Risk Management Option Analysis Conclusion Document

Substance Name: tributyl O-acetylcitrate (ATBC)

EC Number: 201-067-0

CAS Number: 77-90-7

Authority: France

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Foreword

The purpose of Risk Management Option analysis (RMOA) is to help authorities decide whether further regulatory risk management activities are required for a substance and to identify the most appropriate instrument to address a concern.

RMOA is a voluntary step, i.e., it is not part of the processes as defined in the legislation. For authorities, documenting the RMOA allows the sharing of information and promoting early discussion, which helps lead to a common understanding on the action pursued. A Member State or ECHA (at the request of the Commission) can carry out this case-by-case analysis in order to conclude whether a substance is a 'relevant substance of very high concern (SVHC)' in the sense of the SVHC Roadmap to 2020[1].

An RMOA can conclude that regulatory risk management at EU level is required for a substance (e.g. harmonised classification and labelling, Candidate List inclusion, restriction, other EU legislation) or that no regulatory action is required at EU level. Any subsequent regulatory processes under the REACH Regulation include consultation of interested parties and appropriate decision making involving Member State Competent Authorities and the European Commission as defined in REACH.

This Conclusion document provides the outcome of the RMOA carried out by the author authority. In this conclusion document, the authority considers how the available information collected on the substance can be used to conclude whether regulatory risk management activities are required for a substance and which is the most appropriate instrument to address a concern. With this Conclusion document the Commission, the competent authorities of the other Member States and stakeholders are informed of the considerations of the author authority. In case the author authority proposes in this conclusion document further regulatory risk management measures, this shall not be considered initiating those other measures or processes. Since this document only reflects the views of the author authority, it does not preclude Member States or the European Commission from considering or initiating regulatory risk management measures which they deem appropriate.

[1] For more information on the SVHC Roadmap: http://echa.europa.eu/addressing-chemicals-of-concern/substances-of-potential-concern/svhc-roadmap-to-2020-implementation

1. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

ATBC is included in the regulation 10/2011 of 14 January 2011 on plastic materials and articles intended to come into contact with food. ATBC can be used as an additive or polymer production aid. The total specific migration limit is 60 mg/kg.

ATBC use is not forbidden in cosmetic products because not included in the regulation 1223/2009.

EFSA authorizes ATBC as an additive in plastics intended to come into contact with food, with a Tolerable Dose Intake (TDI) of 1.0 mg/kg bw (EFSA, 20025).

Harmonised Classification in Annex VI of the CLP

There is no existing Harmonised Classification for ATBC.

Existing assessments

Several hazard and/or risk assessments have already been conducted:

- In 1999, Joint FAO/WHO Expert Committee on Food Additives evaluated ATBC and, based on current intake, concluded that ATBC represented no safety concern when used as a flavouring agent (JECFA, 1999).

- In 1999, Scientific Committee on Toxicity, Ecotoxicity and the Environment published an "opinion on the toxicological charcateritics and risks of certain citrates and adipates used as a substitute for phthalates as plasticizers in certain soft PVC products" (CSTEE, 1999). The CSTEE concluded that is was not possible to estimate the relationship between exposure levels to ATBC from mouthing soft PVC toys and its NOAEL due to some data gaps. CSTEE was not able to identify migration limits for ATBC from PVC.

- In 2003, Toxicology/Regulatory Services Inc. prepared for Morflex, Inc a report entitled "Assessment of data availability and test plan for acetyl tributyl citrate" and submitted it to the US Environmental Protection Agency (US EPA) to sponsor ATBC in the High Production Volume Challenge Program (US EPA, 2003).

- In 2004, an evaluation concerning ATBC used in children's toys was done by the Scientific Committee on Toxicity, Ecotoxicity and the Environment. CSTEE conclude that there is no safety concern when young children are mouthing PVC-toys containing ATBC as plasticizer (CSTEE, 2004).

- In 2005, an evaluation concerning ATBC was done by the European Food Safety Authority (EFSA) which established a TDI (tolerable daily intake) of 1 mg/kg bw (EFSA, 2005).

- In 2008, Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) assessed the safety of medical devices containing DEHP-plasticized PVC or other plasticizers on neonates and other groups possibly at risk. Several alternative plasticizers were analyzed, among them ATBC (SCENIHR, 2008). Regarding the alternatives, for some compounds including ATBC, sufficient toxicological data is available and indicate a lower hazard compared to DEHP. However, a risk assessment of these alternative plasticizers could not be performed due to a lack of human exposure data.

- In 2010, U.S. Consumer Product Safety Commission (CPSC) published a review on exposure and toxicity data for phthalates substitutes, including ATBC (CPSC, 2010).

- In 2010, Danish Environmental Protection Agency published a report on identification and assessment of alternatives to selected phthalates (No 1341, 2010). Suitable alternative plasticisers have been identified for most applications of the phthalates including ATBC (Danish EPA, 2010).

- In 2012, ECHA published a report entitled "Background document to the Opinion on the Annex XV dossier proposing restrictions on four phthalates". Available information on alternatives including ATBC was collected. Based on these informations ATBC could be an appropriate alternative to DEHP, BBP, DBP and DIBP.

- In 2014, CPSC published a report entitled "Chronic hazard advisory panel on phthalates and phthalate alternatives". According to this report and although data are somewhat limited, there is no evidence that ATBC presents a hazard to infants or toddlers from mouthing toys or child care articles containing ATBC. Therefore, the CHAP (Chronic Hazard Advisory Panel) recommends no action on ATBC. However, information on total exposure to ATBC is not available. The CHAP recommends that the appropriate U.S. agencies obtain the necessary exposure and hazard data to estimate total exposure to ATBC and assess the potential health risks.

- In 2015, SCENIHR does an update on its previous 2008 opinion (SCENIHR, 2015). ATBC has a low toxicity following acute oral administration. In repeated dose studies the oral NOEL was 100 mg/kg kg bw/d, based on decreased body weight, haematological and biochemical changes; increased liver weight at the higher doses. No data are available on humans. The only indication available related to leaching potential from medical devices, suggests a higher rate than DEHP. More information are necessary on this aspect to clarify human exposure in the actual conditions of use of medical device as well as on differences among oral *vs* parenteral route of exposure.

2. CONCLUSION OF RMOA

This conclusion is based on the REACH and CLP data as well as other available relevant information taking into account the SVHC Roadmap to 2020, where appropriate.

For each conclusion selected in the table below a justification needs to be provided in section 3 of this document. Reasons outlining why a particular risk management option was not considered appropriate can also be included in the relevant section; otherwise subsections can be left blank/deleted if not relevant.

Conclusions	**Tick box**
Need for follow-up regulatory action at EU level:	
Harmonised classification and labelling	
Identification as SVHC (authorisation)	
Restriction under REACH	
Other EU-wide regulatory measures	
Need for action other than EU regulatory action	
No action needed at this time	X

3. NEED FOR FOLLOW-UP REGULATORY ACTION AT EU LEVEL

No need for follow-up regulatory action at EU level.

4. NEED FOR ACTION OTHER THAN EU REGULATORY ACTION

No need for action other than EU regulatory action.

5. NO ACTION NEEDED AT THIS TIME

ATBC is an alternative to phthalates in various applications, especially in sensitive ones like medical devices or toys. In the framework on the French National Strategy on Endocrine Disruptors in 2015, the French Competent Authority requested ANSES to evaluate its toxicological profile and verify whether risk management measures should be necessary for this substance.

It should first be recognized that ATBC is a pretty well studied substance for which few recent long term studies have been provided. All the requirements as described in the annexes VII, VIII, IX & X appear to be fulfilled (see preliminary analysis in annex I).

ATBC is not considered as toxic for reproduction and no alert was found on potential endocrine disruption properties, in particular on estrogenic and androgenic activity. However, there is a concern for activation of the PXR pathway but it is currently unclear which adverse effects this may lead to. So, it is not possible to conclude on the endocrine disruptor character of ATBC because there is no solid information on the other ED effects (thyroid, …).
Danish EPA, Swedish chemical agency (KEMI) and Ireland agree with France's conclusions based on the current available data (following ED Expert Group discussions the 2-3 September 2015). In particular, Ireland considers that PXR/ SXR interaction is not endocrine disruption.

Regarding environment, ATBC is not considered as PBT nor vPvB. No alert for endocrine disruptor endpoint has been identified. However, ATBC could be classified as Aquatic Chronic 3 according to CLP if its persistent behavior would be demonstrated. Contradictory results on aquatic biodegradation suggest an alert regarding P criteria of ATBC and further informations would be necessary for clarifications.

Table: SVHC Roadmap 2020 criteria

	Yes	No
a) Art 57 criteria fulfilled?		x
b) Registrations in accordance with Article 10?	x	
c) Registrations include uses within scope of authorisation?	x	
d) Known uses not already regulated by specific EU legislation that provides a pressure for substitution?	x	

The presently available information indicates no alert on potential endocrine disruption properties of ATBC.
Nevertheless, some uncertainties remain:

- For human health, there is no solid information for some ED effects (thyroid, …);
- Concern on the activation of the PXR pathway but it is currently unclear which adverse effects this may lead to;

- There is not enough ED data to conclude an alert for environment;
- Contradictory results on aquatic biodegradation suggest an alert regarding persistence of the substance also the available data seems to show no bioaccumulation.

Based on the available studies, it seems unclear which data to request to diminish the existing uncertainty. Moreover based on the data on exposure (CSTEE, 2004), children exposure *via* toys appear negligible. This substance is therefore judged as low priority for further work.