Proposal to reduce environmental impact from the manufacture of medicines and active pharmaceutical ingredients

- Reducing health risks such as promotion of antimicrobial-resistant bacteria.
- Correcting the situation where industrial discharges of active pharmaceutical ingredients into the environment are not regulated.
- Maintaining a level playing field between nations and companies. Building on existing and functioning regulations accompanied with inspection.
Pollution of the water environment

Pollution from the manufacture of medicinal products has implications far beyond the local environment. For example, in waterways receiving waste from production sites, higher concentrations of antibiotics have been detected than the levels found in the blood of patients undergoing treatment. As a result, antimicrobial resistant bacteria are developing. UN Environment has declared that antimicrobial resistance from environmental pollution is among biggest emerging health threats. Given that antimicrobial resistance is a global threat, the risk to both animal and human health is clear. Industrial discharges of other active pharmaceutical ingredients (APIs, i.e. active substances) into the waterways also add to the negative health and environmental effects.

Active substances are not regulated

Today, there is no regulation governing discharges and emissions of active pharmaceutical ingredients (API) into the environment while manufacturing medicines. In comparison, solvents and other chemicals are regulated by the Industrial Emissions Directive (IED). The IED regulation applies only to manufacturing sites in Europe.

Regulating industrial discharges of active substances

Sweden proposes that the limiting of manufacturing discharges of active substances could be achieved through the introduction of a modified definition of Good Manufacturing Practice (GMP) into the regulation of veterinary and human medicinal products. According to the proposal, within the framework of Good Manufacturing Practices (GMP), there would be requirements imposed on those who manufacture medicinal products to comply with specific requirements limiting discharges and emissions of APIs into the water environment. It is also proposed to amend the regulatory framework so that the definition of GMP is moved to the Human Medicinal Products Directive and the Veterinary Medicinal Products Directive, respectively. A possibility for progress in this direction is included in the new Veterinary Medicinal Products legislation.

In order to avoid overlaps with other legislation, the control should focus on active substances. The proposal is also to be limited to the substances where it is required that the applicants seeking marketing authorisation for medicinal products has to carry out a complete environmental risk assessment (ERA) for the active substances. Connecting control of emissions to the existing regulatory framework of GMP would allow for control of the whole production chain, thus taking advantage of a system of control and action that is already in place. Additional benefits include preserving a level playing field regarding effects on competition between companies or countries within and outside Europe.

How would it work?

Non-compliance by a manufacturer with discharge/emission limits of active substances would mean non-compliance with the GMP regulations. This will affect all manufacturers of medicinal products for the EU/EEA market. Since large parts of the GMP regulations are harmonized through

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2 Emerging issues of environmental concern, UN Environment 2017
4 Platform to enable the initiation of a revision of EU legislation on GMP, in order for legislation also to comprehend environmental considerations. Swedish Medical Products Agency, 2011
5 REGULATION (EU) 2018/... OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of ... on veterinary medicinal products and repealing Directive 2001/82/EC (The regulation will be finalized in 2018).
the International Council of Harmonization (ICH), there are good prospects for establishing global consensus and harmonization.

Potential inspection in practice, suggested model:
Discharge of and emission limits for active substances are to be regulated by the European Commission. An inspector from an accredited organization makes an environmental inspection. This inspection verifies that emission control systems comply with regulations. The GMP inspector relies on the environmental verification during the inspection. Thus the GMP inspector will not perform supervision of the emission control system, but will control the verification.

Benefits of using the GMP regulations
Advantages of introducing environmental aspects into GMP include:

- Reduces the risk of unwanted impact on human and animal health and well-being due to industrial discharges of active substances from manufacturing of medicines.
- Health benefits are achieved regardless of where production takes place – applicable to all production for the EU/EEA markets.
- All manufacturers are bound by the regulation on discharge/emission limits if they want access to EU/EEA market.
- Competition neutral – does not affect competitiveness based on geographic location.
- GMP, a system for control, monitoring and actions regarding non-compliance, is already in place.
- Allows for control of the complete chain of production.
- Well-suited for international harmonization beyond Europe.

Potential disadvantages could be that some manufacturers will not adjust their production to the EU/EAA market. It is therefore important to have parallel discussions and to harmonize with WHO GMP and ICH. Cost of installation and the operation of the facility reducing emissions may influence the price of the medicine. On the other hand, those who have already invested in
optimizing the production and reducing emissions would get credit for their costs. The prize for not limiting the emission on the other hand cannot be calculated in money only.

**Contribution to the Sustainable Development Goals**

To fulfil the promises of the Sustainable Development Goals, to ensure healthy lives and promote well-being for all at all ages, and to ensure clean water and sanitation, we need to reduce the emission of active substances from medicines into the environment and combat antimicrobial resistance. This proposal will promote global health and support access to safe and effective medicines in the future.

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