] Kawall, K., Cotter, J., & Then, C. (2020). Broadening the GMO risk assessment in the EU for genome editing technologies in agriculture. *Environmental Sciences Europe*, *32*(1), 1-24.
[66] RECIPES Guidance on the application of the precautionary principle in the EU, p. 99-100.
[67] Rathenau Institute (2016) Beyond public acceptance Design of a societal incubator for promising (nano)technologies. https://www.rathenau.nl/en/knowledge-democracy/beyond-public-acceptance
[68] Macnaghten, P., & Habets, M. G. (2020). Breaking the impasse: Towards a forward-looking governance framework for gene editing with plants. *Plants, People, Planet*, *2*(4), 353-365.
[69] RECIPES CRISPR CAS9 Case study, p. 24-25
[70] RECIPES Guidance on the application of the precautionary principle in the EU, p. 49.
[71] Aslaksen, I., & Myhr, A. I. (2007). "The worth of a wildflower": Precautionary perspectives on the environmental risk of GMOs. *Ecological Economics*, *60*(3), 489-497.
[72] RECIPES CRISPR CAS9 Case study, p. 12.
[73] RECIPES CRISPR CAS9 Case study, abstract.
[74] RECIPES Guidance on the application of the precautionary principle in the EU, p. 58.
[75] RECIPES CRISPR CAS9 Case study, p. 12.
[76] RECIPES Guidance on the application of the precautionary principle in the EU, p. 75.
[77] RECIPES Guidance on the application of the precautionary principle in the EU, p. 117.
[78] RECIPES CRISPR CAS9 Case study, p. 26.
[79] RECIPES Guidance on the application of the precautionary principle in the EU, p. 118.