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AmCham EU believes legislation applied to pharmaceuticals and medical technologies must consider health implications as well as environmental concerns.

Introduction

AmCham EU's Health Committee member companies support a balanced approach to environment concerns in the field of pharmaceuticals and medical devices and call for an improved cohesion between environment and healthcare policies. The extensive body of EU legislation and guidelines on the development, manufacture or use of pharmaceuticals and medical technologies already provides a framework to ensure that the environmental impact is assessed. Additional provisions must be consistent with and should not duplicate the existing legislation.

In addition, AmCham EU is concerned about the restrictions placed on the use of substances in medical devices and In-Vitro diagnostics (IVDs) as well as dual and competing regulation in the use of radioisotopes for medical purposes..

This paper examines some of these issues and is AmCham EU's first attempt to raise awareness and to call for an informed and science-based dialogue among all stakeholders to explore and develop solutions.

Pharmaceuticals and the environment (PiE)

The possible effects of residues of PiE are a concern to governments and other stakeholders in the EU. The American pharmaceutical industry recognizes this and is committed to advancing the potential environmental impacts posed by the use of pharmaceutical products. Extensive information about the environmental fate and effects of pharmaceutical compounds is contained in the Environmental Risk Assessment (ERA) and the risk-benefit assessment of medicines, i.e. the outcomes of scientific assessments of pharmaceutical substances. It is critical to consider this information when applying the precautionary principle – the basis of many environmental policies in the EU – to this problem. The existing approach will provide patients with quality, safe and effective medicines in a timely manner, while protecting the environment from unanticipated or unacceptable effects.

Pharmaceuticals can enter the environment through different sources. For human pharmaceutical products, the pathway to the environment typically is with domestic wastewater. The main source of entry is through patient excretion: medicines pass through the human body without being metabolized completely and make their way to surface waters through municipal wastewater treatment systems. When pharmaceuticals are discarded (unused or as residual

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in packaging), or released during manufacturing they can also find their way into wastewater treatment systems.

Since 1977, the US Food and Drug Administration (FDA) has regulated PiE through the environmental review process for New Drug Applications submitted to the FDA. In the European Union, the potential environmental risk of human pharmaceuticals is assessed before marketing products. According to the relevant guidelines (EMEA, 2006, 2007), the ERA is a tiered process in which the first phase (Phase 1) is limited to the intended use considering only environmental exposure. If the predicted environmental concentration (PEC) of a pharmaceutical exceeds a defined threshold of environmental concern, such as 0.01 ug/L under the EMEA guidelines, studies on environmental fate and effects must be performed in Phase 2.

Taking into account the existing assessment of medicines, the Water Framework Directive is not the appropriate tool to regulate the issues mentioned above. In its January 2012 proposal for revision of the Water Framework Directive (COM(2011)876), the European Commission proposed that pharmaceuticals that "present significant risk" to the aquatic environment be classified either as: priority substances with measures aimed at reducing their presence in the environment; **or** as priority hazardous substances for which emissions to the environment are eliminated. Ultimately, this action could result in eliminating these products in the EU. The following substances are proposed to be included: Diclofenac (an anti-inflammatory for pain relief in acute and rheumatic conditions); Ethinyl-estradiol (the estrogenic component in practically all modern formulations of combined oral contraceptive pills); and Estradiol (an estrogenic hormone naturally produced and excreted by humans and many animal species, also manufactured synthetically and prescribed for treatment of menopausal disorders - the vast majority of Estradiol present in the environment is naturally occurring).

For years, these substances have been valued treatments for European patients, and it is important that patient access to these medicines continues. Their inclusion in the priority substances list could not only lead to increased surveillance requirements but also to potential restriction of access, putting patients at risk. Since restriction of medicines has also an impact on public health medicines and their potential impact on the environment should be assessed in the context of existing pharmaceutical legislation. A proportionate, balanced and coordinated legal framework will facilitate research and development of pharmaceuticals that meets citizen's needs and ultimately fosters growth while providing environmental protection.

Typically, environmental regulations do not integrate public health aspects and the issue of PiE is handled within an extended pharmaceutical framework. The report of DG Health and Consumer Policy (DG SANCO) as required by the Pharmacovigilance Directive could be an ideal opportunity to assess this issue in more detail and to propose concrete actions to ensure both continued patient access and environmental protection.

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Restrictions on Substances Hazardous to Health (RoHS) and medical devices

The RoHS legislation (Directive 2011/65/EU) restricts the use of six substances in manufacture and design of electric and electronic equipment (EEE). When originally introduced, this legislation sensibly granted the healthcare sector a number of exemptions – until June 2014 – for substances critical to the development of medical products. In some instances there was an expectation that alternative substances could be developed or used to replace prohibited ones. Laws of chemistry and physics have limited the identification of alternatives. For example, lead solder continues to be a necessary component of Magnetic Resonance Imaging (MRI) devices and cadmium still needs to be used in X Ray detector tubes. While the medical devices sector has recently secured additional exemptions in RoHs 2 post-2014 for 8 substance applications, more applications will require assessment and exemption. This might not be possible in the proposed timeframe. All current exemptions should be extended after June 2014 until they have been reviewed.

Article 2(2) of the same legislation (Directive 2011/65/EU) will also have a significant impact on the availability of refurbished medical devices and monitoring equipment. Specifically, medical devices as well as monitoring and control equipments placed on the market before 2014 will not be able to be refurbished, re-sold, repaired, rented or leased. This means that vital and perfectly functional equipments such as Computed Tomography (CT) or MRI scanners cannot be used. While the European Commission has committed to amending Article 2(2), the proposed time period for the legislative process of the amendment (2013-2014) will create significant uncertainty for medical device and IVD manufacturers of EEE. They would need to change complex design, manufacture and supply processes to ensure the continued access for patients of vital medical technology.

Finally, the potential extension of the substance scope of RoHS (by adding more to the 6 substances currently covered by the Directive), will create further uncertainty and R&D challenges to device and IVD manufacturers. Many substances which could be toxic under normal circumstances, can be of tremendous benefit to patients when used in a medical application.. Hence, appropriate transition periods for applying any new substance restrictions for the healthcare sector would be the appropriate step to strike a balance between public health and environmental concerns.

The use of radioisotopes in medical diagnostics and therapy

For historial reasons, environmental aspects on the use of radioisotopes are regulated through the Treaty establishing the European Atomic Energy Community (Euratom) under the responsibility of DG Energy. On the other hand, the control of devices using radioisotopes such as CT scanners and proton beam therapy devices used for the treatment of cancer are regulated by the Medical Devices Directive, supervised by DG SANCO. The regimes lay down two different processes for a markerting authorisation approval with disctinct timescales for assessment and decision, leading to delays and confusion among

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suppliers. Better coordination is needed between DG Energy and DG SANCO to ensure that data is requested in the same format and applications can be run concurrently in the same timescales.

REACH Provisions for Medical Devices and IVDs

Existing environmental legislation (e.g. WEEE, RoHS, REACH) already places significant requirements on Medical Devices and IVD products throughout their life cycle. The medical devices Directives 90/385/EEC, 93/42/EEC and 98/79/EC already set out the requirements on manufacturers for placing safe and efficient products on the European market. This includes stringent and quality manufacturing processes as well as conformity assessment procedures which ensure the safety and efficacy of our products.

The medical devices sector does not manufacture substances as such, but it does predominantly manufacture articles. In the case of the IVD sector they primarily produce preparations (mixtures) rather than substances; hazardous substances could be used in various process steps or products. These substances are either imported directly into the EU or procured from EU manufacturers or distributors. Because the industry is responsible for the registration of substances, we expect our suppliers to be compliant with REACH requirements and we take all necessary measures to communicate with them effectively. In the current legislative regime, devices and IVDs fall only partially under the REACH scope (e.g. when substances in articles have negative environmental impact or when they are used in the manufacturing process).

In this context, the main concerns for devices and IVD manufacturers include:

- **The inclusion of new substances in the REACH authorization process.** In industry's experience with REACH, this is a political issue which often misses a dedicated impact assessment and clearcost-benefit analysis related to patient care. . The exemption for medical devices and IVD medical devices does not automatically extend to process chemicals used in manufacturing of a device and where that substance is not found in the final product. The substance may however be crucial to the manufacturing of the device particularly in biotechnology (this is the case for cobalt salts and borates).
- **Pressures on the supply chain**. While finished devices and IVDs might be exempted from parts of REACH, industry has direct experience with suppliers discontinuing the production of critical chemicals during the SVHC classification stage. As a relative small customer to most chemical manufacturers, the industry would not be able to protect major manufacturing in Europe from using some of these substances. The negative impacts of such a development for both patients and the European economy are unquestionable.
- **REACH review and gaps with sector legislation.** The recent evaluation by the European Commission of the interaction between REACH and sector legislations includes worrying elements as relates to medical devices. It suggests that besides the end product, further safeguards against hazardous substances should be provided (presumably in sectoral legislation) for the formulation and manufacturing stages. In addition,

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testing for the environmental hazards of substances is also proposed. Overall, there is a call to align sectoral legislation further with REACH requirements. While industry respects the goals of REACH, it is our view that medical devices and IVD legislations adequately ensure the safety of our products to patients; this remains the key objective of these regulations. . Including environmental risk assessment in the essential requirements for medical devices would impose an additional layer of burden, slow down the time to market of life-saving technology and ultimately could reduce the availability and/or increase the cost of healthcare. Furthermore medical devices and IVD medical devices are only exempt from authorization requirements when the substances have been listed as an SVHC due to their properties raising concern for human health. Therefore adding the requirement to assess risks to the environment is redundant.

Policy Recommendations

AmCham EU's Healthcare Committee calls for:

- In the short term, removal of Diclofenac, Ethinyl-estradiol and Estradiol from the priority list of substance in the draft Water Framework Directive;
- In the context of RoHS:
  - Accelerate the legislative process for amending Article 2(2)
  - Engage early with healthcare stakeholders in an appropriate impact assessment of any substance additions under the Directive scope.
- In the context of REACH:
  - Assess fully, with industry input, the socio-economic impact to medical devices from the reduction or elimination of supply for critical substances – for which no alternatives exist - as a result of the authorization and restriction processes under REACH.
  - Maintain and ensure clarity of the medical device exemption from authorization, in view of the sector's own strong regulatory framework (Medical Devices and IVD Directives).
  - Align any potential REACH-based regulatory measures – where these concern substances with no safe alternatives – with safety and efficacy requirements found in the medical devices and in-vitro diagnostics sectoral legislations (MD/IVD Directives)
  - Provide adequate transition periods for our industry to find safe alternatives where these exist in response to the inevitable market pressures as a result of SVHC listing.
- In the longer term, an informed and science-based dialogue among all stakeholders should take place to explore and develop solutions to address the potential for pharmaceuticals, IVDs and medical devices to impact the environment within the current pharmaceutical and medical devices legislative frameworks.

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Conclusion

AmCham EU supports a science-based approach to policy making that takes into account the costs and benefits of each legislative proposal, while at the same time favouring a business environment that will meet citizens' needs and foster growth. It is clear that in tackling legislation that could impact the health of the European population environmental **and** health concerns should both be taken into account and given the appropriate weight.

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AmCham EU speaks for American companies committed to Europe on trade, investment and competitiveness issues. It aims to ensure a growth-orientated business and investment climate in Europe. AmCham EU facilitates the resolution of transatlantic issues that impact business and plays a role in creating better understanding of EU and US positions on business matters. Aggregate U.S. investment in Europe totaled €1.7 trillion in 2010 and directly supports more than 4.2 million jobs in Europe.

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