fieldfisher

Annex XV Restriction Report Proposal for a restriction for per- and polyfluoroalkyl substances ("PFASs") - Submission to the public consultation

"*Legal flaws of the Proposal and legal defense of* V1 *products*"

on behalf of V1

1. Context

We refer to the "*Annex XV Restriction Report Proposal for a restriction for per- and polyfluoroalkyl substances (PFASs)*" and its Annexes ("the Proposal") aimed at restricting a wide range of PFAS under Regulation (EC) No 1907/2006[1] ("REACH Regulation" or "REACH"), submitted to ECHA by the competent authorities of Germany, Sweden, the Netherlands, Denmark and Norway ("the Dossier Submitters").

We understand that the Dossier Submitters sent their Proposal to ECHA on 13 January 2023 and that a pre-publication version of the Proposal was made available on ECHA's webpage as of 7 February 2023. Subsequently, the ECHA's Committee for Socio-Economic Analysis ("SEAC") and Committee for Risk Assessment ("RAC") confirmed that the Proposal met the requirements set in Annex XV of REACH during their respective voting meetings on 10 March and on 15 March 2023, in accordance with article 69(4) of REACH.

Consequently, in accordance with article 69(6) of REACH, ECHA re-published an updated version of the Proposal indicating the official date of publication, *i.e.* 22 March 2023 and inviting interested parties to submit comments within six months, *i.e.* until 25 September 2023.

2. V1 and V1 products

V1

V1

[2]

In particular, V1 F2 of virus filter made with hydrophilized polyvinylidene fluoride ("PVDF") hollow fibers, designed to achieve robust retention of parvoviruses and other small viruses under a broad range of operating conditions.[3] This filter is used in nanofiltration, *i.e.* a well-established method allowing the removal of viruses based on size-exclusion that entails filtering of protein solutions through membranes with pores of nanometric sizes that have the capability to effectively retain a wide range of viruses.[4] The use of this filter during nanofiltration is a necessary step in the production of biopharmaceuticals to effectively remove viruses from the end-products, *i.e.* human medicines.

Furthermore, V1 F3 of cell clarification filter for purification of protein solution. It is made with polyvinylidene fluoride ("PVDF") hollow fibers that is designed to have a higher filterability of antibodies. This filter is used in microfiltration, *i.e.* a well-established method that allows the separation of the antibodies (proteins) from the animal cells. The

[1] Regulation (EC) N° 1907/2006 of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), OJ L 396, 30.12.2006, p. 1;
[2] ICH Q5A: ICH harmonised tripartite guideline on Viral safety evaluation of biotechnology products derived from cell lines of human or animal origin, p. 4;
[3] F4
[4] Roth NJ, D. H. (2020). Nanofiltration as a robust method contributing to viral safety of plasma-derived therapeutics: 20 years' experience of the plasma protein manufacturers. *Transfusion*, 60:2661–2674. doi:https://doi.org/10.1111/trf.16022, p. 1;

use of this filter during microfiltration occurs upstream in the filtration of impurities, before the virus removal stage. Therefore, it is a necessary step in the production of biopharmaceuticals aimed to separate the animal cells from the antibodies.

F5 V1) are made with PVDF and are used in the manufacturing of biopharmaceutical drugs, ensuring that biopharmaceuticals are safe, ultimately protecting human health and patient safety.

3. Scope of this paper

V1 strongly supports the objectives of the European Union and the goals of the European Green Deal[5] and the Chemicals Strategy for Sustainability ("CSS").[6] In this regard, V1 welcomes the opportunity to provide comments during the public consultation, opened until 25 September 2023.

With this paper, V1 , assisted by Fieldfisher, hereby submits legal comments to the public consultation in relation to the Proposal to (i) outline the legal flaws of the Proposal and (ii) raise the fact that V1 products should be exempted from the scope of the Proposal, or alternatively, benefit from a time-unlimited derogation for the reasons set out further in this paper.

In accordance with articles 70 and 71(1) of REACH as well as the general principles of EU law, such as due process, right of good administration and right of defense, ECHA, in particular RAC and SEAC, should take into account the information submitted during this public consultation and reflect it in their opinions.

Executive summary:

V1 is one of the world's leading manufacturers of filters employed in the production of biopharmaceuticals, *i.e.* complex medicines derived from characterized cell lines of human or animal origin (*e.g.* mammalian, avian, insect).

V1 products are process filters made with PVDF used in the biopharmaceutical manufacturing, ensuring that biopharmaceuticals are safe, ultimately protecting human health and patient safety.

The REACH restriction Proposal presents serious flaws in terms of methodology, legal principles and scientific rigour for the following eight reasons:

i. There are inaccuracies in the conditions on the proposed restriction - no exemption or derogations for the biopharmaceutical sector and V1 products;
ii. PVDF is generally included among more than 10,000 substances that possess different properties;
iii. PVDF would fall under the scope of the restriction by solely meeting a non-legally binding accepted definition;
iv. The assessment of hazard and risks of PVDF does not appear legally sound;
v. The grouping approach is incorrect;
vi. There is insufficient information on the uses, resulting emissions or exposure of PFAS in the biopharmaceutical manufacture sector;
vii. The information on alternatives is not properly assessed as regards the production of PVDF;
viii. The Proposal does not properly assess the interplay with other EU legislation such as the EU Pharmaceutical legislation.

[5] COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE EUROPEAN COUNCIL, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS The European Green Deal;

[6] COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS Chemicals Strategy for Sustainability Towards a Toxic-Free Environment;

As a consequence, V1 products would unduly fall under the prohibitions laid down in the Proposal.

Within this context, we kindly invite ECHA, in particular RAC and SEAC members, to consider the following options:

a) Option 1: V1 products should be exempted from the Proposal *a priori* as they should not be covered by the REACH Regulation; or

b) Option 2: V1 products should be exempted from the Proposal *a priori* as they are used in a closed system; in alternative,

c) Option 3: V1 products should benefit from a time-unlimited derogation as the same rationale of plant protections products, biocides and human and veterinary medicines should apply.

In support of all three options, ECHA, in particular RAC and SEAC members, should consider that fluoropolymers, such as PVDF, do not pose any risks to the environment and human health.

We ask ECHA, in particular RAC and SEAC members, to carefully take this information into account and reflect it in their opinions, in accordance with articles 70 and 71(1) REACH as well as the general principles of EU law, such as due process, right of good administration and right of defence.

4. Legal flaws of the Proposal

For the reasons set out in this paper, ECHA, in particular RAC and SEAC when preparing their opinions, should acknowledge that the Proposal is **legally flawed** for the **8 reasons** set out below.

i. There are inaccuracies in the conditions on the proposed restriction - no exemption or derogations for the biopharmaceutical sector and V1 products;
ii. PVDF is generally included among more than 10,000 substances that possess different properties;
iii. PVDF would fall under the scope of the restriction by solely meeting a non-legally binding accepted definition;
iv. The assessment of hazard and risks of PVDF does not appear legally sound;
v. The grouping approach is incorrect;
vi. There is insufficient information on the uses, resulting emissions or exposure of PFAS in the biopharmaceutical manufacture sector;
vii. The information on alternatives is not properly assessed as regards the production of PVDF
viii. The Proposal does not properly assess the interplay with other EU legislation such as the EU Pharmaceutical legislation.

i. There are inaccuracies in the conditions on the proposed restriction - no exemption or derogations for the biopharmaceutical sector and V1 products

We take note of the fact that the Proposal only envisages a time-unlimited derogation for "*active substances in human and veterinary medicinal products within the scope of Regulation (EC) No 726/2004, Regulation (EU) 2019/6 and Directive 2001/83/EC*".[7]

However, this derogation does not seem to include the supply chain supporting products covered by Regulation (EU) 528/2012, Regulation (EC) 1107/2009, Regulation (EC) 726/2004, Regulation (EC) 2019/6 and Directive 2001/83/EC.

As a result, all the equipment, reagents and raw materials involved in the manufacturing of the human and medicinal products within the scope of Regulation (EC) No 726/2004, Regulation (EU) 2019/6 and Directive 2001/83/EC, including V1 products, seem to be excluded from the scope of the derogation.

Without this specification, this derogations may be deprived of its *effet-utile*, namely devoid of its practical application. In other words, if upstream products involved in the manufacturing of human and veterinary medicines cannot be derogated, the production of the latter would not be feasible.

Furthermore, the proposed and potential derogations listed in paragraphs 5 and 6 of the Conditions of restrictions in the Proposal do not consider the use of PFAS in the production of biopharmaceuticals.

As a result, in its current status, the Proposal fails to foresee any exemption or derogation for V1 products.

ii. PVDF is generally included among more than 10,000 substances that possess different properties

The Dossier Submitters decided to cover more than 10,000 PFAS substances by grouping PFAS substances on grounds of their structural similarities (primarily related to the alleged "very persistent" property of the substances).[8] However, with this approach, the Dossier Submitters indirectly assume that all PFAS share the same properties.

As a result, PVDF, which is a polymer of low concern[9] and possesses particular properties such as heat resistance, stability, low permeability and chemical resistance, would be included in the scope of the Proposal among more than 10,000 substances that possess other and different properties.

This approach however appears scientifically incorrect as the scope of the restriction Proposal is not defined in sufficient detail and neither in line with Annex XV to REACH, which requires to include the identity of the substance(s) under the restriction.[10]

Additionally, given the large grouping of substances, the scope of the Proposal is unclear. Reference should be made to the Restriction Task Force of ECHA[11]. In particular, it might lead to difficulties for the Committees when analysing the stakeholder comments and preparing their opinions which may relate to specific PFAS substances rather than the whole group.

[7] Annex XV PFAS REACH restriction Proposal, p. 4, Colum 2, paragraph 4;
[8] Annex XV PFAS REACH restriction Proposal, p. 20;
[9] Henry BJ, Carlin JP, Hammerschmidt JA, Buck RC, Buxton LW, Fiedler H, Seed J, Hernandez O. A critical review of the application of polymer of low concern and regulatory criteria to fluoropolymers. Integr Environ Assess Manag. 2018 May;14(3):316-334. doi: 10.1002/ieam.4035;
[10] REACH Regulation, Annex XV, Section II, point (3);
[11] RESTRICTION EFFICIENCY TASK FORCE SETTING A CLEAR SCOPE, A common understanding for a clear scope of Annex XV restriction proposals, Version 3, Dec 2020;

iii. PVDF would fall under the scope of the restriction by solely meeting a non-legally binding accepted definition

In the Proposal, the Dossier Submitters do not specify the IUPAC name, nor EC number nor CAS number of PFAS substances. Instead, they use the following definition "*any substance that contains at least one fully fluorinated methyl (CF3-) or methylene (-CF2-) carbon atom (without any H/Cl/Br/I attached to it"* (with an only exemption for fully degradable PFAS), which resembles the 2021 OECD definition.[12]

Within this context, it should be noted that first, PVDF by solely meeting the above OECD definition, would fall under the scope of the Proposal and second, PVDF is not explicitly listed among the 10,000 substances allegedly covered by the Proposal.

Regarding the first point, it must be pointed out that Dossier Submitters chose the 2021 OECD definition of PFAS,[13] while there is no legally binding accepted legal definition of PFAS. In fact, the 2021 OECD report,[14] from where the definition was taken, was only conceived as a working paper in order "*to provide recommendations and practical guidance to all stakeholders with regard to the terminology of PFASs*"[15] and was not conceived for the purposes of "*regulatory and voluntary actions*".[16] Also, this report does not reach a definite solid and strong scientific conclusion, as it only identifies a standardized system for systematic characterization of different PFASs.[17] Furthermore, it also outlines several areas that warrant further work[18] in a constructive approach, which should be considered work in progress.

Regarding the second point, it should be noted that in global conventions such as the Stockholm Convention[19], implemented in the EU with the POPs Regulation,[20] there is an indicative list of substances which is regularly reviewed (*e.g.* PFOA and related substances indicative list).[21] In the Proposal, the Dossier Submitters failed to provide an analogous list where PVDF would be then explicitly listed.

iv. The assessment of hazard and risks of PVDF does not appear legally sound

The Dossier Submitters failed to explain which hazard properties pose specific PFAS and in turn, which properties lead to risks for specific PFAS substances and related uses.

For instance, it is stated that "*all*" PFAS are persistent, while "*some PFAS*" or "*most of PFAS*" are mobile/ carcinogenic/endocrine disruptors or accumulate in biota, etc[22]. These statements are vague, general in nature and unrelated to specific case-by-case assessments of the various PFAS substances, including PVDF. In fact, it is not clear which are the hazard properties of PVDF that justify its restriction.

In reality, the data demonstrating adverse effects on human health and on the environment used in the Annex XV report relate principally to a few PFAS (most notably PFOA and PFOS).[23]

However, these concerns, which are specific for PFOA and PFOS, have been unduly extended by the Dossier Submitters to all other PFAS, including PVDF, using a "specific-to-general" approach. This

[12] Annex XV PFAS REACH restriction Proposal, p. 4 Column 1;
[13] Any substance that contains at least one fully fluorinated methyl (CF3-) or methylene (-CF2-) carbon atom (without any H/Cl/Br/I attached to it) (OECD, 2021 , Reconciling Terminology of the Universe of Per- and Polyfluoroalkyl Substances: Recommendations and Practical Guidance, OECD Series on Risk Management, No. 61, OECD Publishing, Paris. https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/CBC/MONO(2021)25&docLanguage=En;
[14] *Ibid.*;
[15] *Ibid.* p. 7;
[16] *Ibid.* p. 8;
[17] *Ibid.* p. 8, 29;
[18] *Ibid.* p. 8, 33;
[19] The Stockholm Convention on Persistent Organic Pollutants, *opened for signature* May 23, 2001, UN Doc. UNEP/POPS/CONF/4, App. II (2001), *reprinted in* 40 ILM 532 (2001);
[20] Regulation (EU) 2019/1021 of the European Parliament and of the Council of 20 June 2019 on persistent organic pollutants
[21] Updated indicative list of substances covered by the listing of perfluorooctanoic acid (PFOA), its salts and PFOA-related compounds;
[22] Annex XV PFAS REACH restriction Proposal, p. 13;
[23] Annex B to XV PFAS REACH restriction Proposal;

does not appear scientifically and legally sound.[24] Stated differently, the use of few examples on selected substances to support a concern for all PFAS substances, including PVDF, is scientifically and legally wrong.

Besides, the risks deriving from these properties are combined without a clear link between the alleged hazard properties and derived risks. Indeed, the Dossier Submitters rely on a "combined effect" approach, which is not in line with the requirements for the preparation of an Annex XV dossier.[25]

v. The grouping approach is incorrect

The Dossier Submitters have justified the grouping based on structural similarities of the substances related to alleged "very persistency" criterion, to avoid the regrettable substitution and prevention of future exposure of those PFAS, which are not currently in use.[26]

In doing so, different substances have been unduly and/or arbitrarily grouped together, without a proper case-by-case assessment as required under REACH.[27]

In that regard, such a large grouping under the REACH restriction process is legally questionable. Indeed, the grouping of substances is only foreseen under REACH for purposes of fulfilling data requirements of registered substances. While practice leans towards grouping for REACH restriction purposes, this appears to be driven mostly by reasons of efficiency but is not necessarily scientifically justified. In fact, the clustering of many (and different) substances into a group would make the restriction difficult to meet and falls short to comply with some general REACH and EU principles, such as the One Substance One Registration ("OSOR") principle, proportionality, due process, precautionary, equal treatment and legal certainty. As such, grouping cannot be justified by reference to the literature,[28] let alone to working papers that do not reach a definitive scientific position (much less one that is not accepted as legally binding), in particular the 2021 OECD report[29] and 2018 Ritscher Zurich Statement. [30] In that regard, the fact that RAC in the PFAS restriction in fire-fighting foams refers to such papers does not mean that such definitions are legally sound and definitive.

Moreover, the specific justification provided by the Dossier Submitters to group all 10,000 PFAS altogether is questionable. Indeed, relying on persistency as a standalone criterion to justify a restriction is debatable[31]. Persistency may indeed only operate in combination with other criteria, such as bioaccumulation ("B") or toxicity ("T") or mobility ("M"). This is confirmed both by the text of REACH and Regulation 1272/2008 ("CLP"). On one hand, Annex XIII to REACH lays down the criteria for the identification of Persistent, Bioaccumulative and Toxic substances ("PBT"), and very Persistent and very Bioaccumulative substances ("vPvB"). On the other hand, the CLP Regulation was recently amended to reflect the publication of Commission Delegated Regulation EU 2023/707 introducing new hazard classes and related criteria.[32] In fact, this lays down criteria for Persistent, Bioaccumulative and Toxic substances ("PBT"), very Persistent, very Bioaccumulative substances ("vPvB"), Persistent,

[24] Annex XV PFAS REACH restriction Proposal, p. 13, p. 33;
[25] ECHA Guidance for the preparation of an Annex XV dossier for restrictions (2007), p. 33-34;
[26] Annex B to the Annex XV PFAS REACH restriction Proposal, p. 5;
[27] ECHA Guidance for the preparation of an Annex XV dossier for restrictions (2007), p. 32;
[28] For instance, Cousins I.T., DeWitt J.C., Gluge J., Goldenman G., Herzke D., Lohmann R., Miller M., Ng C.A., Scheringer M., Vierke L., and Wang Z. (2020a): Strategies for grouping per- and polyfluoroalkyl substances (PFAS) to protect human and environmental health. Environmental science. Processes & impacts 22 (7), 1444-1460. doi: 10.1039/d0em00147c;
[29] OECD, 2021, Reconciling Terminology of the Universe of Per- and Polyfluoroalkyl Substances: Recommendations and Practical Guidance, OECD Series on Risk Management, No. 61, OECD Publishing, Paris. https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/CBC/MONO(2021)25&docLanguage=En;
[30] Ritscher A, Wang Z, Scheringer M, Boucher JM, Ahrens L, Berger U, Bintein S, Bopp SK, Borg D, Buser AM, Cousins I, DeWitt J, Fletcher T, Green C, Herzke D, Higgins C, Huang J, Hung H, Knepper T, Lau CS, Leinala E, Lindstrom AB, Liu J, Miller M, Ohno K, Perkola N, Shi Y, Småstuen Haug L, Trier X, Valsecchi S, van der Jagt K, Vierke L. Zürich Statement on Future Actions on Per- and Polyfluoroalkyl Substances (PFASs). Environ Health Perspect. 2018 Aug;126(8):84502. doi: 10.1289/EHP4158;
[31] Annex XV PFAS REACH restriction Proposal, p. 1;
[32] Commission Delegated Regulation (EU) 2023/707 of 19 December 2022 amending Regulation (EC) No 1272/2008 as regards hazard classes and criteria for the classification, labelling and packaging of substances and mixtures, *OJ L 93, 31.3.2023, p. 7–39*;

Mobile and Toxic substances ("PMT"), very Persistent, very Mobile substances ("vPvM"). These criteria should be considered in the Proposal.

Taking all of this into account, it should be noted that the Dossier Submitters failed to clarify which specific PFAS, in particular PVDF, are either PBT, vPvB, PMT or vPvM in the Proposal. In fact, ECHA is wrong in stating that the Proposal "*does not only rely on persistence*",[33] as the Dossier Submitters failed to explain the combination of persistency with other concerns and relied on the literature supporting the P-sufficient approach.[34]

vi. Insufficient information on the uses, resulting emissions or exposure of PFAS in the biopharmaceutical manufacture sector

The Dossier Submitters claim to have covered rather exhaustively all PFAS uses, but in fact, they only covered 14 uses and 78 sub-uses as indicated in Table 2 of the Proposal.[35]

Among these uses and sub-uses, the biopharmaceutical sector does not seem to have been taken into account.

In fact, it seems that the Dossier Submitters arbitrarily chose to focus on these specific uses while stating that "*all uses of PFASs are covered by this restriction proposal, regardless of whether they have been specifically assessed by the Dossier Submitters and/or are mentioned in this report or not, unless a specific derogation has been formulated*".[36]

This approach is not in line with the requirements set out for the preparation of an Annex XV, *i.e.* providing deep analysis of the information of the use of the substances.[37]

vii. Information on alternatives is not properly assessed as regards the production of PVDF

The Dossier Submitters allege that there is "*sufficiently strong evidence*" that technically and economically feasible alternatives exist for non-polymeric PFAS as polymerisation aids in the production of PTFE, PVDF and FKM.[38] In that regard, the following aspects should be noted.

Firstly, in order to qualify evidence as "*sufficiently strong*", it is clear that information should not only come from one source as this approach is not reflective and representative of the market.

Secondly, Annex E to the Proposal contains a contrary statement. Specifically, this annex states that "*it is not clear whether all PTFE, PVDF and FKM can already be produced without PFAS polymerisation aids at industry level".*[39]

Therefore, it remains unclear whether the production of PVDF can be done without PFAS polymerisation aids and whether alternatives can lead to the same quality of PVDF. Also, we take note of the fact that the effectiveness of many proposed derogations,[40] which may rely on the availability of PVDF, may be put at risk.

As such, it can be concluded that a thorough analysis of the possible alternatives was not conducted, in breach of one of the requirements set out in the Guidance for the preparation of Annex XV.[41]

[33] ECHA Webinar: Restriction of per- and polyfluoroalkyl substances (PFAS) under REACH Questions and answers, p. 14, reply to question 1.4.4;
[34] Annex XV PFAS REACH restriction Proposal, p. 24;
[35] Annex XV PFAS REACH restriction Proposal, p. 53 Table 2;
[36] *Ibid.*, p. 2;
[37] ECHA Guidance for the preparation of an Annex XV dossier for restrictions (2007), p. 108;
[38] Annex XV PFAS REACH restriction Proposal, p. 81 Table 8;
[39] Annex E to the Annex XV PFAS REACH restriction Proposal, p. 2;
[40] Annex XV PFAS REACH restriction Proposal, p. 4, Colum 2, paragraphs 5 and 6;
[41] ECHA Guidance for the preparation of an Annex XV dossier for restrictions (2007), p. 69;

viii. The Proposal does not properly assess the interplay with other EU legislation such as the EU Pharmaceutical legislation

The Dossier Submitters failed to analyze other Risk Management Options ("RMOs") by inadequately assessing the EU regulatory framework applicable to PFAS. Indeed, in the text of the Proposal there is no proper and exhaustive assessment of the overlap between the Proposal and other existing EU legislation[42].

As further developed in Option 3 below, there is no proper analysis of the interaction between REACH and the Pharmaceutical legislation.[43] A proper analysis would have in fact removed V1 products from the Proposal, as they are already regulated under the applicable Pharmaceutical Legislation at EU level.

By failing to fully acknowledge the overlap between the Proposal and the Pharmaceutical Legislation, the Dossier Submitters breached the principle of over regulation, affirming that double regulation should be avoided.[44]

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The analysis above has evidenced that the Dossier Submitters did not adequately follow the EU principles, as well as the rules in REACH and the ECHA Guidance for the preparation of an Annex XV dossier for restrictions for the eight reasons specified above. As a consequence, V1 products unfairly fall under the scope of the restriction.

4. Legal defense of V1 products

With the following assessment, we will demonstrate that V1 products shall be exempted from the Proposal or shall benefit from a time-unlimited derogation. In that respect, we kindly invite ECHA, in particular RAC and SEAC members, to consider the following options:

a) **Option 1**: V1 products should be exempted *a priori* from the Proposal as they should not be covered by the REACH Regulation; or,

b) **Option 2**: V1 products should be exempted *a priori* from the Proposal as they are used in a closed system; in alternative,

c) **Option 3**: V1 products should benefit from a time-unlimited derogation in relation to the Proposal as the same rationale of plant protections products, biocides and human and veterinary medicines should apply.

a) Option 1: V1 products should be exempted *a priori* as they should not be covered by the REACH Regulation

Human medicines are defined in the EU as "*(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or (b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis*". Medicines can be authorised at Union level, *i.e.* through a centralised procedure or at Member-State level.

While at Member-State level, a national authorization is simply made by reference to a Union authorized medicinal product, the Union authorization procedure entails several steps and different actors to ensure that the medicines are safe. In fact, the EMA's Committee for Medicinal products for Human

[42] *Ibid.*, p. 70;
[43] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency
[44] Commission understanding paper on the relationship between REACH and POPs;

Use ("CHMP") carries out a thorough scientific assessment and gives a recommendation on whether the medicine should be authorized. The final authorization involves dialogue between the Member States, the Commission and the Standing Committee on Medicinal Products for Human Use.

V1 products, by constituting a necessary step of the production of biopharmaceuticals, should be regarded as medicines and treated as such by the competent EU and national authorities.

In that respect, it should be noted that article 2(5)(a) REACH exempts medicinal products for human use from certain REACH requirements such as registration, evaluation and authorisation.

Since medicines are indeed excluded from the registration and evaluation procedures, they should also be excluded from restriction. Indeed REACH restrictions correspond to one of the steps of a single continued procedure: if the evaluation and registration cannot be carried out, it seems difficult to continue from a practical point of view with the restriction procedure. Stated differently, the restriction process is based on the outcome of the registration and evaluation. In fact, the rules set out in the REACH Regulation are based on the principle that each single substance needs to be registered in order to be manufactured, imported or placed on the market and that the assessment of each substance, including in Title VIII (Restriction), is based on the information submitted on the relevant substance for registration purposes.

Also, it is worth noting that 2(5)(a) REACH exempts medicinal products for human use from authorisation. Since the authorisation process is explicitly excluded, the same rationale should apply for restrictions as both processes aim at replacing the most harmful chemicals with less harmful ones. In addition, the two processes present some similarities, such as the actors involved.

For the reasons outlined above, V1 products should be exempted *a priori* as they should not be covered by the REACH Regulation.

b) Option 2: V1 products should be exempted *a priori* as they are used in a closed system

It is settled case law that the main purpose for introducing new restrictions and amending existing restrictions is to ensure a high level of protection of human health and the environment.[45]

Indeed, under Article 68(1) of REACH, for a restriction to be adopted, there needs to be: (a) an unacceptable risk to human health or to the environment; (b) a causal link between that risk and the manufacture, use or placing on the market of the substance concerned; and (c) that risk needs to be addressed on a EU-wide basis.[46] If at least one of those conditions is not fulfilled, a REACH restriction cannot occur.

As regards V1 products, we believe that the first condition, *i.e.* (a) the presence of an "*unacceptable risk*",[47] is not fulfilled as these products are used in a closed system, where no emissions and exposure occur to the general population. In fact, the risks are already controlled firstly during use and secondly at the end-of-life.

Firstly, the use of V1 products takes place upstream in the production of human medicines, which is addressed under the respective Medicines Regulation. In fact, it should be noted that both F6 are used in the manufacture of biopharmaceuticals, which are then placed on the EU market in accordance with the Medicines Regulation, *i.e.* Regulation EC No 726/2004.[48]

As explained above, nanofiltration with the use of F7 are necessary steps in the manufacturing process of human medicines. In other words,

[45] Case T-226/18, *Global Silicones Council and Others v Commission*, paragraph 73; Case T-661/19, *Sasol Germany and Others v Commission*, para. 141;
[46] REACH Regulation, article 68(1);
[47] *Ibid.*;
[48] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency

without these steps, the biopharmaceuticals cannot be manufactured. In that regard, it should be born in mind that the product information of some biopharmaceuticals often states that "*Manufacturers of these medicines also include steps in the processing of the blood or plasma that can inactivate or remove viruses*".[49] This means that (i) these types of filters are already evaluated by the competent medicinal agencies, at European and national level, and (ii) risks for human health are controlled in the evaluation of the final end-product, the medicines.

As such, there is no exposure to humans and risks are controlled under the Medicines Regulation and eventually other EU applicable legislation.

Secondly, V1 products are incinerated after use to avoid contact with humans and the environment. In the EU, they should be regarded as "*hazardous waste*" under the Waste Framework Directive ("WFD").[50] The latter establishes a legal framework for treating waste in the EU to protect the environment and human health by emphasizing the importance of proper waste management, recovery and recycling techniques to reduce pressure on resources and improve their use. In particular, V1 products are regarded as hazardous waste as they meet the criteria laid down in Annex III to the WFD, in particular "*H9 Infectious – waste containing viable micro-organisms or their toxins which are known or reliably believed to cause disease in man or other living organisms*".[51]

Since the WFD is an EU Directive, it establishes general rules and objectives, while the Member States should concretely carry out an assessment to determine if the waste should be regarded as hazardous based on the criteria of the WFD.[52] For instance, in Germany there are special rules for the classification as hazardous waste, which may only be transported from the waste producer to an authorised recovery or disposal facility with an official permit and proof should be kept by means of the electronic waste records procedure ("eANV")[53].

Therefore, no emissions and/or leakage occur during end-of-life phase and risks are controlled under the EU applicable legislation on end-of-life.

For the reasons outlined above, V1 products should be exempted from the Proposal *a priori* as they are used in a closed system.

c) Option 3: V1 products should benefit from a time-unlimited derogation as the same rationale of plant protections products, biocides and human and veterinary medicines should apply

According to the Dossier Submitters, there is an overlap between the Proposal and the EU legislation concerning the approval of plant protection products ("PPP"),[54] biocidal products[55] ("BP") and human and veterinary medicinal products ("MP")[56].

In fact, they consider that active substances in PPP, BP and human and veterinary MP are already exhaustively regulated by an approval system under their respective regulations. They note in fact that "*in contrast to (industrial) chemicals, active substances will not be marketed in the EU or any of the Member States unless a product authorization has been granted by the national competent authorities in collaboration with European agencies EFSA, ECHA or EMA"*.[57]

[49] EMA, Product information of hizentra;
[50] Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives
[51] *Ibid.*, article 3(2) and Annex III;
[52] *Ibid.*, article 7(2);
[53] AVV Abfallchlussel, § 3 para. 2;
[54] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC
[55] Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the making available on the market and use of biocidal products
[56] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use; Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency;
[57] Annex XV PFAS REACH restriction Proposal, p. 72;

In particular, the Dossier Submitters state that "*for PPP and BP mainly a risk assessment is made. A risk/benefit analysis for PPP and BP is considered for candidates for substitution, in the form of a comparative assessment at product level. The risk/benefit analysis of the active substances in MP is performed as part of the assessment under the corresponding directive/regulation*".[58]

Ultimately, they recognize that a general PFAS restriction on the application for human and veterinary MP would not be necessary as it "*would impact the security of supply of both human [and veterinary] medicines and their alternatives*".[59] They also observe that although "*during the assessment of medicines possible negative effects on the environment are indicated, however they have no decisive effect on the authorization process*", this does not affect the ultimate goal, *i.e.* avoiding the disruption of medicines supply.

As a consequence, the Dossier Submitters conclude that "*PFAS used as active substance (but not as co-formulants) in PPP, BP and human and veterinary MP should be generally derogated from this REACH restriction*".[60] Generally, these active substances are substances that are characterized by the presence of one or more CF3-group(s) in their molecular structure, mostly aromatics.[61] Examples of PFAS used as active substances in medicines is given in Table A.110 of Annex A to the Proposal,[62] which however does not mention PVDF.[63]

As such, they propose a time-unlimited derogation for the active substances in PPP, BP and human and veterinary MP with certain reporting requirement, *i.e.* the obligation for manufacturers and importers of the active substances for PPP and human and veterinary MP to submit to ECHA the following information every two years: (a) the derogation that the intended use belongs to; (b) the identity and quantity of the active substance placed on the market.[64]

Since the use of V1 products constitute a necessary step of the manufacturing of medicinal products for human use, the same rationale of PPP, BP and human and veterinary MP should apply. Indeed without the use of V1 products, the production of medicines would not be possible. As a result, the security of supply would be put at risk, with consequences on human health and patient safety.

Also, since risks are already controlled both during use and at the end of life as explained in Option 2 above, V1 products should be considered safe. Additionally, it should be noted that PVDF is not bioavailable and cannot accumulate in human tissues,[65] as it is considered a polymer of low concern. Finally, it should be recalled that medicinal regulatory authorities require further assurances of the safety of these types of products and have adopted extended guidance on the subject.[66]

In this regard, we consider that the text of the time-unlimited derogation for PPP, biocides and human and veterinary medicines should be clarified to include upstream products, such as V1 products. Indeed, without this inclusion the supply of medicines would be put at risk and the derogation in itself would be deprived of its *effet utile*.

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[58] *Ibid.*, p. 73;
[59] *Ibid.*;
[60] *Ibid.*, p. 75;
[61] Annex A to the Proposal, p. 152;
[62] Annex A to Annex XV PFAS REACH restriction Proposal, Table A.110, p. 282;
[63] Annex A to the Proposal, Table A.110, p. 282;
[64] Annex XV PFAS REACH restriction Proposal, p. 4, Colum 2, paragraph 4;
[65] Korzeniowski SH, Buck RC, Newkold RM, Kassmi AE, Laganis E, Matsuoka Y, Dinelli B, Beauchet S, Adamsky F, Weilandt K, Soni VK, Kapoor D, Gunasekar P, Malvasi M, Brinati G, Musio S. A critical review of the application of polymer of low concern regulatory criteria to fluoropolymers II: Fluoroplastics and fluoroelastomers. Integr Environ Assess Manag. 2023 Mar;19(2):326-354. doi: 10.1002/ieam.4646;
[66] ICH Q5A(R2): VIRAL SAFETY EVALUATION OF BIOTECHNOLOGY PRODUCTS DERIVED FROM CELL LINES OF HUMAN OR ANIMAL ORIGIN Draft version, Endorsed on 29 September 2022, Currently under public consultation; GUIDELINE ON VIRUS SAFETY EVALUATION OF BIOTECHNOLOGICAL INVESTIGATIONAL MEDICINAL PRODUCTS, London, 24 July 2008 Doc. Ref. EMEA/CHMP/BWP/398498/2005;

For the reasons outlined above, V1 products should benefit from a time-unlimited derogation in relation to the Proposal as the same rationale of plant protections products, biocides and human and veterinary medicines should apply.

In support of all three options, ECHA, in particular RAC and SEAC members, should also consider that fluoropolymers, such as PVDF, do not pose any risks to the environment and human health. In particular, it is worth noting that there is considerable data, demonstrating that fluoropolymers do not degrade in the environment or release substances of toxicological or environmental concern.[67]

5. Conclusion

In light of all the above, there is enough evidence that the Proposal presents serious flaws in terms of methodology, legal principles and scientific rigour for the eight reasons presented in this paper.

As a consequence, V1 products would unduly fall under the prohibitions laid down in the restriction.

Therefore, we kindly ask ECHA, in particular RAC and SEAC members, to consider the following options:

a) Option 1: V1 products should be exempted *a priori* from the Proposal as they should not be covered by the REACH Regulation; or,

b) Option 2: V1 products should be exempted *a priori* from the Proposal as they are used in a closed system; in alternative,

c) Option 3: V1 products should benefit from a time-unlimited derogation in relation to the Proposal as the same rationale of plant protections products, biocides and human and veterinary medicines should apply.

[67] Korzeniowski SH, Buck RC, Newkold RM, Kassmi AE, Laganis E, Matsuoka Y, Dinelli B, Beauchet S, Adamsky F, Weilandt K, Soni VK, Kapoor D, Gunasekar P, Malvasi M, Brinati G, Musio S. A critical review of the application of polymer of low concern regulatory criteria to fluoropolymers II: Fluoroplastics and fluoroelastomers. Integr Environ Assess Manag. 2023 Mar;19(2):326-354. doi: 10.1002/ieam.4646;

We ask ECHA, in particular RAC and SEAC members, to carefully take this information into account and reflect it in their opinions, in accordance with articles 70 and 71(1) REACH as well as the general principles of EU law, such as due process, right of good administration and right of defence.

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