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FROM THE BARONESS PENN
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Dear Natalie,

Thank you for the valuable points you put forward during Tuesday's Report Stage, on protection of the environment.

I committed to write to you to provide further detail on the different approaches taken in the Bill with regards to the regulation of Human Medicines and Devices and Veterinary Medicines and consideration of the environment.

Veterinary Medicines

The regulatory systems for veterinary medicines and human medicines, whilst broadly similar, have some major distinctions that warrant including explicit protection of the environment within the veterinary medicines clause of the Bill. As I mentioned during Tuesday's debate, the environmental safety aspects of the regulatory framework for veterinary medicines relate to the potential impact of such medicines on the terrestrial and aquatic ecosystems and their flora and fauna – soil micro-organisms, fungi, algae, plants, invertebrates, fish etc. Chemicals used as veterinary medicines in food-producing animals, and/or their metabolites, can enter the environment through the application to land of manure and slurry from treated animals, through direct excretion by grazing animals, or through loss of the medicine during application. Furthermore, in aquaculture veterinary medicines may need to be applied directly to the water. These treatments have a high potential to reach the aquatic environment and any residues in manure or slurry may also enter the aquatic environment indirectly via surface runoff or leaching to groundwater. As such, there is more direct exposure to the environment when it comes to veterinary medicines as compared to human medicines. All conditions applied to manufacture and disposal of human medicines (discussed below) also apply to veterinary medicines.

The Veterinary Medicines Directorate (VMD) protects not just animal health but also public health and the environment. It is therefore only right that when we make regulations under the Bill that relate to veterinary medicines, we need to be satisfied that they would promote one or more of the following: the health and welfare of animals, the health and safety of the public and the protection of the environment.

Human Medicines

Direct exposure to the environment is significantly less for human medicines, as human medicines are administered directly to patients. However, the risk of their environmental exposure in clinical use still needs to be evaluated and robust arrangements are already in place.

The Baroness Bennett of Manor Castle
House of Lords

An environmental risk assessment (ERA) is already part of the requirements when applying for marketing approval in the UK. Many medicines taken by patients, irrespective of their administration route (oral, intravenous, subcutaneous, etc.), are excreted in urine and faeces and so their impact on sewage treatment and how they enter the environment (soil, surface water and ground water) must be risk assessed.

UK pharmaceutical regulatory guidance has adopted European guidance, the *Guideline on the environmental risk assessment of medicinal products for human use*, which was introduced in 2006[1], with a Q&A document first published in 2011[2]. An updated document with more detailed guidance on reviewing the risk of endocrine disrupting drug substances on the environment, such as oestrogen, is currently in draft form and is yet to be formally adopted[3]. This regulatory guidance provides a framework of the types of environmental studies a pharmaceutical company should undertake in order to assess the impact of their medicine on micro-organisms, plants and animals that would live in the affected environment. These studies are internationally standardised and follow the most recent test guidelines issued by the Organization for Economic Co-operation and Development (OECD) and to comply with Good Laboratory Practice (GLP) standards.

The presence of the ERA acts as a formal regulatory document for each human medicine approved for marketing in the UK, detailing any environmental risks, and includes any specific arrangements to limit the environmental impact. This could include appropriate product storage, appropriate measures regarding the use of the medicine, and appropriate disposal of the used or unused medicine.

UK manufacturers are also required to comply with Good Manufacturing Practice (GMP) guidelines and MHRA inspectors will inspect manufacturing sites for compliance. GMP is very clear in providing robust measures that ensure manufacturers safely and responsibly dispose of waste materials during the process of manufacturing human medicines. For example, drainage systems must be designed so that effluents can be effectively neutralised or decontaminated to minimise the risk of environmental contamination. There should be written procedures for the safe and documented storage and disposal of waste, disposable and rejected items, such as units from infected donors or out of date blood.

Baroness Jolly raised specific concerns about wastewater, citing oestrogen finding its way into local rivers. Through GMP guidelines outlined above, there are stringent measures already in place on the disposal of waste material including drainage systems. Furthermore, the NHS Community Pharmacy Contractual Framework deals with the collection and disposal of waste medicines from pharmacies and aims to ensure the public has an easy method of safely disposing of unwanted medicines, reducing the environmental damage caused by the use of inappropriate disposal methods for unwanted medicines. The Environmental Risk Assessment, which forms part of the requirements when applying for marketing approval in the UK, also specifically includes requirements for the evaluation of precautionary and safety measures to be taken regarding the environmental release from use in patients. This measure addresses the risks of environmental exposure from traces of drugs excreted from patients by evaluating the predicted environmental concentration of the drug in question.

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[1] Guideline on the environmental risk assessment of medicinal products for human use. EMA, 2006. www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500003978.pdf

[2] Questions and answers on 'Guideline on the environmental risk assessment of medicinal products for human use'. EMA, 2016. www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/06/WC500207858.pdf

[3] Guideline on the environmental risk assessment of 5 medicinal products for human use https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-environmental-risk-assessment-medicinal-products-human-use-revision-1_en.pdf

Metabolism and excretion data is taken into account to assess the persistence and accumulation of the drug substance or its relevant metabolites in the environment, and to also consider its potential removal in sewage treatment plants.

You asked how this is covered by the Bill, and I would like to reassure you that the enabling powers under clause 1 of the Bill provide the necessary powers to make changes to the Human Medicines Regulations 2012 (HMRs) and the Medicines for Human Use (Clinical Trials) Regulations 2004 (CTRs) , should there be need to amend or introduce new provisions with regards to waste disposal or wider environmental issues, where this is specifically concerned with human medicines. For example, we have the ability under clause 2(1)(a) to update the requirements needed to obtain and hold a manufacturing licence; this could include requirements with regards to waste disposal.

You asked specifically how research is regulated with regards to environmental protection. The Regulations for human medicines that are in scope of the power in this Bill, for example the HMRs and CTRs, regulate medicines once they reach the stage of clinical trials or supplying a medicine in the UK, rather than early research activities.
The regulatory framework for human medicines in the UK already provides safeguards to ensure appropriate consideration of the environmental impact of the manufacture of medicines. These safeguards are also relevant when considering the import of medicines from around the world. All medicinal products placed on the UK market, whether manufactured domestically or imported, must comply with the UK requirements. This includes the requirements outlined above in GMP and an Environmental Risk Assessment.

I will place a copy of this letter in the Library of the House and have copied it to Noble Lords who spoke during the debate. I sincerely hope the contents of this letter provide some clarity on the issues you and Noble Lords raised.

Very best wishes,

BARONESS PENN