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To European Commission; Directorate-General for Health and Food Safety, Unit "Medicines: policy, authorisation and monitoring" (SANTE.D.1)

Date 22 of January, 2025

Subject Reply to reaction EC on joint open letter from COGEM and ZKBS on the environmental risk assessment of new vaccine developments based on self-replicating mRNAs and viral replicon systems

Dear Ms. Salomon,

The Netherlands Commission on Genetic Modification (COGEM) and the German Central Committee on Biological Safety (ZKBS) want to thank you for your response to the joint open letter that we sent to Ms. Sacristán Sánchez, Directorate-General for Health and Food Safety Biotechnology unit (SANTE.E.3).[a]

COGEM and ZKBS expressed their concerns regarding the marketing authorisation of medicinal products based on viral replicons and self-amplifying mRNAs (samRNAs) without undergoing an environmental risk assessment (ERA), using Kostaive – a samRNA vaccine against COVID-19 – as an example. We are of the opinion that an ERA of self-propagating molecules such as samRNAs and similar medicinal products currently under development is imperative, as specific risks to third parties and the environment can arise from those medicinal products.

Your response clarified that the EC considers that Kostaive, being a self-amplifying mRNA sequence encapsulated in a lipid nanoparticle, does not fulfil the definition of a GMO as set under Directive 2001/18/EC.

As Kostaive is considered a non-GMO, an ERA under guideline EMEA/CHMP/BWP/473191/2006[b] was not conducted before the approval of Kostaive and the GMO competent authorities were not involved.

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a COGEM and ZKBS (2025). Joint open letter from COGEM and ZKBS on the environmental risk assessment of new vaccine developments based on self-amplifying mRNAs and viral replicon systems. 13 May 2025

b European Medicines Agency (EMA). Environmental risk assessments for medicinal products containing, or consisting of, genetically modified organisms (GMOs) – Scientific guideline. https://www.ema.europa.eu/en/environmental-risk-assessments-medicinal-products-containing-or-consisting-genetically-modified-organisms-gmos-scientific-guideline (accessed 2 December 2025)

In your response, you mention that the Committee for Medicinal Products for Human Use (CHMP) assessed the risks of recombination of the vaccine with the wildtype Venezuelan equine encephalitis virus (VEEV), in case a patient is infected before or after vaccination with Kostaive, and considered the risk to be low.

COGEM and ZKBS appreciate that the risks of recombination of Kostaive with wildtype VEEV were evaluated during the market approval process. However, in the ERA typically also other risks beyond recombination are assessed, such as complementation and – specifically for RNA constructs derived from alphaviruses – the ability to form virus-like vesicles (VLVs).[c] Apparently, these aspects were not assessed by the CHMP,[d] and an ERA was not fully conducted.

COGEM and ZKBS would also like to emphasize that the issues raised in their open letter do not only relate to the marketing authorisation process of Kostaive but do concern also any other viral replicons and samRNA vaccines.

COGEM and ZKBS stress the importance to develop guidelines for an ERA of self-propagating molecules to ensure that possible environmental risks of future samRNA vaccines and similar medicinal products are assessed and that such medicinal products are approved in a robust authorisation process.

To discuss this subject with other advisory bodies from EU member states a workshop was organized recently. The aim was to further update our knowledge on the latest developments and potential environmental risks of viral replicons and samRNAs, and to discuss how advisory bodies can deal with these developments. Given the complexity of the subject, the outcomes of the discussion will be further elaborated on in the near future. We would like to involve the EC in this discussion in due course.

Yours sincerely,

Professor Thomas W. Vahlenkamp
Chair of ZKBS

Professor Sybe Schaap
Chair of COGEM

c As set out in our joint letter and accompanying appendix, VLVs can spread in the body; it is currently unclear whether they can also be transmitted to third parties. These viral replicons are usually regulated as GMOs under directives 2009/41/EC and 2001/18/EC. VLVs are also being developed as vaccines.

d Kostaive: EPAR - Public assessment report. https://www.ema.europa.eu/en/documents/assessment-report/kostaive-epar-public-assessment-report_en.pdf (accessed 16 December 2025)