Blood Transfusion Association

FACT SHEET

On the Application for Authorisation (AfA) for the continued use of DEHP in blood bag sets

Understanding REACH

The regulation on the Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH) is a European Union (EU) legislation that was enacted to improve the protection of human health and the environment from the hazards that chemicals can cause, while also increasing the competitiveness of the EU chemicals sector.

Companies have the burden of evidence under REACH. Companies must identify and manage the risks associated with the chemicals they manufacture and market in the EU in order to comply with the legislation. They must show the European Chemicals Agency (ECHA) how the chemical may be used safely, and they must convey the risk management measures to the users.

If the hazards cannot be addressed, authorities might impose various restrictions on the use of chemicals. In the long term, the most toxic compounds should be replaced with less hazardous ones.

What is the Application for Authorisation (AfA)?

The Authorisation process aims to ensure that "the risks associated with Substances of Very High Concern (SVHC) are properly managed throughout their life cycle"[1], and when "technically and economically feasible"[2], SVHC are gradually replaced with appropriate alternatives (low risk substances, new technologies and processes).

The AfA allows organisations to continue using substances on the REACH authorisation list after the sunset date. The AfA must be completed and submitted by the respective applicant(s) by the latest application date (LAD). In case the AfA is granted by ECHA, the submitting applicant(s), the immediate supplier of the applicant(s) (as long as this supplier is not using the substance itself) and the entire downstream supply chain of the applicant(s) are allowed to use this substance beyond the sunset date, until a suitable replacement is found. ECHA typically grants authorisation periods of 4, 7 or 12 years, depending on each individual case. The sunset date differs from the date of restriction, which is the date by which a substance is completely restricted from being used or placed on the market.

DEHP

Di-2-ethylhexylphthalate (DEHP) is a member of the phthalate family of compounds, which are used to make certain plastics more flexible. Due to DEHP contamination of the environment, concerns were raised pertaining to the continued exposure of the human population to DEHP. Concerns about the health effects of DEHP that could lead to endocrine-disruptive consequences have resulted in European legislation aiming to diminish or ban the use of this substance.

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[1] Authorisation process - ECHA (europa.eu)
[2] Ibid

DEHP has been used for over 60 years in blood bags to make the PVC blood bag sets flexible. This allows the processing of the drawn donor blood in a closed system into various blood components for the transfusion to patients. Additionally, studies have demonstrated that DEHP extends the shelf life of the stored red blood cells (RBCs) up to 49 days (depending on the storage conditions and the preservative solution used) by interacting with, and stabilising the membrane of these cells, making them more resistant.[3] Consequently, the use of DEHP decreases the rate of haemolysis. This is beneficial for patients as transfusing free haemoglobin (that has separated from RBCs) can have toxic effects, particularly in patients receiving multiple transfusions. In this sense, the use of DEHP in blood bag sets is an important aspect of assuring the quality of collected and stored blood products.

Until recently, DEHP-containing medical devices have been exempted from the authorisation requirement of the REACH Regulation.

AfA and DEHP

Following the recommendation of the ECHA in 2019, the European Commission adopted Commission Regulation (EU) 2021/2045 amending Annex XIV to Regulation (EC) No 1907/2006 concerning REACH, which entered into force on 13 January 2022. Regulation (EU) 2021/2045 removes the exemption from the authorisation requirement of medical devices, including blood bag sets containing DEHP. Since the endocrine disruptive effects of DEHP are not only related to human health, but also to the environment, the use of DEHP in blood bag sets also falls under the REACH Regulation (as well as the Medical Devices Regulation), meaning that some previously exempted uses, such as blood bag sets, are now required to have an authorisation.

As a result, the use of DEHP for the manufacturing of medical devices in Europe will be prohibited after 27 May 2025, unless an authorisation is granted under REACH, or unless an AfA was submitted before the Latest Application Date (LAD), which is 27 November 2023.

Plastic blood bag sets containing different sterile plastic transparent parts were developed in the 1940s and broadly introduced in all markets in the early 1960s to facilitate the collection, separation and storage of blood and blood components. From the start, and despite potential toxicity concerns, DEHP was used to plasticise the PVC in the production of the bags and other plastic parts because of the high clinical efficacy, reduced haemolysis levels and extended blood storage times enabled by this substance. Over time, the Industry has gained considerable experience with the use of DEHP. Manufacturers of blood bag sets are careful not to introduce new unknown risks that could possibly lead to a higher rate of critical defects. The rate of critical defects is very low for the current generation of PVC-DEHP blood bag sets and such defects are often not detected until millions of units have been produced.

In the EU, approximately 20 million blood bag sets are used each year. Alternative materials are continuously being examined as potential replacements for DEHP, but more data is needed to better understand their leaching properties and potential toxicity, as well as their impact on the medical effectiveness of treatments. When replacing DEHP in blood bag sets, it is important not to change to an alternative material that may result in higher mean levels of haemolysis or a reduction in storage time.

[3] Lagerberg, J. W., Korsten, H., Van Der Meer, P. F., & De Korte, D. (2017). Prevention of red cell storage lesion: a comparison of five different additive solutions. *Blood transfusion = Trasfusione del sangue*, *15*(5), 456–462. https://doi.org/10.2450/2017.0371-16

The Application for Authorisation process

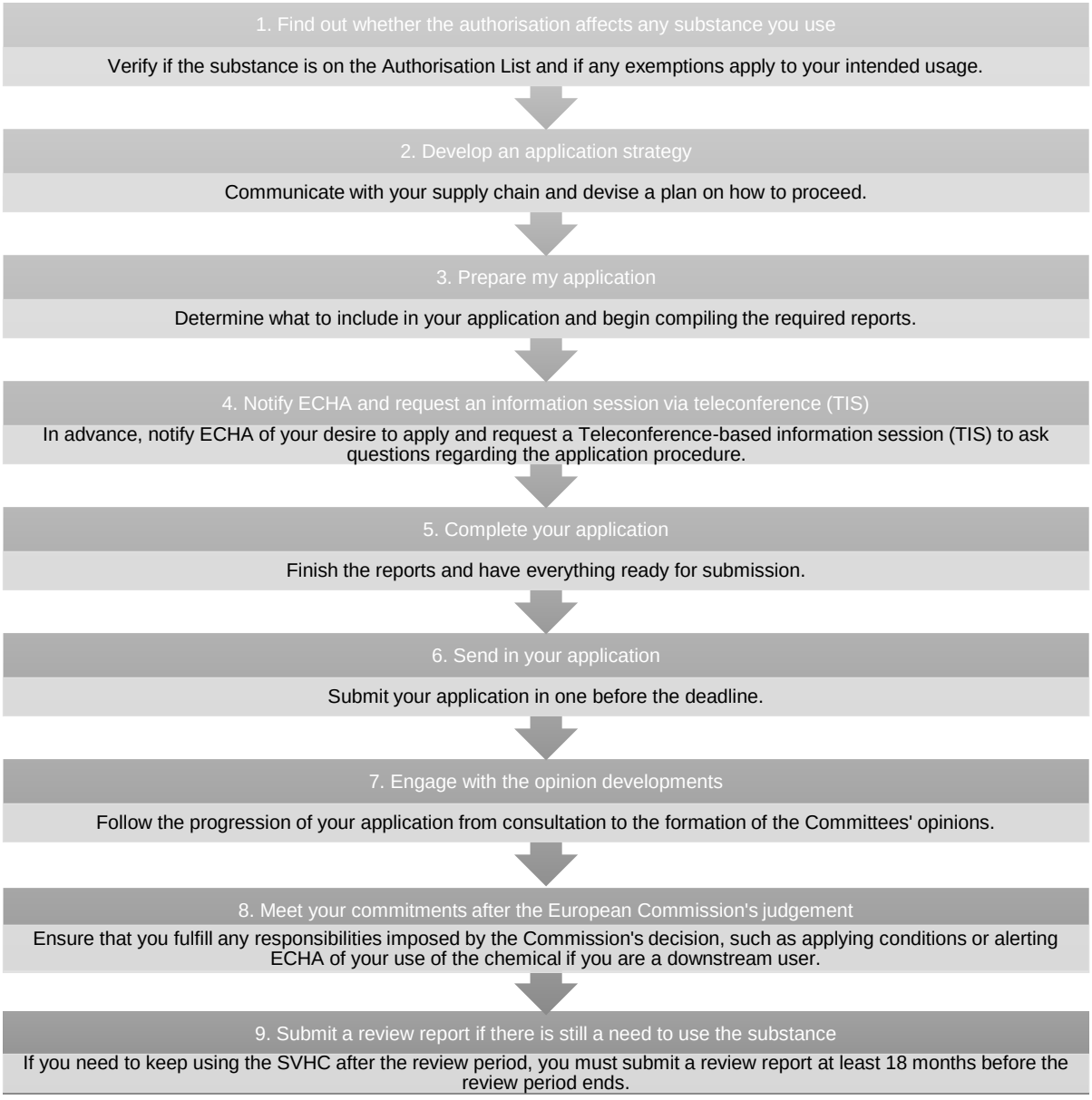
An AfA can be submitted for one or several uses for one or a group of (similar) substances. Applicants may apply for authorisation for their own use or for the intended use of the substance on the market.

Companies need to check if the substances that they use or place on the market are in the list of substances requiring an authorisation. If the substances are subject to authorisation, the next step is to develop a strategy on how to proceed. This strategy consists of two phases:

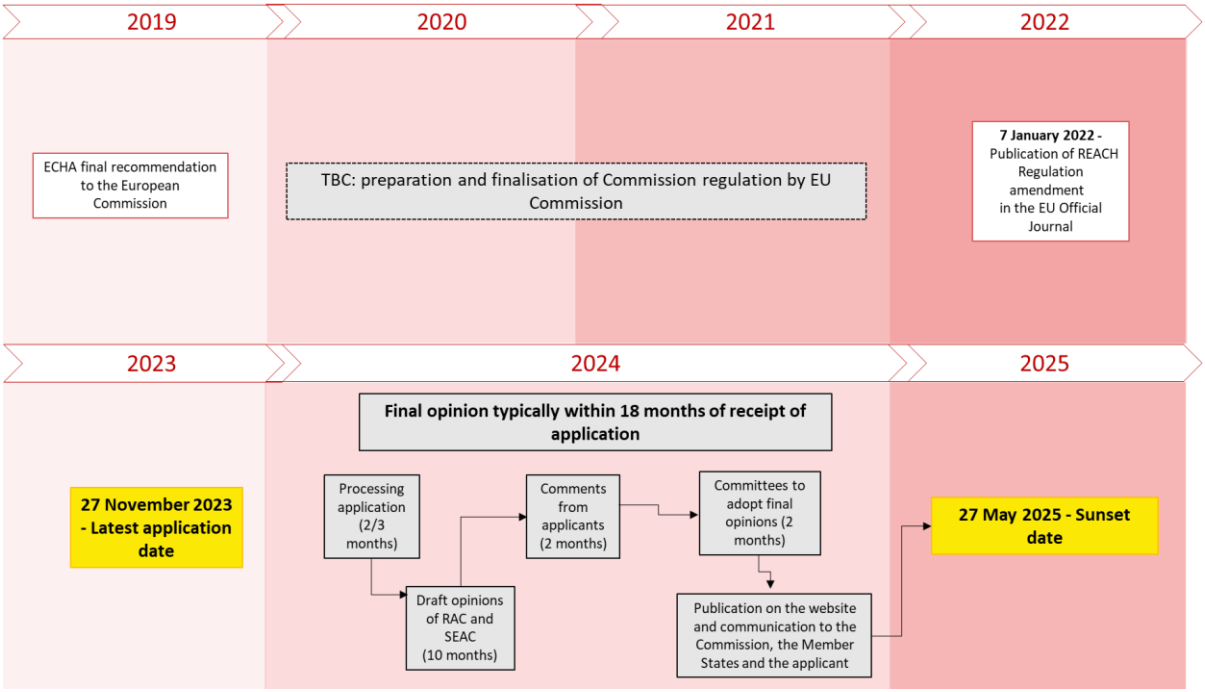
I. Look for safer alternatives and evaluate if they can be replaced.

II. Assessment of the importance of substances to the company and supply chain.

If it is concluded that the substance will continue to be used or put on the market after the sunset date, the company must apply for authorisation.[4][5]



[4] Information reproduced from: Develop an application strategy - ECHA (europa.eu)
[5] Table reproduced from: How to apply for authorisation - ECHA (europa.eu)



For more information:
https://echa.europa.eu/documents/10162/17229/apply_for_authorisation_en.pdf

Preparing an Application for Authorisation

Pursuing an AfA is a complex process undertaken by an applicant or applicants that requires considerable commitment from all parties to be completed.

The amendment that the Commission adopted entered into force on 13 January 2022 with 27 November 2023 as the latest application date (LAD) for an AfA. The processing time following submission of the AfA is between 2 to 3 months. At this stage a public consultation would open, lasting for 8 weeks allowing all interested parties to make an opinion for the Commission's consideration. Simultaneously, the Committee for Risk Assessment (RAC) and the Committee of Socio-Economic Analysis (SEAC) would take 4 to 10 months to develop official opinions. The applicant then will have 1 to 4 months to comment on the draft opinion, which would lead to the final opinion being published by ECHA, usually within 18 months of receipt of the application. The Commission then has 6 months to publish its final decision.

The AfA for blood bag sets in Europe

Certain blood bag set manufacturers are working with the supplier of DEHP to support the AfA for the continued use of DEHP to ensure continuity of supply beyond the sunset date. This topic was presented during a series of meetings with the EU Commission informing them of their intent to convert their EU portfolios to non-DEHP. These meetings were also attended by the European Blood Alliance (EBA) representing blood establishments in the EU. Both the Industry and the EBA shared their concerns regarding their ability to meet the sunset date based on the changing regulatory landscape (up-classification of some blood bag sets in the MDR (Regulation (EU) 2017/745), revision of the EU legislation on blood, tissues, and cells (Directive 2002/98/EC and Directive 2004/23/EC), and the revision of the EU general pharmaceuticals legislation (Directive 2001/83/EC1 and Regulation (EC) No 726/2004).

Glossary

Application for Authorisation (AfA) – An AfA allows companies to apply for an authorisation to continue or start using and placing substances on the market that are included in the REACH Authorisation List

Applicant – The entity submitting an AfA to ECHA

Sunset date – The date after which the use or placing on the market of a substance in the EU will be prohibited unless an authorisation is granted under REACH, or unless an AfA was submitted before the latest application date (LAD)

Date of restriction – The date by which a substance is completely restricted from being used or placed on the market in Europe

Diethylhexyl phthalate (DEHP) - DEHP is one of the most important plasticisers based on phthalate and is widely used in medical devices such as blood bag sets

Haemolysis – the breakdown of red blood cell membranes which causes the release of haemoglobin into the plasma

Latest application date (LAD) – The deadline by which an AfA must be made to continue using or placing a restricted substance on the market

REACH – The regulation on the Registration, Evaluation, Authorisation, and Restriction of Chemicals, which entered into force in 2007