Report on the request to review a derogation request for the restriction of PFOA, its salts and PFOA-related substances (entry 68 of Annex XVII to REACH)

24 May 2018

REQUEST FOR ADDITIONAL DEROGATION TO ENTRY 68 OF ANNEX XVII OF REACH

1. Background

Annex XVII restriction on Perfluorooctanoic acid (PFOA), its salts and related substances (entry 68 of Annex XVII) entered into force in June 2017. It includes several derogations for different industrial sectors and uses. The entry is presented in chapter 2.

On 30 April 2018 ECHA received a request from the Commission to review a derogation request for additional use provided to the Commission by AstraZeneca. The company uses perfluorooctane bromide (PFOB) for the manufacturing of pharmaceutical products for the treatment of pulmonar diseases. PFOB is excluded from the scope of the PFOA restriction[1], but it contains perfluorooctane iodide (PFOI) as an impurity in concentrations above the concentration threshold in the PFOA restriction. PFOI is a PFOA-related substance that is covered by the restriction.

PFOA is currently proposed to be included to the Stockholm convention, and this derogation request is also under consideration for that legislation[2]. However, the amendment of the Stockholm convention will not take place before the PFOA restriction becomes effective in 2020, and a review of the restriction entry in REACH is needed if the use of PFOB should continue.

This report analyses if the requested derogation is justified based on the requirements and current practises under the restriction process. In other words, the analysis gives similar emphasis and results as to what would have taken place if the information would have been provided during the processing of the PFOA restriction proposal.

2. Current PFOA restriction entry

Table 1 gives the Annex XVII restriction entry 68. The substances excluded include C8F17-X, where X = Br. This is PFOB, which is used by AstraZeneca. "Any related substance (including its salts and polymers) having a linear or branched perfluorooctyl group with the formula C8F17- as one of the structural elements" include PFOI, which is present as an impurity in PFOB used by the company.

Table 1: Entry 68 of the Annex XVII of the REACH regulation restricting the use of PFOA, its salts and related substances.

'68.Perfluorooctanoic acid (PFOA) CAS No 335-67-1 EC No 206-397-9	1.Shall not be manufactured, or placed on the market as substances on their own from 4 July 2020.

[1] C_8F_{17}-X, where X = F, Cl, Br are excluded (see the entry).
[2] Following previous precedent, substances included in the POPs convention are included in Regulation 850/2004 and the relevant entry is deleted in Annex XVII of REACH.

and its salts. Any related substance (including its salts and polymers) having a linear or branched perfluoroheptyl group with the formula C_7F_{15}- directly attached to another carbon atom, as one of the structural elements. Any related substance (including its salts and polymers) having a linear or branched perfluorooctyl group with the formula C_8F_{17}- as one of the structural elements. The following substances are excluded from this designation: — C_8F_{17}-X, where X = F, Cl, Br. —C_8F_{17}-C(=O)OH, C_8F_{17}-C(=O)O-X′ or C_8F_{17}-CF_2-X′ (where X′ = any group, including salts).	2.Shall not, from 4 July 2020, be used in the production of, or placed on the market in: (a) another substance, as a constituent; (b) a mixture; (c) an article, in a concentration equal to or above 25 ppb of PFOA including its salts or 1 000 ppb of one or a combination of PFOA-related substances. 3.Points 1 and 2 shall apply from: (a)4 July 2022 to: (i)equipment used to manufacture semi-conductors; (ii) latex printing inks. (b)4 July 2023 to: (i)textiles for the protection of workers from risks to their health and safety; (ii)membranes intended for use in medical textiles, filtration in water treatment, production processes and effluent treatment; (iii) plasma nano-coatings. (c)4 July 2032 to medical devices other than implantable medical devices within the scope of Directive 93/42/EEC. 4.Points 1 and 2 shall not apply to any of the following: (a)perfluorooctane sulfonic acid and its derivatives, which are listed in Part A of Annex I to Regulation (EC) No 850/2004; (b)the manufacture of a substance where this occurs as an unavoidable by-product of the manufacture of fluorochemicals with a carbon chain equal to or shorter than 6 atoms; (c)a substance that is to be used, or is used as a transported isolated intermediate, provided that the conditions in points (a)

	to (f) of Article 18(4) of this Regulation are met; (d) a substance, constituent of another substance or mixture that is to be used, or is used: (i) in the production of implantable medical devices within the scope of Directive 93/42/EEC; (ii) in photographic coatings applied to films, papers or printing plates; (iii) in photo-lithography processes for semiconductors or in etching processes for compound semiconductors; (e) concentrated fire-fighting foam mixtures that were placed on the market before 4 July 2020 and are to be used, or are used in the production of other fire-fighting foam mixtures. 5. Point 2(b) shall not apply to fire-fighting foam mixtures which were: (a) placed on the market before 4 July 2020; or (b) produced in accordance with point 4(e), provided that, where they are used for training purposes, emissions to the environment are minimised and effluents collected are safely disposed of. 6. Point 2(c) shall not apply to: (a) articles placed on the market before 4 July 2020; (b) implantable medical devices produced in accordance with point 4(d)(i); (c) articles coated with the photographic coatings referred to in point 4(d)(ii); (d) semiconductors or compound semiconductors referred to in point 4(d)(iii).'

3. Proposed additional derogation

The analyses and justification provided in chapter 4 supports inclusion of the following derogation to entry 68 of the Annex XVII of the REACH regulation:

> Point 2 shall not apply to import and use of perfluorooctane bromide (PFOB) containing perfluorooctane iodide (PFOI) in concentration lower than 250 ppm for the purpose of producing pharmaceutical products.

The derogation could be implemented for example as an addition to existing derogation 4(d). Both import and use should be derogated as PFOB is imported to the EU and used here. Derogation from point 1 (substances on their own) is not necessary as PFOI is an impurity in PFOB.

4. Justification for a derogation

This chapter summarises the analyses of and justification for derogation. It is based on chemical safety report (CSR), analysis of alternatives (AoA) and socio-economic analysis (SEA) provided by AstraZeneca to the Commission. These assessment reports are annexed to this report (Annexes 1 to 3).

4.1. Description of the use

AstraZeneca uses perfluorooctyl bromide (PFOB) as a processing aid in the manufacture of porous particles, which are a functional component in pressurised metered-dose inhaler (pMDI) medicines. These porous particles provide a uniform suspension inside a pMDI, which is able to deliver an optimal distribution of drug crystals in the lungs for alleviation of lung diseases such as COPD. The technology also enables consistent delivery of multiple active ingredients from a single pMDI.

The manufacture of the porous particles uses PFOB as a processing aid, which is critical to delivering the unique aerodynamic properties of the porous particles, which ensure the efficient delivery of the medicine to the lungs. The PFOB is produced outside the EU and typically contains up to 200 ppm PFOI as an impurity, and the concentration should always be below 250 ppm. This exceeds the threshold of 1 ppm set in the current restriction on PFOA.

4.2. Human health and environmental impacts

In the opinion on PFOA, the focus in the evaluation of the risk reduction capacity is in estimating the releases of the covered substances. This follows the current practise on the evalution of PBT and vPvB cases under REACH.

AstraZeneca estimates their use is up to 10 tonnes of PFOB per year at their site in Sweden. The PFOI concentration in PFOB is typically below 200 ppm. This gives a maximum of 2 kg of PFOI that could be expected to be present as impurity in PFOB.

AstraZeneca reports that they have the best available technology to ensure there are negligible releases to the environment. It estimates that less than 4 grams of PFOI is released to the environment per year. In addition to that, even lower quantities of PFOI are placed on the market in the final products (<2 ppb). The management of the gaseous and liquid waste streams leading to such low emissions is described in the CSR.

Human health impacts are not discussed here as the PFOA restriction proposal is focusing on concerns based on the PBT properties of the covered substances. Nevertheless, the CSR provided by AstraZeneca (Annex 2) contains assessment concluding that handling of PFOB represents a minimal risk to workers.

4.3. Economic impacts

AstraZeneca could manufacture porous particles in the USA but expansion opportunities are limited at their existing facility. The site in Sweden is planned to produce most of the porous particles. For this, AstraZeneca will need to invest in an additional production site to meet the expected demand.

The following economic impacts are identified by AstraZeneca:

- Loss of sales if the manufacturing capability does not meet the demand,
- Cancelled investment in a second manufacturing site in Sweden, and
- High equipment relocation costs and significant investment in a new production plant outside Europe, or significant R&D costs to develop a process with an alternative to PFOB with interrupt in the supply of medicine to patients.

Furthermore, AstraZeneca describes possible social and wider economic impacts in its SEA (see Annex 3) including loss of employment opportunities in Sweden, France and the UK and possible decrease in the possibilities for patients to manage their symptoms.

4.4. Analysis of alternatives

AstraZeneca considered four alternative scenarios in their AoA (see Annex 2):

1. PFOB which is further purified to reduce residual levels of PFOI,

2. PFOB that is manufactured via alternative synthetic routes,

3. PFOE used instead of PFOB,

4. Use of structurally different alternatives to PFOB.

The first scenario will be followed but it is very unlikely to provide PFOB that meets the impurity thresholds in the PFOA restriction. The second option is rejected as it shortfalls in technical suitability and there are potential risks with the use of an alternative intermediate. Also option 3, use of PFOE, fails to address current risks while introducing new ones. Use of alternative agents (scenario 4) is expected to be too expensive and it would require a long time to get regulatory re-approvals.

5. Conclusions

ECHA Secretariat agrees with AstraZeneca that the estimated annual releases of 4 grams of PFOI represents a minimal risk to human health and the environment. The amount is similar or lower to those in applications (semiconductors, photographic coatings and implantable medical devices) for which RAC recommended derogation in their opinion based on the estimated emissions. The risk management measures in place appear to be appropriate to minimise the releases. Furthermore, ECHA Secretariat considers that

restricting this use is not proportionate to the risks posed by these limited releases. Because of this, ECHA Secretariat supports the request to add a derogation into the existing entry 68 of Annex XVII of REACH Regulation.

Annex 1: Chemical safety report (CSR) provided by AstraZeneca

Annex 2: Analysis of alternatives (AoA) provided by AstraZeneca

Annex 3: Socio-economic analysis (SEA) provided by AstraZeneca