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Review

When similar chemicals meet different rules: Environmental standards in the licensing of medicinal and plant protection products in the EU and USA

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ABSTRACT

This article presents a comparative analysis of environmental standards employed in the licensing of human medicinal products (HMPs), veterinary medicinal products (VMPs), and plant protection products (PPPs) across the European Union (EU) and United States of America (USA). Despite structural and functional similarities, these chemicals are regulated separately, resulting in divergent environmental (risk) assessment (E(R)A) procedures. Using a qualitative case study approach, this research examines domestic licensing procedures across four thematic areas: institutional context, E(R)A requirements, post-authorisation obligations, and the treatment of legacy and generic products. We frame our analysis through the lens of three policy design concepts — integration, participation, and stringency — revealing that PPPs are subject to the most stringent environmental standards, followed by VMPs, and HMPs subject to the least. EU regulations are generally more stringent than those in the USA, particularly regarding E(R)A data requirements, substitution obligations, and the practical weight of the E(R)A in influencing licensing decision making. Our study identifies regulatory gaps, especially in the treatment of legacy products, co-formulants and categorical exclusions. We thus propose five policy recommendations to enhance the stringency of environmental standards in the licensing of these products: legislative enshrinement of E(R)A data requirements for pharmaceuticals; reduction of E(R)A categorical exclusion eligibility; extension of substitution obligation to pharmaceuticals; periodic licence renewals for medicinal products involving re-evaluation of E(R)A data; and E(R)As covering complete product formulations, not only active substances. This research contributes a novel cross sectoral and cross-jurisdictional perspective on synthetic chemicals regulation and environmental governance.

1. Introduction

Medicinal and plant protection products – two related groups of synthetic chemicals – have both been linked to recent advancements in human lifespan, healthspan, and in maintaining the health and welfare of farmed animals (Campos et al., 2019; Cooper and Dobson, 2007). Human life expectancy globally has more than doubled over the last two centuries (Dattani et al., 2023a), and child mortality has fallen to 4.3% from a rate of up to 50% among hunter-gatherer societies (Dattani et al., 2023b). Over the last six decades, global production of crops and livestock (including from aquaculture) has risen nearly four-fold (Fuglie et al., 2024), with cereal yields alone increasing by 209% (Ritchie et al., 2022a). Meanwhile, dependence on these chemicals is growing: the use of pesticides globally increased by 97% between 1990 and 2021 (Ritchie et al., 2022b); consumption of human pharmaceuticals grew by 14% between 2018 and 2023, with a further 12% increase expected by 2028 (IQVIA, 2024); and it's estimated that global use of antibiotics in livestock by 2040 could be 30% higher than in 2019 (Acosta et al., 2025).

Chemically, medicinal and plant protection products are highly similar, differing in some cases by just a single functional group (Hao et al., 2011; Tice, 2001). Their molecular, structural, and functional similarities have led to overlapping research and development, with

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Table 1
Overview and description of codebook themes (source: own representation)

Theme	Description
Institutional Context	Encompasses the formal and informal structures that influence domestic regulatory outcomes, providing an overview of the contextual framework within which product licensing takes place.
Environmental (Risk) Assessment	Contains criteria relating to the E(R)A of medicinal and plant protection products in their respective licensing procedures, including testing requirements and the extent to which findings can influence licensing decision-making.
Post-Authorisation	Covers ongoing environmental standards post-licensing, including criteria on licence renewal and licence holder obligations.
Legacy & Generic Products	Covers the treatment of medicinal and plant protection products granted marketing authorisation before current E(R)A standards came into force, as well as the licensing of generics based on already-licensed products.

newly synthesized chemicals often evaluated for both pharmaceutical and pesticidal applications (Swanton et al., 2011). Despite their similarities in chemical makeup and metabolic function, medicinal and plant protection products are treated distinctly from one another in licensing procedures, often under the jurisdiction of different regulatory bodies and subject to varying levels of environmental safety testing (Oelkers, 2021; Swanton et al., 2011). As a result, the environment is left vulnerable to different levels of exposure to these chemicals, and non-target species at varying risk of adverse physiological effects (Lenzen et al., 2020; Stehle and Schulz, 2015b). In the short-term, non-target species can suffer from, among other things, reproductive problems, genetic mutations and excess mortality (Wood and Goulson, 2017). In the longer-term, these effects can compound, causing species-, population-, or ecosystem-level impacts (Green et al., 2004; Newton, 1979). Sometimes these population effects involve bioaccumulation of toxic residues, with resulting propagation effects across successive links on the food chain (Newton, 1979).

To our knowledge, a multi-jurisdictional comparison and analysis of environmental standards employed in the licensing of human medicinal products (HMPs), veterinary medicinal products (VMPs), and plant protection products (PPPs) – collectively referred to as medicinal and plant protection products – has yet to be undertaken. The extant literature has so far been limited by substance (Chen et al., 2023; de la Casa-Resino et al., 2021; Gildemeister et al., 2023), geographic scope (Fabrega and Carapeto, 2020; Moore et al., 2021; Stehle and Schulz, 2015b), environmental compartment (Oelkers, 2021; van Dijk et al., 2021), or policy breadth (Botos et al., 2019). We therefore pose the following question: *how do environmental standards vary in the licensing of medicinal and plant protection products across the European Union (EU) and United States of America (USA)?* To answer this, we first review the extent and nature of variance in licensing standards for these products across two of the world's largest economies – the EU and USA – and then frame our discussion through analysis of three policy design concepts: integration, participation, and stringency. We end with our conclusions and policy recommendations.

2. Methods

We took a qualitative, comparative case study approach to investigate the environmental standards employed in the licensing of medicinal and plant protection products across two contexts – the EU and USA – which were selected as case studies due to their market dominance (EFPIA, 2025; Ritchie et al., 2022a) and global leadership on this issue (Walter and Mitkidis, 2018), contrasted with their differential approaches to the management of environmental risk (Baylis et al., 2008; Kelemen and Vogel, 2010).

Data collection involved the review of documents spanning policy, academic, and grey literature. We used a hybrid search strategy combining snowballing with database searches (e.g., EUR-Lex, U.S. Code) (Wohlin et al., 2022), covering the outputs of the legislative (statutes, bills), executive (regulations), and judicial (decisions, rulings) branches of government. Data were then analysed using the qualitative coding software MAXQDA (VERBI Software, 2024). Coding was an iterative process; we first derived four themes (as codes) inductively, by screening and collating our data, to compare our case studies. Described in Table 1, these themes include the institutional context within which licensing occurs, the core aspect of environmental standards – the Environmental (Risk) Assessment[1] (E(R)A) process – and further nuances such as post-authorization requirements and the approach to legacy and generic products. These themes were further subdivided into subcodes, the full list and definitions of which can be found in Appendix 1. The use of MAXQDA was structural rather than quantitative: codes and subcodes assisted in grouping conceptually related material. We did not use code frequencies to make comparative claims, as these would risk overstating precision and conflating document volume with regulatory weight. Instead, coding supported the transparent, reproducible organisation of evidence from which we developed the analytical comparison presented in the Results & Discussion.

In a second step, we drew on three policy design concepts relevant to environmental protection to structure our analysis, namely integration and participation for the first (institutional context) theme, and stringency for the latter three (Table 1). In the context of this research, these policy design concepts are defined as follows.

- *Integration*: the degree of unification and coordination between institutional decision-making loci in licensing processes (Bouckaert et al., 2010; Hooghe et al., 2003). Our focus is on institutional integration, particularly multi-level (high integration) versus horizontal (low integration) governance structures, not on integration as defined in the European environmental policy discourse (Jordan and Lenschow, 2010; Lafferty and Hovden, 2003).
- *Participation:* the involvement of citizens in the design, implementation and evaluation of environmental policies (Newig et al., 2023). Arnstein's (1969) eight-rung ladder of citizen participation varies in gradations ranging from non-participation through to degrees of tokenism (low participation: informing, consultation, placation) and citizen power (high participation: partnership, delegation, citizen control).
- *Stringency*. Referring to the level of coerciveness or constraint a policy imposes on actors; stringency pertains to the strictness of regulatory standards or requirements. Often operationalised as a spectrum or continuum, stringency is a matter of degree: the tighter the policy's requirements or the higher its explicit or implicit price on environmentally harmful behaviour, the more stringent it is (Botta and Koźluk, 2014).

We then compared the degree of stringency in a final step to delineate the most significant differences in licensing standards overall, both inter- and intra-jurisdictionally. Rather than numerical scoring, we operationalize stringency qualitatively, employing a criteria-based scale

[1] For the purposes of comparison in this research, 'environmental (risk) assessment' ('E(R)A') will be used as a catch-all term to describe the process of evaluation of environmental risks for HMPS, VMPS and PPPs in both the EU and USA. While not officially labelled as an 'environmental risk assessment' (the term used in the EU) or an 'environmental assessment' (the term used for medicinal product licensing in the USA), licensing of PPPs in the USA nonetheless requires an assessment of environmental risk (Schierow and Esworthy, 2012).

Table 2
Degrees of stringency (source: own representation, adapted from Botta and Koźluk's (2014) EPS Index)

Degree of Stringency	Qualities of Licensing Procedures
Very Low	Very weak standard; voluntary, symbolic or purely informational; very weak enforcement; no cost or coerciveness
Low	Weak standard; often voluntary, symbolic or purely informational; weak enforcement; minimal cost and minimal coerciveness
Moderate	Relatively robust standard with clear regulatory limits; mix of binding and voluntary; some flexibility or offset mechanisms; moderate non-compliance cost and moderate coerciveness
High	Strong standard with binding regulatory limits; little flexibility or scope for offset mechanisms; strong enforcement; sanctions for non-compliance and high coerciveness
Very High	Very strong standard with strict quantitative limits; no flexibility or scope for offset mechanisms; very strong enforcement; high sanctions for non-compliance; maximum coerciveness

Table 3
Summary of institutional context factors (source: own representation)

Jurisdiction	Criterion	HMP	VMP	PPP
EU	Responsible body	European Commission, European Medicines Agency, National Competent Authorities		European Commission, European Food Safety Authority, National Competent Authorities
	Government system	Supra-national organisation, multi-level representative democracy		
	Principal legislation	Directive, 2001/83/EC, Regulation (EC) 726/2004	Regulation (EU) 2019/6	Regulation (EC) No 1107/2009
	Interstate licensing variance	National, decentralised and mutual recognition procedures allow licensing at the Member State level		Product authorisations granted by National Competent Authorities at Member State or zonal level
	Public consultation pre-licensing	No	No	Yes
USA	Responsible body	Food & Drug Administration		Environmental Protection Agency
	Government system	Constitutional federal republic, representative democracy		
	Principal legislation	Federal Food, Drug and Cosmetics Act (FDCA), National Environmental Policy Act (NEPA)		Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)
	Interstate licensing variance	States cannot license pharmaceuticals independently		State licensing decisions at least as stringent as federal licensing
	Public consultation pre-licensing	Conditional	Conditional	Yes

to compare regulatory stringency across product classes and jurisdictions. The rationale for this decision is two-fold: first, the heterogeneity of instruments and legal architectures across sectors makes cardinal weighting difficult; and second, a quantitative approach risks over-precision where indicators are not directly comparable and evidence is document-based. We therefore qualitatively describe degrees of stringency and classify these into ordinal categories reflecting relative coerciveness, while refraining from interval interpretations (Table 2). Our comparative claims are explicitly relational and policy design-focused and do not reflect causal outcomes.

3. Results & Discussion

We first present results on the institutional context behind licensing procedures which relate to the policy design concepts of integration and participation. Then we delineate the aspects related to the product's marketing authorisation application (e.g., E(R)A), which we discuss in terms of stringency. Finally, we provide an inter- and intra-jurisdictional comparative analysis of degrees of stringency in licensing procedures.

3.1. Institutional Context

The regulation of medicinal and plant protection products in both the EU and USA largely falls under the jurisdiction of national or supra-national government organisations (Karamfilova, 2023; Moore et al., 2021). Table 3 summarises the bodies responsible and principal legislation governing the licensing of these products.

3.1.1. Integration and multi-level governance

The integration of governance structures in medicinal and plant protection product licensing differs significantly across the two jurisdictions, offering insights into how institutional design shapes environmental regulation. In the EU, licensing procedures operate within a multi-level system in which the European Commission acts as the final arbiter (Fig. 1). HMP, VMP and PPP licensing decisions are based on the conclusions of assessment authorities, namely the European Medicines Agency (EMA) and the European Food Safety Authority (EFSA) (Handford et al., 2015; Oelkers, 2021; van Dijk et al., 2021). Within the EMA, the Committee for Medicinal Products for Human Use (CHMP) and the Committee for Veterinary Medicinal Products (CVMP) formulate opinions on HMPs and VMPs. For PPPs, there is a dual system in place: the European Commission, supported by EFSA, centrally licenses PPP active substances at the EU-level and Member States (MSs) then authorise PPPs at the national level (de la Casa-Resino et al., 2021; EFSA, 2018; Oelkers, 2021).

By contrast, licensing procedures in the USA follow a less integrated governance structure in which no single federal body spans both pharmaceuticals and PPPs. As shown in Fig. 2, the Food and Drug Administration (FDA) – an operating division of the Department of Health and Human Services – is the responsible federal agency for the licensing of pharmaceuticals, within which sits the Center for Drug Evaluation and Research (CDER) and the Center for Veterinary Medicine (CVM) (Bergeron, 2024; McVey, 2012). The licensing of PPPs, meanwhile, falls under the purview of the Environmental Protection Agency (EPA) which is an independent agency reporting directly to the Executive (Donley, 2019; Handford et al., 2015).

The presence of the European Commission as a bridging authority means licensing decision-making loci are more integrated in the EU than in the USA. The environmental policy integration literature argues that such institutional integration should enhance environmental protection by internalising cross-sector externalities, reducing veto points and increasing coherence (Lafferty and Hovden, 2003). Greater integration may therefore yield greater upward harmonisation of environmental standards in the EU compared to the USA, although integration is necessary but not sufficient for environmental protection (Jordan and Lenschow, 2010).

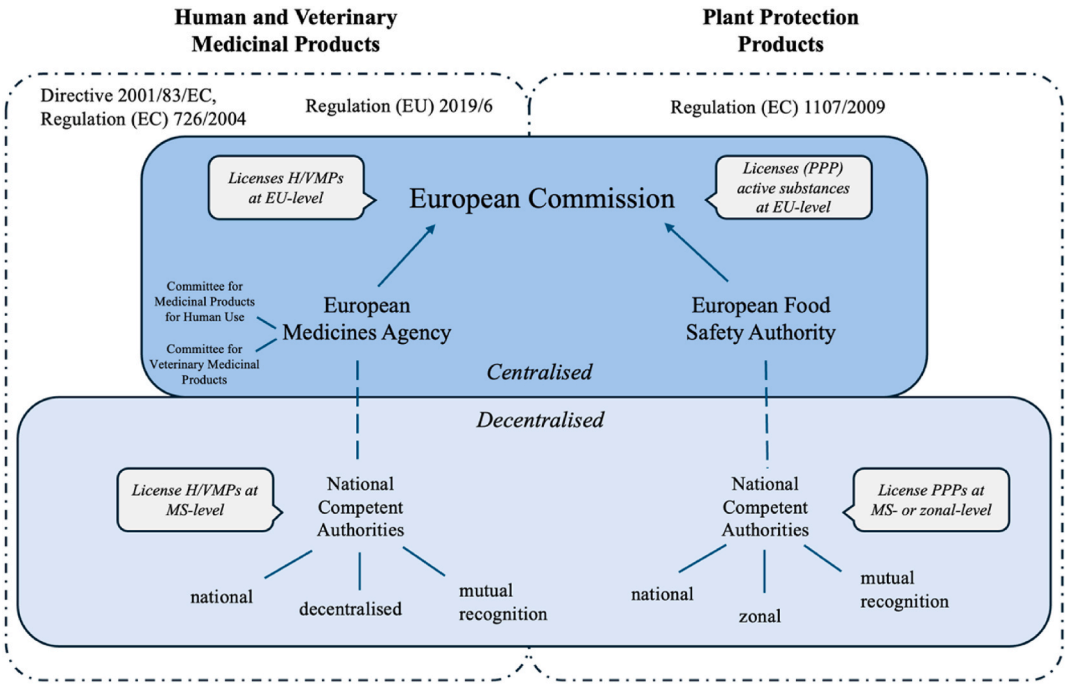

Fig. 1. Schematic representing the multi-level governance structure for medicinal and plant protection product licensing in the EU (source: own representation)

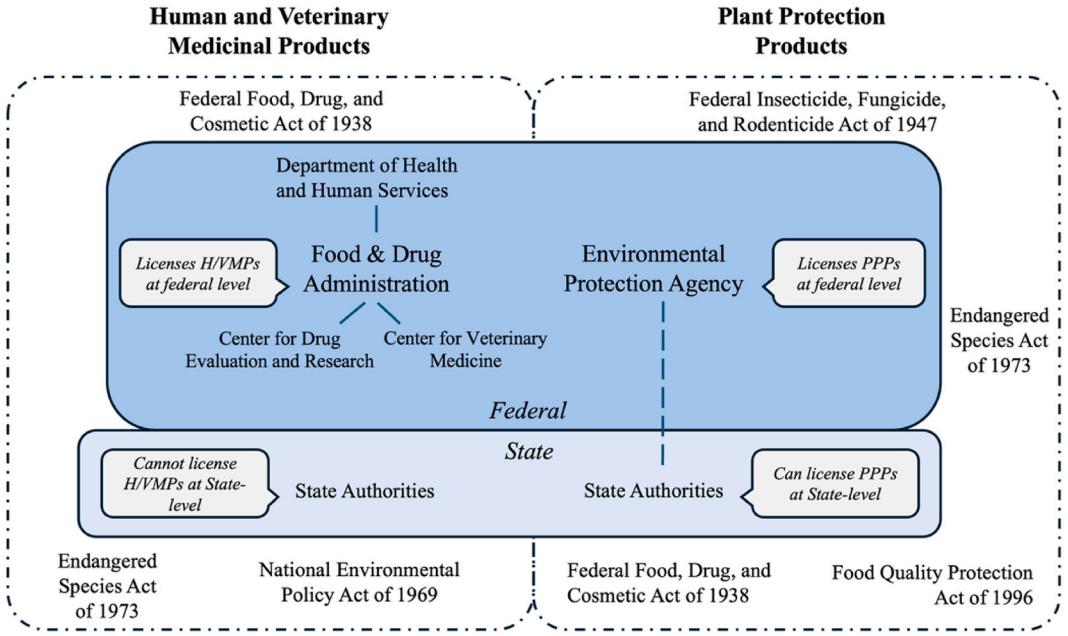

Fig. 2. Schematic representing the multi-level governance structure for medicinal and plant protection product licensing in the USA (source: own representation)

In practice, however, the involvement of MSs introduces opportunities for divergence. This can be seen in decentralised authorisation pathways which give national competent authorities (NCAs) capacity for product licensing. PPP authorisation in particular is explicitly structured around MS involvement: while active substances are licensed centrally, products themselves are authorised at either the MS- or zonal-level, giving countries multiple formal veto points under Regulation 1107/2009 (Doussan et al., 2024; Schriever et al., 2025). Certain medicinal products can also be licenced at the MS-level under the national, decentralised, or mutual recognition procedures (Directive 2001/83/EC; Regulation (EU) 2019/6).

Such multi-level governance structures create a more vertically integrated system than that found in the USA, but they can generate fragmentation (Lee, 2013). Divergent administrative capacities, risk management cultures and enforcement practices across NCAs can hinder consistent implementation of Commission-level decisions. One consequence, particularly evident in pharmaceutical licensing, is the frequent absence of complete E(R)A data in decentralised authorisations, demonstrating the limits of institutional integration when operational responsibilities are dispersed (Gildemeister et al., 2023). Thus, while EU governance supports upward harmonisation in principle, this outcome is contingent on MSs' ability to implement and enforce shared standards

consistently (Jordan, 1999).

In the USA, by contrast, PPPs must be federally registered by the EPA before they can be sold or distributed (7 U.S.C. § 136-136y). Individual states may subsequently license or restrict PPPs under FIFRA § 24(a) (Moore et al., 2021), provided state regulations are at least as stringent as federal regulations (7 U.S.C., § 136v(a); Ambrozaite et al., 2023). Certain states require additional state-level registration before sale (e.g., California F.A.C. § 12811), and FIFRA § 24 permits additional PPP registrations for localised needs unless pre-empted by the EPA (EPA, 2025b; Osteen, 1994). For pharmaceuticals, however, the FDCA grants the FDA exclusive authority to licence medicinal products for interstate marketing; states cannot independently license HMPs or VMPs (21 U.S.C., § 301 et seq.; *Mutual Pharmaceutical Co. v. Bartlett, 2013*). Only once a medicinal product is federally licensed may states regulate its sale, distribution or use (21 U.S.C., § 301 et seq.).

Overall, the EU's multi-level governance structure combines higher vertical integration with a greater role for MSs than in the USA, where licensing is more hierarchical and federally pre-emptive. While these EU structures may enhance context-sensitivity and encourage MS ownership of decision-making (Newig and Fritsch, 2009), they also create additional veto points and variability in implementation. The USA's system, by contrast, offers fewer opportunities for states to reshape licensing decisions. While the initiatives of individual US states have occasionally led to the ratcheting up of nationwide policies ('California effect' (Vogel, 2000)), policy studies widely agree that the EU's multi-level governance system fosters upward harmonisation by raising lagging MSs to stricter standards (Jordan and Lenschow, 2010; Lee, 2013). Yet these benefits are conditional: multi-level systems can just as easily produce fragmentation and lowest-common-denominator outcomes when coordination mechanisms are weak or enforcement capacities diverge (Jordan, 1999; Jordan and Lenschow, 2010; Lee, 2013; Squintani, 2022). The European Commission's bridging role therefore enhances integration only insofar as NCAs implement decisions consistently and robust mechanisms exist for managing intergovernmental and intersectoral conflicts.

3.1.2. Public participation

Public consultation is an explicit part of PPP licensing procedures in both the EU and USA. In the EU, EFSA must publish their draft assessment report on the licensing or renewal of an active substance which is then typically open to public comment for sixty days (Regulation (EC) No 1107/ 2009, Art. 12(1)). Alongside their conclusion, EFSA must publish "an explanation of how the comments received have been taken into account or why they have been disregarded" (Regulation (EC) No 178/2002, Art. 32b(1)(c)). Likewise in the USA, FIFRA requires the EPA to make their provisional decision available for public comment before a final registration decision is made (7 U.S.C. § 136 et seq.). This final decision must be supported by a public docket showing how the feedback received was addressed (EPA, 2020; Moore et al., 2021). In the past, courts have struck down EPA PPP approvals when it was judged that public concerns were not properly considered (*NRDC v. EPA, 1984*; EPA, 2025e.

Licensing procedures for pharmaceuticals in both jurisdictions, by contrast, do not contain provision for public participation. In the EU, neither HMP nor VMP licensing involves public consultation (Oelkers, 2021), although it is often part of the development of new EU guideline documents. For example, the most recent update to the EMA's HMP guidelines included a public consultation period of seven months before a revised draft was published alongside a document summarising how the comments received had been addressed (CHMP, 2024). In the USA, there is similarly no formal public comment period required during the evaluation of a new HMP or VMP application set out in the FDCA. However, when licensing of a pharmaceutical triggers preparation of an Environmental Impact Statement (EIS) by the FDA (see further details on EISs below), a draft of this document must be published for public comment before a final decision is made (21 C.F.R. § 25.40(d); Bergeron, 2024). Along with this final decision, the FDA must publicly set out how it has addressed the comments received (40 C.F.R. § 1503.4; 42 U.S.C. § 4332).

There is thus more provision for public participation in the licensing procedures of PPPs compared to pharmaceuticals in both the EU and USA, although the form of participation involved – consultation – remains on the lower, tokenistic rungs of Arnstein's ladder (Arnstein, 1969). As stressed by Newig et al. (2023), the effectiveness of stakeholder participation in improving environmental governance not only hinges on *who* is involved, but on *how* they are involved; they emphasise the importance of power delegation in predicting environmental governance outcomes, explaining that actual influence over tokenistic consultation is a particularly strong predictor (Newig et al., 2023). Higher levels of citizen participation involving power sharing and joint decision-making are therefore missing in the licensing procedures of both medicinal and plant protection products across both jurisdictions (Arnstein, 1969).

3.2. Environmental (Risk) Assessment

An assessment of the environmental risks of the use of a medicinal or plant protection product is required as part of the product or substance's marketing authorisation application in both the EU and USA. Table 4 summarises aspects relating to this E(R)A.

3.2.1. Product- vs. substance-based E(R)A

In both the EU and USA, the E(R)A of medicinal products takes a product-based approach while PPPs are assessed based on the active substance(s) they contain (Ågerstrand et al., 2015; Bruce et al., 2023; Oelkers, 2021). Existing research has discussed the advantages and drawbacks of both systems. The active substance-based approach offers efficiency: it avoids replication of assessment for products containing the same active ingredient(s) (Ågerstrand et al., 2015), and is more easily standardised, making it well-suited to centralised licensing procedures (Oelkers, 2021). However, this approach risks overlooking formulation-specific hazards, including combination effects or the environmental risk of co-formulants (Walter and Mitkidis, 2018). Empirical studies show that co-formulants can alter toxicity, persistence, or bioavailability of active substances (Bruce et al., 2023; Mesnage and Antoniou, 2018), and that full formulations can exhibit higher toxicity than the isolated active ingredient (Klátyik et al., 2023). These findings indicate that assessment of the active substance alone may underestimate environmental risks.

Cox and Surgan (2006) highlight the misleading use of the word 'inert' in reference to co-formulants ('adjuvants') used in medicinal products in the USA; in fact, many of these so-called inert ingredients have been or are also used as active ingredients and are listed on the Hazardous Substances Data bank owing to their own biological activity and associated risks to human or environmental health (Bruce et al., 2023; Cox and Surgan, 2006; Mesnage and Antoniou, 2018). Such terminology can obscure the contribution of co-formulants to overall product toxicity, limiting the effectiveness of substance-focused E(R)A frameworks in protecting non-target organisms.

A product-based approach is therefore better able to assess formulation-specific risks, although this comes at the cost of assessment repetition, potential inconsistencies in interpretation, and longer approval times (de la Casa-Resino et al., 2021; Oelkers, 2021). For example, as noted by Ågerstrand et al. (2015), the assessment of estradiol in Sweden by eight different pharmaceutical companies resulted in four different environmental risk conclusions. This variability underscores both the influence of co-formulants and the lack of standardised methodology in product-based assessments. The EU may capture the benefits of both risk assessment approaches through their dual system of centrally licensing PPP active substances at the EU-level and commercial products at the MS/zonal-level. This approach is more stringent than the US approach to the E(R)A of PPPs which remains

Table 4
Summary of E(R)A factors (source: own representation). Where table entries are not referenced in the main text, references are provided in the table's footnotes.

Jurisdiction	Criterion	HMP	VMP	PPP
EU	E(R)A requirement since X	2005[a]	1993[b]	1993[c]
	Product- or substance-based E(R)A	Product	Product	Active substance (products authorised by Member States)
	Burden of proof	Licence applicant	Licence applicant	Licence applicant
	Explicit environmental protection goal stated in principal legislation	No	No	Yes[d]
	E(R)A data requirement enshrined in legislation	No (sub-legal EMA guidelines since 2006)[e]	No (sub-legal guidelines since 1998, VICH since 2000)[f]	Yes (Regulation (EU) 283/2013 and 284/2013)
	Categorical exclusion possible	No	No	No
	Incomplete or inadequate E(R)A sufficient for licence refusal	No	Yes	Yes
	Findings of ERA sufficient grounds for licence refusal	No	Yes (benefit-risk assessment)	Yes
	Threshold value for in-depth E(R)A	Predicted Environmental Concentration in surface water (PEC_{sw}) $\geq$ 0.01 µg/L[g]	$PEC_{soil} \geq$ 100 µg/kg (terrestrial), $EIC_{aquatic} \geq$ 1.00 µg/L (aquatic)[h]	Risk Quotient $\geq$ 1[i]
	Chronic ecotoxicity assessed	Yes (conditional)[e]	Yes[j]	Yes[d]
	Hazard assessment (PBT/vPvB)	Implicit[e]	Yes[j]	Yes[d]
	Risk to endangered species and their habitats considered	Only if Natura 2000 site affected	Only if Natura 2000 site affected	Implicit; explicit if Natura 2000 site affected
	Endocrine disruption assessed	Yes (conditional, benefit-risk assessment)[e]	Yes (benefit-risk assessment)[j]	Yes[k]
USA	E(R)A requirement since	1977[l]	1977[l]	1972[m]
	Product- or substance-based E(R)A	Product	Product	Active substance
	Burden of proof	Licence applicant for EA, CDER for FONSI or EIS	Licence applicant for EA, CVM for FONSI or EIS	Licence applicant
	Explicit environmental protection goal stated in principal legislation	No	No	Yes[n]
	E(R)A data requirement enshrined in legislation	No (sub-legal guidelines since 1980)[o]	No (sub-legal guidelines since 1985)[p]	Yes (40 C.F.R. § 158)
	Categorical exclusion possible	Yes	Yes	No
	Incomplete or inadequate E(R)A sufficient for licence refusal	Yes	Yes	Yes
	Findings of ERA sufficient grounds for licence refusal	Yes (in theory)	Yes (in theory)	Yes (cost-benefit analysis)
	Threshold value for in-depth E(R)A	Expected Introduction Concentration (EIC) $\geq$ 1.00 µg/L[o]	$PEC_{soil} \geq$ 100 µg/kg (terrestrial), $EIC_{aquatic} \geq$ 1.00 µg/L (aquatic)[p]	Risk Quotient > EPA's defined Levels of Concern[q]
	Chronic ecotoxicity assessed	No[o]	Yes[p]	Yes[r]
	Hazard assessment (PBT/vPvB)	Implicit[o]	Implicit[p]	Implicit[s]
	Risk to endangered species and their habitats considered	Yes	Yes	Yes
	Endocrine disruption assessed	No[t]	No[t]	Yes[u]

[a] EMA, 2016b.
[b] Directive 92/18/EEC.
[c] Directive 91/414/EEC.
[d] Regulation (EC) No 1107/2009.
[e] EMA, 2024.
[f] EMEA, 1998, 2000, 2004.
[g] EMA, 2006.
[h] EMA, 2016a.
[i] Regulation (EU) No 283/2013.
[j] Regulation (EU) 2019/6.
[k] Regulation (EU) 2018/605.
[l] 21 C.F.R. § 25.
[m] FIFRA § 2(bb), 3(c)(5)(C).
[n] FIFRA § 3(c)(5)(C).
[o] FDA, 1998.
[p] FDA, 2001, 2006.
[q] EPA, 2025d.
[r] 40 C.F.R. § 158.630.
[s] EPA, 2025a.
[t] 21 U.S.C. §§ 355, 360b.
[u] via Endocrine Disruptor Screening Program (21 U.S.C. § 346a(p)).

focused on the assessment of active substances.

3.2.2. *E(R)A objectivity & categorical exclusions*

For medicinal products in the USA, once the licence applicant has provided their E(R)A, the FDA (specifically the CDER or CVM) will evaluate it to ensure objectivity and accuracy, before producing either an Environmental Impact Statement (EIS) or Finding of No Significant Impact (FONSI) (EPA, 2025c; Walter and Mitkidis, 2018). An EIS is required when a product may "significantly affect the quality of the human environment" (21 C.F.R. § 25.15(b)), whereas a FONSI is issued in the absence of such findings (21 C.F.R., § 25.41). Walter and Mitkidis (2018) argue that the FDA's evaluation process, in contrast to the EU where authorities do not prepare independent environmental assessments following applicant submissions, means the US system is more likely to yield an E(R)A of high standard. However, this advantage in the USA's framework is substantially undermined by the extensive use of

categorical exclusions, which allow many applicants to forgo submitting an E(R)A altogether (Walter and Mitkidis, 2018).

Only for medicinal products in the USA is categorical exclusion from completion of an E(R)A possible (FDA, 2022). Under NEPA, categorical exclusions may be granted when a requested federal action does not "individually or cumulatively have a significant effect on the human environment", thereby eliminating the requirement for submission of an E(R)A by the licence applicant or preparation of an EIS by the FDA (FDA, 2017). Although the FDA retains the right to request an E(R)A when there is the "the potential for serious harm to the environment" or when an action will "adversely affect a species or the critical habitat of" an endangered or protected species (21 C.F.R. § 25.21), this authority is seldom invoked. Between 1970 and 2015, the FDA issued just one EIS relating to the licensing of an HMP, with all other cases resulting in categorical exclusions or FONSIs (Eckstein, 2015).

The list of categories covering eligibility for categorical exclusion is long and includes pharmaceutical substances new to market provided it can be shown that they will not enter the aquatic environment in quantities exceeding one part per billion (21 C.F.R. § 25.31(b); Bergeron, 2024). The scientific derivation for this regulatory cutoff lacks transparency (FDA, 1998), suggesting the value functions as an administrative screening threshold rather than a risk-based criterion. Furthermore, as this threshold applies to individual substances, multiple products may each qualify for categorical exclusion despite cumulatively exceeding the threshold concentration in receiving watersheds. Whereas VMPs are granted categorical exclusions less frequently, applications for VMPs for use in non-food animals automatically qualify (21 C.F.R. § 25.33). Therefore, although E(R)A requirements in the USA appear robust and on par with the stringency of EU regulations in many areas, few product applications are subject to them in practice.

3.2.3. Prioritisation and balance of risk

The weight and practical influence of the E(R)A on licensing decision-making is another key feature that differs between the EU, USA, and the products licensed therein. These differences shape not only the likelihood that environmental considerations will affect product authorisation but also reveal underlying political and ethical choices regarding how these jurisdictions prioritise human health, economic interests, and environmental protection.

(i) Only in EU PPP licensing is the environmental risk quotient a mandatory standalone requirement for marketing authorisation, making the findings of the E(R)A sufficient grounds for licence refusal and not something which can be offset by benefits from the product's use (EFSA, 2018; Regulation 1107/2009, Art. 4). This reflects a precautionary, hazard-based approach where environmental protection goals cannot be overridden by product benefit arguments.

(ii) By contrast, PPP licensing in the USA and VMP licensing in the EU incorporates environmental risks into broader balancing frameworks. If these risks cannot be offset by benefits or controlled with appropriate mitigation measures (EMA, 2012; Moermond et al., 2023), the licence can be denied on environmental grounds (BIOIS, 2013; Fabrega and Carapeto, 2020). For PPPs in the USA, environmental impacts are weighed as part of a cost-benefit analysis under FIFRA: the ERA cannot register a PPP which causes "unreasonable adverse effects on the environment" (7 U.S. C. § 136a(c)(5)), defined as risks evaluated in light of the "economic, social, and environmental costs and benefits of the use of any pesticide" (EPA, 2025c; FIFRA § 2(bb)). For VMPs in the EU, the findings of the E(R)A form part of a benefit-risk assessment which considers benefits of therapeutic efficacy against risks to the target animal, consumer, and wider environment (Regulation 2019/6, Art. 37). Notably, unlike the USA's cost-benefit assessment, this benefit-risk assessment does not permit the weighting of environmental harm against economic value.

(iii) For medicinal products in the USA, while the E(R)A is in theory grounds for licence refusal under NEPA, this requirement for consideration of environmental impact is purely procedural and not in itself an independent statutory ground for licence refusal (21 C.F.R. § 25). Environmental risks of medicinal products, especially VMPs, are instead usually resolved via implementation of risk mitigation measures rather than outright licence refusal (21 C.F.R. § 25.40(e); FDA, 1997). Moreover, the frequency of categorical exclusions granted, particularly for HMPs, means that refusal of their licensing on environmental grounds is extremely unlikely (21 C.F.R. § 25.31).

(iv) Similarly, for HMP licensing in the EU, the environmental risk quotient does not form part of the product's benefit-risk assessment, nor can the E(R)A stand alone as sufficient grounds for licence refusal (Directive 2001/83/EC). Proposition of risk mitigation measures by the licence applicant is required under Article 8(3) of Directive 2001/83/EC. Environmental concerns may therefore be acknowledged but cannot affect the licensing outcome.

The hierarchy of concern attached to the findings of a product or active substance's E(R)A creates a spectrum on which therapeutic benefits, environmental risks, and in some cases economic returns, are weighed. Environmental risks cannot currently justify refusing authorisation for HMPs in the EU because EU law structurally prioritises public health and uninterrupted access to medicines, while treating environmental impacts as secondary, mitigable side-effects. This approach is in direct contradiction with the EU's precautionary principle and although acknowledged as a shortcoming by the European Pharmaceutical Strategy, environmental risks have yet to be given determinative weight over therapeutic benefits in HMP licensing (European Environment Agency, 2013; Harrison et al., 2025). By contrast, EU VMP and USA PPP environmental risks may be offset by benefits (including economic returns in the USA) or risk mitigation measures. Such mitigation measures are often included but rarely accompanied by monitoring or enforcement mechanisms, limiting their real-world environmental effectiveness (Gildemeister et al., 2023; Moermond et al., 2023).

3.2.4. Incomplete or inadequate E(R)A as grounds for licence refusal

In contrast to HMPs, the E(R)A forms part of the decision-making process in the licensing of VMPs and PPPs, and therefore it follows that an incomplete or inadequately conducted E(R)A is also sufficient grounds to refuse their marketing authorisation (BIOIS, 2013; EFSA, 2018; Regulation 2019/6, Art. 37). Conversely, for HMPs in the EU, just as the results of an E(R)A cannot constitute grounds for licence refusal, neither can an incomplete or scientifically unacceptable E(R)A (Gildemeister et al., 2022; Walter and Mitkidis, 2018). Any request made for the provision of missing information after the licence has been granted is non-binding and failure to provide this information has no consequences on the licence holder (Gildemeister et al., 2022). Gildemeister et al. (2023) found that an absence of E(R)A information at the time of licensing was particularly common in decentralised EU procedures: in Germany for example, of 113 applications assessed between 2018 and 2020 which required an E(R)A, 49% had no E(R)A available at the time of marketing authorisation (Gildemeister et al., 2023). However, there is also evidence of this phenomenon in the centralised marketing procedure: Caneva et al. (2014) found that 37% of centralised applications between 2011 and 2012 were submitted after the deadline and 83% of those submitted were of inadequate or unsatisfactory quality. As the E(R)A does not form part of the benefit-risk calculation for HMP licensing in the EU, the findings of the E(R)A do not play a determinative role in the licensing process (Caneva et al., 2014; Gildemeister et al., 2023).

3.2.5. Data requirements

The data required for an E(R)A are enshrined in law for PPPs in the

Table 5
Summary of post-authorisation factors (source: own representation)

Jurisdiction	Criterion	HMP	VMP	PPP
EU	Initial MA grant period	5 years	Unlimited (5 years for a limited market)	10 years
	Subsequent renewal timeframe	Unlimited	Unlimited	15 years
	E(R)A data required for renewal	No	N/A	Yes
	Substitution obligation	No	No	Yes
USA	Initial MA grant period	Unlimited	Unlimited	15 years
	Subsequent renewal timeframe	N/A	N/A	15 years
	E(R)A data required for renewal	N/A	N/A	Yes
	Substitution obligation	No	No	No

EU (Annexes of Regulation (EU) No 283/2013 for active substances and Regulation (EU) No 284/2013 for PPPs) and the USA (40 C.F.R. § 158; EPA, 2025a). However, for medicinal products in both jurisdictions, such requirements are instead set out in sub-legal guidelines, i.e., 'soft law' instruments which guide best practice without being legally enforceable. In both the EU and USA, there was a time lag between the publication of these guidelines and the date at which an E(R)A became a mandatory part of licensing applications, meaning a gap exists between the onset of the obligation and circulation of the instructions on how to fulfil that obligation (de la Casa-Resino et al., 2021; Gildemeister et al., 2023). This time lag was 3 years and 8 years for HMPs and VMPs respectively in the USA, and 1 year and 5 years for HMPs and VMPs in the EU. These lag periods may have led to licence applications being granted with insufficient E(R)As, thereby reducing the stringency of medicinal product regulations when compared to PPPs.

Data requirements themselves also differ greatly in terms of stringency, both inter- and intra-jurisdictionally (Table 4). The threshold value for an HMP's E(R)A to progress to later-phase testing in the EU, for example, is when the predicted environmental concentration (PEC) in surface water exceeds 0.01 μg/L (EMA, 2006). The equivalent value is 100 times higher in the USA (1.00 μg/L) and only serves as a screening benchmark to determine whether an E(R)A is required under NEPA (FDA, 1998). Specific screening requirements (e.g., endocrine-disrupting chemicals, chronic ecotoxicity, hazardous properties) are generally more stringent in the EU than in the USA and in both cases, PPP requirements tend to be more stringent than medicinal product requirements (Table 4).

A notable exception is the USA's more stringent requirements for consideration of risk posed to endangered species and their habitats. Under Section 7 of the Endangered Species Act, all federal agencies must consult the U.S. Fish and Wildlife Service or National Marine Fisheries Service to ensure that their proposed action "is not likely to jeopardize the continued existence of any endangered or threatened species or result in the destruction or adverse modification of designated critical habitat" (16 U.S.C. § 1536). However, the FDA has not published guidance on when it considers such consultation necessary, bringing the stringency of this obligation into question (Bergeron, 2024). Meanwhile, there is no equivalent blanket obligation on licensing authorities in the EU for the protection of endangered species. The nearest equivalent is found in Article 6(3) of the EU Habitats Directive which confers a legal duty on MSs to "ensure that any plan or project likely to have a significant effect on a Natura 2000 site is subject to an appropriate assessment of its implications for the site in view of the site's conservation objectives" (Directive 92/43/EEC). It could also be argued that endangered species have implicit protection under the general obligation to avoid unacceptable effects on non-target species under Article 4 of the EU's PPP Regulation 1107/2009.

3.3. Post-Authorisation

Post-authorisation, ongoing monitoring of environmental impacts dictated by license renewal procedures vary; PPP regulations are more stringent than medicinal product regulations, particularly in the EU (Table 5).

3.3.1. Periodic E(R)A review

As shown in Table 5, the licences of PPPs in both the EU and USA must be renewed periodically (7 U.S.C. § 136a(g); Regulation 1107/2009, Art. 14). By extension, this includes reassessment of the product's E(R)As: in the EU, as at first licensing, the outcome of the updated E(R)A can form grounds for renewal refusal (Oelkers, 2021), whilst in the USA renewal involves recalculation of the product's cost-benefit ratio (Donley, 2019; Moore et al., 2021). Medicinal products, by contrast, can be granted indefinite marketing authorisation from the outset in the USA (FDA, 2025), and after an initial 5-year period for HMPs and VMPs for a limited market in the EU (Karamfilova, 2023; Regulation 2019/6, Arts. 5, 24). There is therefore no continued oversight of developing E(R)A data for medicinal products, making PPP regulations more stringent in this regard. However, if new information relevant to the E(R)A comes to light post-authorisation, the licence holder of an HMP, VMP or PPP in the EU or USA must report this information to the relevant licensing authority, regardless of licence renewal intervals (21 C.F.R. §§ 25.21, 314.81(b)(2)(i); Oelkers, 2021; Schierow and Esworthy, 2012). In all cases, the impact of this new information on a product's licensing status will depend on the weight afforded to the E(R)A.

3.3.2. Substitution obligation

In the EU, a substitution obligation exists for PPPs shown to cause environmental risk when there is a less environmentally damaging alternative available. Under Article 50 of Regulation 1107/2009, if a PPP contains an active substance identified as a 'candidate for substitution', MSs must conduct a comparative assessment when granting or renewing a PPP authorisation and if a safer alternative is available the proposed active substance must be substituted. Annex II defines candidates for substitution as those that meet one or more criteria including toxicological concerns, hazardous properties, or other environmental concerns. The initial licence and subsequent renewal timeframe of candidates for substitution is shortened to seven years (Regulation 1107/2009, Art. 24). However, no equivalent substitution obligation applies to medicinal products in the EU nor to products in the USA (Oelkers, 2021; Walter and Mitkidis, 2018). Risk mitigation measures may instead be implemented to mitigate the likelihood of environmental harm (Walter and Mitkidis, 2018).

In practice, this means when there are safer alternatives available, there is no obligation on a medicinal product licence holder in the EU, or a medicinal or PPP licence holder in the USA, to substitute. A real-world example of the implications of this shortcoming in regulatory stringency is the ongoing use of a VMP with widely documented toxicity to vultures in the EU: veterinary diclofenac, known to have decimated vulture populations on the Indian Subcontinent (Green et al., 2004; Oaks et al., 2004), has held marketing authorisation in Spain since 2013 despite the Iberian Peninsula being home to over 90% of Europe's vultures (Moreno-Opo et al., 2021). Two equivalent veterinary drugs – meloxicam and tolfenamic acid – are available and vulture-safe yet the marketing authorisation for diclofenac remains valid (Cook et al., 2024; Green et al., 2016). The increased stringency of PPP licensing standards in the EU means this situation would not have occurred if the pharmaceutical in question were a PPP as substitution for safer alternatives

Table 6
Summary of legacy & generic product factors (source: own representation). Where table entries are not referenced in the main text, references are provided in the table's footnotes.

Jurisdiction	Criterion	HMP	VMP	PPP
EU	Retrospective E(R)A required for legacy products	No	Case-by-case basis	N/A (no legacy products without ecotoxicity data)
	E(R)A required for licensing of generic based on legacy product	No	Yes	Yes (unless bridging justification)[a]
	E(R)A required for licensing of generic based on non-legacy product	Yes	No (aligned with E(R)A of reference product)	Yes (unless bridging justification)[a]
USA	Retrospective E(R)A required for legacy products	No (unless safety concern triggers re-evaluation)	No (unless safety concern triggers re-evaluation)	Yes
	E(R)A required for licensing of generic based on legacy product	Most granted categorical exclusion	Yes	Yes, if product differs significantly from reference product[b]
	E(R)A required for licensing of generic based on non-legacy product	Most granted categorical exclusion	Yes	Yes, if product differs significantly from reference product[b]

[a] FAO, 2018; Regulation (EC) 1107/2009.
[b] 40 C.F.R. § 152.44.

would have been obligatory.

3.4. Legacy & Generic Products

Medicinal products licensed before current marketing authorisation procedures came into force – so-called 'legacy products'– were not subject to the same environmental standards at the time of their licensing. Generic products, meanwhile, are those containing the same active ingredient as a previously registered product, and whose chemical and functional equivalence mean they are licenced under the same use conditions. Generic products often come to market after the patent or data protection period of the previously registered product – known as the 'reference product' – has expired and the generic can be produced at a lower cost. A summary of the treatment of legacy and generic products in EU and USA licensing procedures is set out in Table 6.

3.4.1. Uncertain legacy of legacy products

Medicinal products considered legacy products in the EU are those licensed pre-2005. For legacy HMPs, only an 'indication of any potential risks presented by the medicinal product for the environment' was required in their original marketing authorisation application (Directive 93/39/EEC). There is no requirement for an E(R)A to be conducted retrospectively and hence many such products remain on the market without ecotoxicity data (BIOIS, 2013). Indeed, the medicinal products found in the highest concentrations in European surface water, groundwater and drinking water are predominantly legacy products, including widely used analgesics like ibuprofen, paracetamol, diclofenac, and naproxen (Graumnitz and Jungmann, 2021). Furthermore, an E(R)A is not required for the licensing of today's generic HMPs based on these legacy products, meaning both the reference products and their generics remain on the market without having been evaluated under modern E(R)A standards (EMA, 2016b; Oelkers, 2021; Walter and Mitkidis, 2018).

Ågerstrand et al. (2015) highlight the flawed conflation of the absence of ecotoxicity data for many such legacy products with the absence of environmental risk, which directly contradicts the EU's precautionary principle and is instead more aligned with the reactionary approach of the USA to environmental risk (Kelemen and Vogel, 2010). This regulatory gap persists despite growing recognition that legacy pharmaceuticals contribute substantially to environmental concentrations and ecological risks (Graumnitz and Jungmann, 2021).

This shortcoming in the stringency of HMP licensing in the EU has been rectified in the equivalent provisions for VMPs: an E(R)A must be performed for the licensing of generic products based on legacy products (BIOIS, 2013; de la Casa-Resino et al., 2021; European Commission, 2009). However, the retrospective E(R)A of legacy VMPs themselves is still approached on a case-by-case basis: the process must be initiated by a willing NCA after an identification of risk to the environment, and the conditions under which such a reassessment is triggered have not been defined (de la Casa-Resino et al., 2021; Oelkers, 2021; Regulation (EU) 2019/6).

As in the EU, there is no automatic requirement for the retrospective E(R)A of legacy medicinal products in the USA unless specific safety concerns emerge (Jose et al., 2020). Categorical exclusions granted to generic HMPs (whether based on a legacy product or not) further reduce the likelihood of environmental review: an E(R)A is only required if the generic HMP differs from the reference product in active ingredient, dosage, strength, administration, use conditions, or if there is an expected increase in environmental exposure (21 C.F.R. § 25.31(b)). Categorical exclusions for generic VMPs, however, are less common and will only be considered by the FDA's CVM when the proposed generic is identical to the reference product in formulation, use, and expected environmental exposure level (21 C.F.R. § 25.33). The above demonstrates that in both the EU and USA, there is a lack of stringency in the treatment of legacy medicinal products and the generic products for whom they serve as reference product. These notable regulatory gaps result in systemic under-assessment of the environmental risks of long-standing and widely used pharmaceuticals.

3.4.2. Periodic PPP review ensures retrospective assessment

In contrast to medicinal products, the periodic 15-year renewal period required in the licensing of PPPs in both the EU and USA ensures there are no products on the market without ecotoxicity data, meaning the above conflation of 'no data' with 'no risk' is less of a concern (Ambrozaite et al., 2023; Angelo, 2008; Oelkers, 2021). Although these efforts are ongoing – Schierow and Esworthy (2012) point out the immense cost involved in meeting FIFRA's § 4 obligation on the EPA to reregister all PPPs licensed pre-1984 – the more stringent approach to legacy PPPs in the EU and USA reduces the risk that legacy substances persist without sufficient environmental risk assessment. This periodic reassessment model is akin to the treatment of industrial chemicals under REACH (the EU's Regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals) where there is no differential treatment of legacy products and all chemicals must meet consistent risk assessment requirements (Ågerstrand et al., 2015). The success of REACH in addressing historic data gaps demonstrates that lifecycle-based regulatory frameworks are feasible and can better address chemical risks over time. Despite these precedents, no equivalent renewal or periodic reassessment requirements exist for pharmaceuticals in either jurisdiction.

3.5. Comparative Analysis of Stringency

As described across the latter four themes above, the level of stringency in the licensing procedures of medicinal and plant protection products varies by both product type and jurisdiction. This intra- and

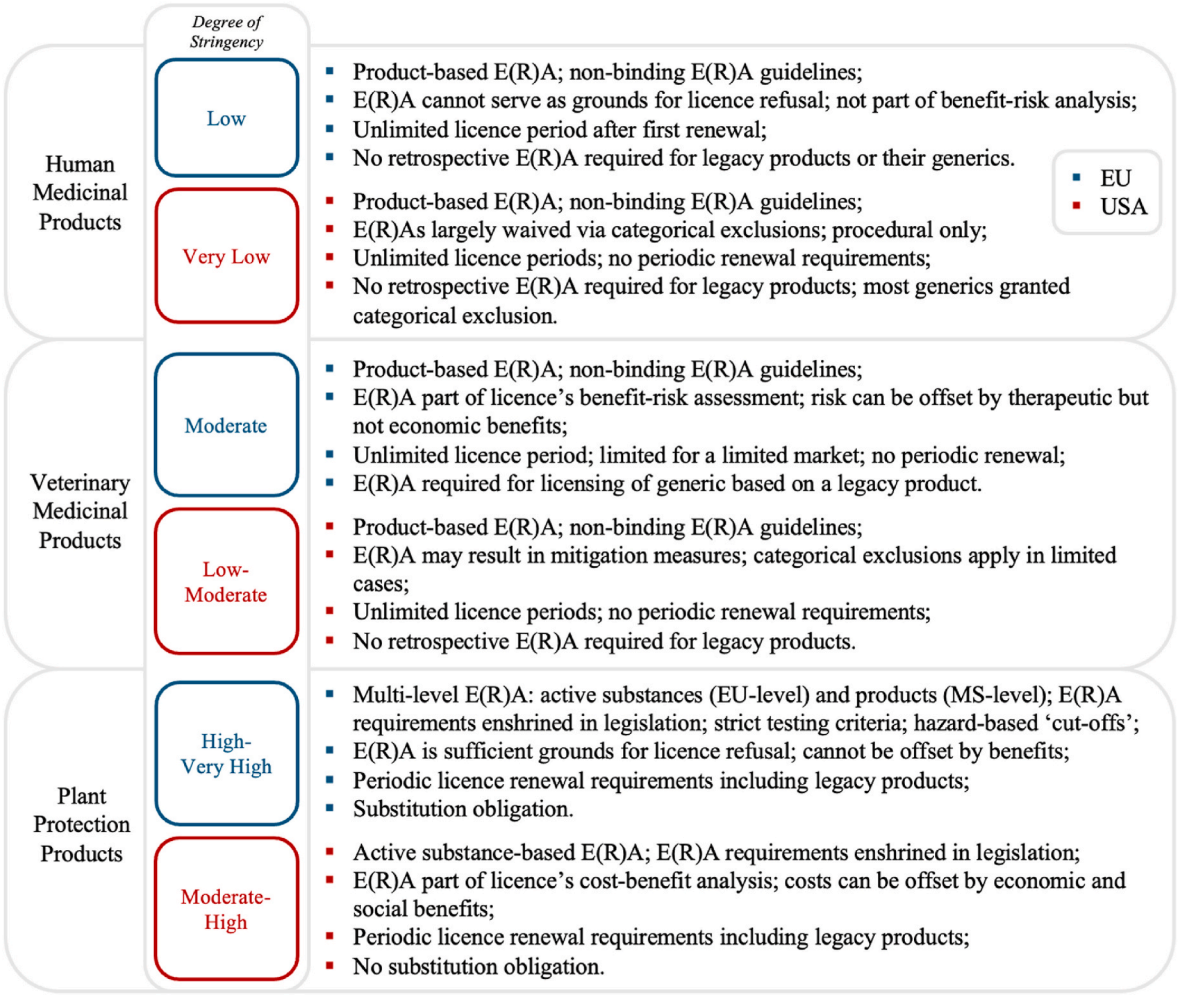

Fig. 3. Comparing the stringency of environmental standards in the licensing of medicinal and plant protection products in the EU and USA (source: own representation)

inter-jurisdictional variance in stringency is summarised in Fig. 3 and illustrated in Fig. 4, using the spectrum of stringency defined in Table 2.

Fig. 4 shows that across the two case studies, environmental standards in licensing procedures are more stringent in the EU than in the USA across all three classes of products. Across both jurisdictions, PPP requirements are most stringent, HMP requirements least stringent, and VMP requirements at an intermediate level of stringency. As stringency increases across both product and jurisdiction, the practical influence of the E(R)A on licensing decision-making increases: we see a general shift from risk-based to more hazard-based assessments; the introduction of automatic 'cut-offs' and stricter testing thresholds; the E(R)A becoming sufficient grounds for licence refusal, or at least part of the product's risk- or cost-benefit assessment; and greater controls on ensuring products on the market have up-to-date ecotoxicity data (Fig. 3).

3.5.1. Policy stringency vs. environmental protection

It is important to stress that the 'High-Very High' degree of stringency attributed to EU PPPs is relative to the other products and jurisdictions analysed above. Although a full assessment of policy performance lies outside the scope of this study, the literature widely documents the shortcomings of EU PPP policy in terms of real-world environmental protection (Scheringer and Schulz, 2025). EU PPPs therefore emerge as the most stringent only in a comparative policy design sense, not as an indication of superior environmental protection. Indeed, although EU PPP policies include several hazard-based and legally codified features, long-term monitoring studies indicate persistent exceedances of regulatory thresholds, underscoring a gap between policy design and environmental outcomes. Stehle and Schulz's (2015b) EU meta-analysis found that measured insecticide concentrations between 1972 and 2012 exceeded regulatory acceptable concentrations in 45% of cases, while a global meta-analysis found exceedances in 53% of measured insecticide concentrations between 1962 and 2012 (n = 11, 300) (Stehle and Schulz, 2015a). These findings highlight that even comparatively stringent licensing frameworks do not automatically translate into improved environmental effectiveness, which also depends on factors such as implementation, enforcement, and patterns of use (Gray and Shimshack, 2011).

4. Limitations

4.1. Qualitative comparative study

Our analysis is based on the qualitative comparison of a large document corpus, and several limitations follow from this approach. First, qualitative coding inevitably involves interpretive judgement, even when supported by systemic structuring in MAXQDA. Second, achieving true like-for-like comparison across sectors is inherently limited as product licensing frameworks are grounded in different statutory regimes, procedural requirements, regulatory terminologies and evidentiary standards. Third, the analysis is constrained by what is publicly documented, leaving implementation practices, enforcement variability and information on the quality of submitted E(R)As only

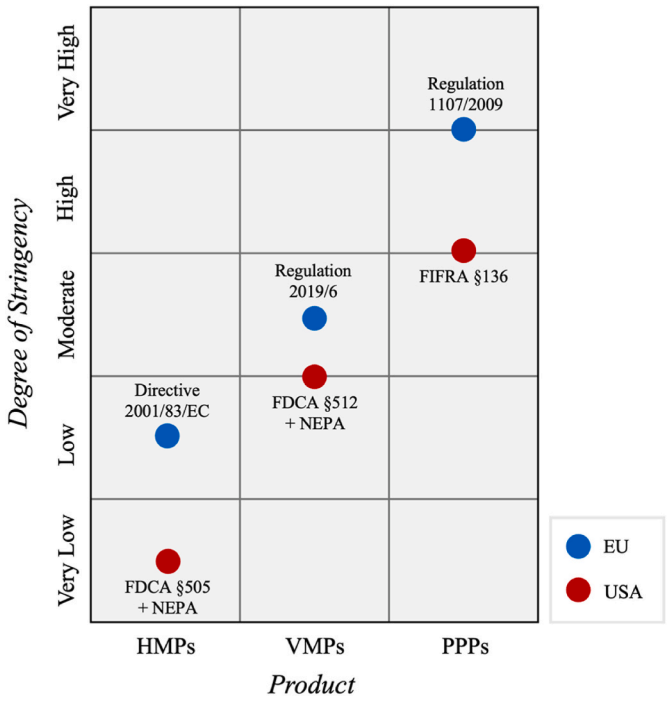

Fig. 4. Comparative overview of stringency in environmental standards in the licensing of medicinal and plant protection products across the EU and USA (source: own representation)

partially visible. This restricts our ability to generalise beyond documented provisions. Finally, there is limited outcome-level evidence directly linking specific policy design features to environmental protection outcomes, and we therefore restrict our claims to policy design, not realised environmental concentrations of chemicals.

4.2. Stringency analysis

Our stringency comparison is qualitative and ordinal: we do not ascribe numeric scores or claim interval comparability. This choice avoids arbitrary weighting across non-comparable indicators, but it also entails trade-offs: first, qualitative categories may appear less definitive than a numeric index; second, borderline classifications can remain debatable when cases straddle category thresholds; and third, our focus on policy design – rather than monitored environmental outcomes - means stringency should not be read as a proxy for effectiveness.

5. Conclusions

This research examined how environmental safety standards vary within the licensing frameworks of medicinal and plant protection products across two of the world's largest economies – the EU and USA. Our analysis shows that institutional contexts vary in their degree of integration and participation: while EU licensing procedures are multi-level compared to the more hierarchical structure found in the USA, citizen participation in the licensing process across both jurisdictions remains tokenistic for PPPs and wholly absent for medicinal products. Our analysis of policy stringency found variance in E(R)A-related requirements, refusal grounds, renewal obligations, and substitution provisions. Across both case studies, environmental standards in PPP licensing requirements are the most stringent, HMP requirements the least stringent, and VMP requirements at an intermediate level of stringency. Between the two case studies, we find that EU frameworks are generally more stringent than their USA equivalents across all three classes of products. These findings reflect differences in statutory foundations, procedural triggers, and the legal force of environmental obligations – not realised environmental outcomes.

Our results highlight significant shortcomings in the stringency of current licensing frameworks, particularly in the treatment of legacy products, co-formulants and categorical exclusions. Moreover, the politically constructed regulatory hierarchy weighing environmental risk against therapeutic, social, and economic benefits generates ethical tensions between ecological protection, public health, fairness, and long-term sustainability which warrant further discussion.

In light of these results, we outline several targeted policy recommendations for strengthening the regulatory architecture governing the licensing of medicinal and plant protection products. These complement recommendations already made in the extant literature in research focusing on specific products or geographic regions (Ågerstrand et al., 2015; Ambrozaite et al., 2023; de la Casa-Resino et al., 2021; Gildemeister et al., 2023; van Dijk et al., 2021). They are also put forward in the context of the proposed overhaul of EU pharmaceutical legislation under the European Commission's Pharmaceutical Strategy for Europe, which may address shortcomings in the stringency of existing HMP regulations, including introducing retrospective E(R)A requirements for legacy products and adding grounds for licence refusal if environmental risks cannot be sufficiently mitigated (Harrison et al., 2025). The direct comparison between HMPs, VMPs, and PPPs across the EU and USA in this research allowed the addition of novel recommendations, all of which aim to bolster the stringency of existing regulations and many of which aspire to bring environmental standards in medicinal product licensing closer to the level of those already employed in the licensing of PPPs.

1. Enshrine E(R)A data requirements for medicinal products in legislation rather than relying on ‘soft law’ guidelines to ensure obligations are codified and prevent data gaps.
2. Reduce the number of medicinal products, especially HMPs, eligible for categorical exclusion from E(R)A in the USA to increase environmental scrutiny and close systemic assessment gaps.
3. Extend the EU's substitution obligation – currently applied to PPPs – to medicinal products to create a structured pathway for the phase out of environmentally harmful pharmaceuticals when safer alternatives exist.
4. Introduce periodic licence renewal periods for medicinal products requiring re-evaluation of E(R)A data, in line with the more precautionary PPP and REACH models, to ensure older pharmaceuticals are reassessed using the latest scientific methods and data sources.
5. Require E(R)As of complete product formulations, not only active substances, to capture the risks associated with co-formulants.

CRediT authorship contribution statement

Sophie E. Cook: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Martin Scheringer:** Writing – review & editing, Supervision, Conceptualization. **Eva Lieberherr:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jenvman.2026.129319.

Data availability

Data will be made available on request.

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