Stakeholder Engagement for OneHealthDrugs Action

Brussels meeting 07/07/25

Integrating Ecotoxicity in Early-Stage Drug Development

Integrating Ecotoxicity in Early-Stage Drug Development

OneHealthdrugs Stakeholder Meeting

Date: 7 July 2024
Venue: COST Association Premises, Brussels

1. Welcome & Opening Remarks

Theo Zacharis

Stakeholder Engagement for OneHealthDrugs Action

27 Feb 2025

2. Context & Current Landscape

The Hidden Impact of Pharmaceuticals on the Environment

▶ Pharmaceuticals persist in the environment, affecting ecosystems and human health.

• **Fact 1:** Over **4,000** active pharmaceutical ingredients (APIs) are in use globally, many of which are detected in water bodies. *(Source: WHO, 2022)*

• **Fact 2:** A **2022 study** found pharmaceutical contamination in **over 258 rivers across 104 countries**, with antibiotics, antidepressants, and painkillers present at harmful levels. *(Source: University of York, 2022)*

• **Fact 3:** The European Environment Agency (EEA) reports that **less than 50%** of pharmaceutical compounds in wastewater are removed by conventional treatment plants.

▶ 📌 **Why It Matters to Policymakers?**

• **Unregulated pharmaceutical pollution** can lead to antibiotic resistance, endocrine disruption, and biodiversity loss.

• **Economic cost**: Water treatment costs rise as pharmaceutical residues accumulate.

• **Regulatory gap**: Current laws focus on human safety but ignore long-term environmental risks.

The Hidden Impact of Pharmaceuticals on the Environment (VBD and anti-parasitic)
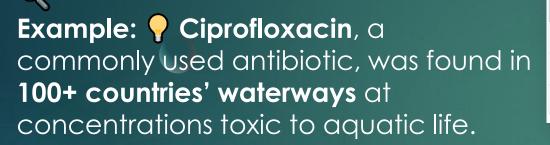
- **Over 75%** of VBD drugs are excreted in active form, entering **soil, water, and food chains** *(WHO, 2023)*.

- **Antiparasitic residues (e.g., ivermectin, fipronil)** detected in **livestock runoff, impacting insect biodiversity** *(EU Environment Agency, 2022)*.

- **Antibiotic pollution accelerates antimicrobial resistance (AMR)**, reducing the efficacy of drugs against VBD-associated microbial infections *(Lancet AMR Report, 2023)*.

- 📌 **Why It Matters to Policymakers?**

- **Regulatory gap**: Most drug approvals assess **human/veterinary safety** but overlook **ecosystem impact**.

- **Biodiversity risk**: Vector-control pesticides & antiparasitics **harm pollinators & aquatic species**, reducing **natural disease regulation**.

- **Public health challenge**: AMR from pharmaceutical waste **threatens global efforts against emerging infections**.

What Is Missing in Current Drug Development?

▶ **Key Message:** The environmental impact of new drugs is considered **too late** in the approval process.
📊 **Current Process vs. Needed Process**

🔍

Example: 💡 **Ciprofloxacin**, a commonly used antibiotic, was found in **100+ countries' waterways** at concentrations toxic to aquatic life.

Phase	Current Process	What Needs to Change?
Preclinical	No requirement for environmental risk screening	Require **in silico & assay-based ecotoxicity**
Clinical	Focuses only on host safety (human/veterinary)	Include **AMR & bioaccumulation** impact
Regulatory	EMA/FDA approvals exclude long-term effects	Integrate **One Health-based risk evaluation**

No early-stage ecotoxicity screening was done before its approval.
Policy Need: If early predictive tools had been used, such issues could have been identified **before mass production**.

▶ 📌 **Policy Action**:

• Implement **early-phase ecotoxicity screening** as part of regulatory approval.

• Encourage pharmaceutical companies to **adopt predictive modelling** for environmental impact.
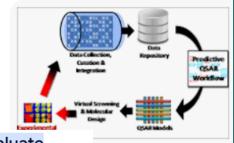
In Silico and Assay-Based Ecotoxicity Tools

▶ Cutting-edge tools can predict environmental risks **before** drugs reach the market.

▶ 🔬 **Available Tools Policymakers Can Leverage:**

1. **QSAR Models** *(OECD Toolbox, VEGA, ECOSAR)* → Predict toxicity based on molecular structure.

Structure-activity relationship (SAR) and quantitative structure-activity relationship (QSAR) models - collectively referred to as (Q)SARs - are mathematical models that can be used to predict the physicochemical, biological and environmental fate properties of compounds from the knowledge of their chemical structure. The VEGA platform provides predictive QSAR models to evaluate chemical properties and predict biological activity. VEGA includes models for hydrophobicity (LogP), bio-concentration factor, aquatic toxicity, mutagenicity, carcinogenicity, developmental toxicity and skin sensitisation. The ECOlogical Structure-Activity Relationship Model (ECOSAR) Class Program is a computerized version of the ecotoxicity analysis procedures as currently practiced by the Office of Pollution Prevention and Toxics (OPPT) when data are lacking for risk assessment development.

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2. **High-Throughput Screening** *(OECD Test Guidelines, EPA Models)* → Rapidly assesses bioaccumulation potential.

3. **AI & Machine Learning in Toxicology** *(e.g., DeepTox, REACH Models)* → Improves risk prediction for regulators.

▶ 📌 **How Policymakers Can Act:**
✅ Require early-phase **environmental impact assessment** for **high-risk drug categories**.
✅ Allocate **EU Horizon funding** for AI-driven ecotoxicology tools.
✅ Encourage pharmaceutical **self-regulation incentives** (e.g., tax benefits for sustainable drug development).

Regulatory Gap & How to Address It

▶ Existing regulations **lack enforcement mechanisms** for pharmaceutical pollution control.

🔴 **Current Weaknesses in EU Policy:**

> The Regulation on the **registration, evaluation, authorisation and restriction of chemicals** (REACH) is the main EU law to protect human health and the environment from the risks that can be posed by chemicals.

• **REACH & EMA regulations** focus on human safety, **not long-term ecosystem impact**.

• **Pharmaceuticals exempt** from key environmental policies (e.g., EU Water Framework Directive).

• **Inconsistent monitoring** across EU member states.

▶ ✅ **Proposed Policy Actions:**

1. **Legislate Early-Phase Ecotoxicity Assessment** → **Amend EMA Guidelines** to include environmental screening as part of new drug approval.

2. **Require Public Disclosure of Environmental Impact** → Encourage pharmaceutical companies to **publish ecotoxicity reports** alongside clinical data.

3. **Expand EU Water Framework Directive** → Include **pharmaceutical-specific pollution controls** in environmental legislation.

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Regulatory Gap & How to Address It

▶ 📌 **Next Steps for Policymakers:**

• **Support integration of in silico & assay-based tools** in the EMA approval process.

• **Promote cross-industry collaboration** to develop sustainable pharmaceuticals.

• **Fund pilot programs** testing new regulations before widespread implementation.

▶ **Key Takeaways for Policymakers:**
✓ **Early ecotoxicity screening** prevents long-term environmental damage.
✓ **Existing regulatory frameworks are outdated** and require urgent updates.
✓ **New in silico and AI-driven models** offer a **cost-effective** solution to predict pharmaceutical pollution before market approval.

▶ **Next Steps:**
🚀 **Form a working group** to draft policy recommendations.
📢 **Engage pharmaceutical stakeholders** to ensure industry compliance.
🔬 **Launch an EU-wide pilot** for **mandatory environmental impact screening** in drug development.

Regulatory Gap & How to Address It

▶ **Why Now?**

💡 **The Next Pandemic May Come from Vector-Borne AMR**

- Without action, **pharmaceutical pollution & AMR** will create **untreatable vector-borne infections**.

- The EU must **lead the global effort** in **eco-conscious drug development.**

- With **OHD COST Action support**, we can **develop policies that balance innovation & sustainability**.

- This **policymaker-friendly approach** focuses on:

✅ **Clear data-driven urgency** (e.g., AMR, One Health risks).
✅ **Practical regulatory solutions** (e.g., integrating risk screening early).
✅ **Policy incentives** (e.g., funding & pharma collaborations).

3. Industry & Scientific Perspectives

Theo Zacharis

Industry & Scientific Perspectives – The Role of Pharmaceuticals in Environmental Health

▶ The pharmaceutical industry is at a crossroads—balancing drug efficacy with environmental sustainability.

📌 **Why This Matters?**

- **Pharmaceutical waste is a major contributor to environmental contamination**, yet industry adoption of ecotoxicology in drug discovery remains **voluntary, not mandatory.**

- **Veterinary and agricultural pharmaceuticals** impact **both ecosystem biodiversity & One Health initiatives.**

- **Industry can drive innovation** by integrating **green chemistry principles & predictive ecotoxicity modelling**.

- 📊 **The Challenge: Balancing Drug Effectiveness with Environmental Safety**

✅ **Industry Opportunity:**

Factor	Current Industry Focus	Proposed Sustainable Approach
Drug Development	Focus on efficacy & safety for human/animal health	Include **early ecotoxicity screening**
Environmental Regulation	Only required at **late regulatory stages**	Integrate in **preclinical design**
Drug Residue Monitoring	Monitored post-market in wastewater	Design **biodegradable formulations**

- Shift from **reactive** environmental risk management to **proactive** green drug design.

How Pharma Integrates Ecotoxicity – Current Practices

▶ Leading pharmaceutical companies **recognize** the need for ecotoxicology but

lack standardized guidelines.

▶ 🔬 **Current Approaches in the Pharma Pipeline**
✓ **Predictive In Silico Modelling**

• Some companies **voluntarily** use **QSAR & molecular simulations** to predict environmental impact.
Example: **AstraZeneca uses ECOSAR models** to screen potential toxicity before preclinical development.

▶ ✓ **Green Chemistry in Drug Formulation**

• Novartis & GSK are investing in **biodegradable APIs** to reduce environmental accumulation.
Example: **Merck reduced solvent waste by 40%** through green chemistry initiatives.

▶ ✓ **Industry-Led Risk Assessments**

• Pfizer & Bayer conduct **in-house risk studies**, but these are **not industry-wide standards**.

• Limited collaboration between pharma & regulators on **uniform early-phase guidelines**.

▶ 📌 **Regulatory Challenge:** No global standard enforces **early-stage** ecotoxicity screening in pharma pipelines.

The Regulatory Gap & Industry Challenges

► 📉 **Why Aren't Companies Fully Adopting Ecotoxicology?**
[1] **Lack of Incentives:** Companies **prioritize market speed over environmental screening** due to **cost & regulatory pressure**.
[2] **Regulatory Inconsistency: EMA & FDA do not require** ecotoxicity testing before **late-phase drug approval**.
[3] **Data Gaps in Risk Modelling: Lack of historical ecotoxicity data** limits accurate predictions for **new molecular entities (NMEs)**.

► 📌 **Key Industry Barriers:**
🚧 **High costs** of experimental ecotoxicity assays.
🚧 **Limited data-sharing** between industry & regulators.
🚧 **Competing priorities**—focus remains on efficacy & market access.

► ✅ **Proposed Industry Shift:**

• **Integrate mandatory ecotoxicity modelling into preclinical assessments**.

• **Create shared databases** for pharma to contribute environmental impact data.

• **Develop financial incentives** (e.g., tax relief for eco-conscious drug design).

Veterinary & Agricultural Pharmaceuticals – A Growing Environmental Concern

Veterinary pharmaceuticals used in livestock & agriculture **contribute significantly to ecosystem pollution**.

▶ 📌 **Why This Is a Priority?**

- **80% of antibiotics sold worldwide are used in livestock**, impacting **water systems & soil biodiversity** *(FAO, 2023)*.
- **Antiparasitics like ivermectin persist in animal feces**, affecting insect populations essential for waste breakdown.
- **Lack of wastewater treatment in agriculture** leads to pharmaceutical runoff into natural ecosystems.

  ▶ 🔬 **Key Veterinary Drug Risks:**
  ✓ **Antiparasitics (e.g., Ivermectin, Fipronil)** → Bioaccumulate in livestock manure, harming dung beetles & soil health.
  ✓ **Antibiotics (e.g., Tylosin, Tetracyclines)** → Lead to antimicrobial resistance (AMR) hotspots in agricultural runoff.
  ✓ **Hormones (e.g., Estradiol, Trenbolone)** → Found in groundwater, affecting fish reproduction & ecosystem balance.

▶ 📌 **Industry Challenge: Veterinary drugs have even fewer environmental regulations than human pharmaceuticals**.

A Call to Action for Pharma & Veterinary Sectors

▶ 📌 **How Industry Can Lead Change**

▶ **Integrate ecotoxicology into preclinical drug development.**
Collaborate with regulators to establish universal industry standards.
Invest in eco-friendly formulations & biodegradable alternatives.
Engage veterinarians & farmers in sustainable pharmaceutical practices.

▶ 💡 **Key Takeaways:**
✓ **Pharma companies must go beyond compliance** to lead environmental responsibility.
✓ **Veterinary pharmaceuticals remain largely unregulated**—this must change.
✓ **Collaboration across industry, regulators & veterinarians is essential** for sustainable One Health drug development.

▶ **Next Steps:**
📣 **Industry, veterinarians & regulators must establish a joint working group** to develop **eco-conscious drug development policies**.
📣 **Encourage pharmaceutical companies to invest in early-stage ecotoxicity testing**.
📣 **Advocate for One Health-based pharmaceutical regulation reforms** in EMA & FDA frameworks.

4. Stakeholder Engagement & Strategic Plan

Stakeholder Engagement & OHD Strategic Plan

▶ Successful integration of ecotoxicity in drug development requires **policy support, regulatory action, and multi-sector collaboration.**

▶ 📌 **Three Key Goals of OHD Strategy:**
🔲 **Influencing Regulatory Bodies** → Securing policy backing for **mandatory early-stage ecotoxicity screening**.
2️⃣ **Ensuring OHD COST Action Sustainability** → Establishing a long-term framework beyond Action.
3️⃣ **Building a Multi-Sector Coalition** → Bringing together **industry, academia, regulators, and veterinarians**.

▶ ✅ **Ultimate Objective:** Move from voluntary adoption to **structured regulatory inclusion of ecotoxicity assessments**.

Engaging Policymakers & Regulatory Bodies

▶ Policymakers **set the legal foundation** for industry-wide change.

▶ 📢 Who Do We Need to Engage?

✓ **EU Commission – Directorate-Generals (DGs)** → Specifically **DG ENV (**Environment**), DG AGRI (**Agriculture & Rural Development) **& DG SANTE (**Health & Food Safety**)** or even **DG CLIMA** – Climate Action and **DG MARE** – Maritime Affairs & Fisheries.

✓ **European Parliament Committees** → **Committee on Environment, Public Health & Food Safety (ENVI)**.

✓ **National & Regional Regulatory Authorities** → Agencies **responsible for pharmaceutical approvals**.

✓ **OECD, EMA, and WHO Working Groups** → Global influence for **harmonized policy adoption**.

Building a Coalition for Regulatory & Industry-Wide Adoption

▶ **Cross-sector collaboration** accelerates regulatory change & industry adoption**.**

▶ 🔍 **Key Stakeholders to Engage:**

✓ **Regulatory & Policy Experts** → European Commission, EMA, OECD, national agencies.

✓ **Pharmaceutical Industry** → R&D leaders, sustainability teams, regulatory affairs.

✓ **Veterinary & Medical Associations** → Human & animal health representatives advocating for drug safety.

✓ **Environmental Monitoring Bodies** → EU Environment Agency, water quality monitoring agencies.

✓ **SMEs & Biotech Innovators** → Pioneering companies developing sustainable pharmaceuticals.

Building a Coalition for Regulatory & Industry-Wide Adoption

▶ 📣 **How to Align Efforts for a Collective Push?**

   ▶ 🚀 **Establish a Permanent OHD Policy Forum** → Regular meetings between industry, regulators, and scientists.

   🚀 **Launch a Multi-Sector White Paper** → A unified recommendation document to **push regulatory change**.

   🚀 **Secure Financial Backing for Sustainable Pharma Development** → Attract EU & private investment in **eco-conscious drug R&D**.

▶ ✅ **Outcome Goal:** Align stakeholders under **one agenda** to standardize **early-phase ecotoxicity assessment across Europe**.

5. Next Steps & Action Items

Stakeholder Outreach & Engagement Roadmap – Brussels Meeting (June 2024)

▶ **Objective:** Successfully invite and engage **10 key stakeholders** from regulatory, industry, veterinary, and environmental sectors to a high-impact meeting in Brussels focused on **integrating ecotoxicity in early drug development**.

▶ 📌 **Phase 1: Stakeholder Identification & Prioritization (March - Early April 2024)**

▶ 🎯 **Goal:** Identify, map, and prioritize **top 10 influential stakeholders** for direct engagement.

🔍 **Target Stakeholder Groups: Regulatory Authorities** (EMA, EU Commission DG SANTE, DG ENV, OECD, National Health Agencies), **Pharmaceutical Industry Leaders** (R&D Heads, Regulatory Affairs Executives from GSK, Novartis, Bayer, Pfizer), **Veterinary & Medical Associations** (European Veterinary Federation(FVE), One Health Initiative), **Environmental & Ecotoxicology Experts** (EU Environment Agency, Water Framework Directive representatives), **Policymakers & Parliament Representatives** (MEPs from the SANTE, ENVI & AGRI Committees).

Stakeholder Outreach & Engagement Roadmap – Brussels Meeting (June 2024)

▶ 📌 **Practical Steps:**

✅ **Create a Stakeholder Matrix** – Rank potential attendees based on **influence, relevance, and engagement likelihood**.

✅ **Personalized Outreach List** – Identify key contact persons within target organizations.

✅ **Prepare Initial Engagement Materials** – Draft short **invitation letters, briefing notes, and a one-page concept note** explaining meeting objectives.

▶ 📌 **Phase 2: Initial Outreach & Personal Invitations (Mid-April – May 2024)**

▶ 🎯 **Goal:** Send out personalized invitations and secure RSVPs for the Brussels meeting.

📣 **Outreach Strategy:**

✓ **Personalized Emails to High-Priority Stakeholders** – Send targeted invitations **signed by senior OHD representatives**

✓ **Official Endorsements** – Secure backing from a relevant EU agency or COST representative for credibility.

✓ **Follow-Up Calls & Meetings** – Schedule **short online calls with key invitees** to address concerns and build commitment.

✓ **Leverage Industry & Policy Networks** – Use **existing contacts in pharmaceutical, veterinary, and environmental policy circles** to facilitate introductions.

Stakeholder Outreach & Engagement Roadmap – Brussels Meeting (June 2024)

▶ 📌 **Practical Steps:**

✅ **Draft & Send Invitation Letters** – Explain the significance of the meeting and the impact of their participation.

✅ **Prepare Talking Points for Direct Calls** – Summarize **what's in it for them** (e.g., policy influence, industry standards, regulatory alignment).

✅ **Monitor & Track Responses** – Maintain a **real-time RSVP tracker** to ensure outreach success.

Stakeholder Outreach & Engagement Roadmap – Brussels Meeting (June 2024)

▶ 📌 **Phase 3: Pre-Meeting Engagement & Agenda Refinement (Late May – Early June 2024)**

▶ 🎯 **Goal:** Ensure stakeholders are well-prepared and committed to active participation.

📢 **Engagement Actions:**

✓ **Send Pre-Meeting Briefing Materials** – Include a short **policy briefing, draft agenda,** and expected outcomes.

✓ **Organize a Pre-Meeting Virtual Q&A Session** – Address **questions, concerns, and expectations** of confirmed participants.

✓ **Confirm Final Attendee List** – Ensure at least **10 high-profile stakeholders** commit to attending.

✓ **Develop Stakeholder-Specific Talking Points** – Tailor key **discussion themes based on confirmed attendees**.

Stakeholder Outreach & Engagement Roadmap – Brussels Meeting (June 2024)

▶ 📌 **Practical Steps:**

✅ **Finalize the Meeting Agenda** – Reflect participant interests to maximize engagement.

✅ **Share Background Materials** – Send **one-pagers on ecotoxicity in drug development**.

✅ **Prepare Moderator & Speaker Notes** – Ensure **structured discussion and clear action points**.