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Methodology for comparison of alternative substances to Formaldehyde

Revised collective expert assessment report

December 2020

INVESTIGATE, EVALUATE, PROTECT

Methodological document for comparison of alternatives to hazardous substances

Request n°2014-SA-0236 – Formaldehyde and substitutes

Revised[1] collective expert appraisal REPORT of December 2017

Expert Committee (CES) on "Characterisation of substance hazards and toxicity reference values" and "Health reference values"

Working Group on "Formaldehyde and substitutes"

December 2020

[1] « Supersedes the appraisal report of December 2017 published in May 2018 » (cf. table in appendix 25)

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Presentation of participants

PREAMBULE : The expert members of the Expert Committees and Working Groups or designated rapporteurs are all appointed in a personal capacity, *intuitu personae*, and do not represent their parent organisations.

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Acronyms and abbreviations

AGS	:	German Committee on Hazardous Substances
ANSES	:	French Agency for Food, Environmental and Occupational Health & Safety
BAuA	:	German Federal Institute for Occupational Safety and Health
C2C	:	Cradle to Cradle
CES	:	Expert Committee
CLP	:	Classification, labelling and packaging
CMR	:	Carcinogenic, Mutagenic, Reprotoxic
CPA	:	Clean Production Action
CTSA	:	Cleaner Technologies Substitutes Assessment
DEHP	:	Di(2-ethylhexyl) phthalate
DfE	:	Design for the Environment
DGCCRF	:	Directorate General for Competition, Consumer Affairs and Fraud Control
DGPR	:	Directorate General for Risk Prevention
DGS	:	Directorate General for Health
DGT	:	Directorate General for Labour
ECHA	:	European Chemicals Agency
EU	:	European Union
GSLT	:	GreenScreen List Translator
HCA	:	Hazardous Chemical Agent
IARC	:	International Agency for Research on Cancer
IC2	:	Interstate Chemicals Clearinghouse
IFA	:	Institute for Occupational Safety and Health of the German Social Accident Insurance
INRS	:	National Research and Safety Institute [for the prevention of occupational accidents and diseases]
LCA	:	Life-Cycle Assessment
MSD	:	Musculoskeletal disorder
NRC	:	National Research Council
NTP	:	National Toxicology Program
OEL	:	Occupational exposure level
P2OSH	:	Pollution Prevention - Occupational Safety and Health
PARIS	:	Program for Assisting the Replacement of Industrial Solvents
POP	:	Persistent organic pollutant

PT	:	Product type
QCAT	:	Quick Chemical Assessment Tool
R&D	:	Research and development
REACh	:	Registration, evaluation, authorisation and restriction of chemicals
RoSH	:	Restriction of Hazardous Substances
RSC	:	Royal Society of Chemistry
SCIL	:	Safer Chemical Ingredients List
SCJ	:	US Company SC Johnson & Son
SCRAM	:	Chemical Scoring and Ranking Assessment Model
SME	:	Small and medium-sized enterprise
SMI	:	Small and medium-sized industry
SNAP	:	Significant New Alternatives Policy
SVHC	:	Substance of very high concern
TURI	:	Toxic Use Reduction Institute
TRGS	:	Technical Rules for Hazardous Substances
UCLA	:	University of California Los Angeles
US EPA	:	United States Environmental Protection Agency
US OSHA	:	United States Occupational Safety and Health Administration
WG	:	Working Group

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1 Background, purpose, and processing of the request

1.1 Background of the request

Formaldehyde was classified as a Group 1 known carcinogen in humans by the IARC (International Agency for Research on Cancer) in 2004 and this classification was confirmed in October 2009 on the basis of induction of nasopharyngeal tumours and leukaemia. At the European level, a change in classification from a Category 2 carcinogen to a Category 1B carcinogen was adopted in Commission Regulation (EU) No 605/2014 of 5 June 2014 amending the CLP Regulation for the purposes of its adaptation to technical progress.

In France, the Order of 13 July 2006 added “work involving exposure to formaldehyde” to the list of carcinogenic substances, mixtures and processes under the terms of Article R. 4412-60 of the Labour Code. Identifying substitutes for Category 1A or 1B carcinogenic, mutagenic or reprotoxic agents (CMRs) in the workplace is an obligation for employers. It is referred to in the general principles for prevention in Article L. 4121-2 of the Labour Code and is reinforced in Article R. 4412-66. As a result, the employer must be able to justify all successful or unsuccessful efforts made with the purpose of substituting all Category 1A or 1B CMR agents or processes identified in the workplace. The outcome of these investigations must appear, in particular, in the single risk assessment document. Only a substantiated technical justification is acceptable to justify non-substitution of a Category 1A or 1B CMR agent or process by a non-hazardous or less hazardous agent or process.

When the principle of substitution cannot be applied, the employer must implement all possible measures to reduce exposure by means of suitable prevention and protection measures (closed systems, other collective protection measures, followed by personal protection measures but also training and providing information to employees, as well as medical monitoring).

1.2 Purpose of the request

In view of these new data on the hazardous properties of formaldehyde and the priority given to substitution in terms of occupational risk management, a formal request was made to ANSES on 09 October 2014 (received by letter on 22 January 2015) for an “Opinion on the use of substitutes for formaldehyde in various sectors of activity”. The request was made jointly by the Directorate General for Labour (DGT), the Directorate General for Health (DGS), the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF), and the Directorate General for Risk Prevention (DGPR).

ANSES was requested to provide the public authorities with an expert opinion on:

- the benefit of formaldehyde compared to other substitutes in **the area of diagnostics in pathological anatomy and cytology** in routine situations and in specific situations that should be indicated in which formaldehyde remains essential;
- the benefit of formaldehyde compared to other substitutes for **embalming processes**, with a summary of the studies under way at the European level in the framework of the biocide regulation in terms of assessment of the active substance formaldehyde (PT2,

3, 20 and 22). Moreover, in the framework of the studies carried out on formaldehyde substitutes in pathological anatomy and cytology, the directorates would like to have an analysis of the possible use of these substitutes in certain types of biocidal products, and in particular PT22, and on the potential consequences in terms of toxicity and ecotoxicity;

- the benefit of formaldehyde compared to other substitutes for use in **animal feed** as a processing aid for protection against ruminal degradation, as a preservative additive, as a silage additive, and as an additive aimed at limiting or reducing the microbial load of pathogenic organisms found in animal feed;
- the benefit of formaldehyde compared to other substitutes for use in **food for human consumption** as a processing aid for the manufacture of certain alginates and for use as a bacteriostatic agent in the sugar sector.

If formaldehyde substitutes can be used, the directorates requested an evaluation of their toxicity for workers and the general population.

1.3 Processing of the request: means implemented and organisation

ANSES tasked the Working Group (WG) on “Formaldehyde and substitutes”, within the Expert Committees (CES) on “Characterisation of substance hazards and toxicity reference values”, then on “Health reference values” with carrying out the work to respond to this request.

The methodological review of the WG, described in this report, was followed-up and presented to the CES on “Characterisation of substance hazards and toxicity reference values” on 12 May 2016 and 09 June 2016.

This review was validated for public consultation by the CES on “Characterisation of substance hazards and toxicity reference values” on 07 July 2016.

This report was made available for public consultation from 08 August 2016 to 30 September 2016. The list of individuals or bodies that contributed to the public consultation is shown in Annex 24. The comments received were examined and discussed by the CES on “Characterisation of substance hazards and toxicity reference values”, which adopted this version of the report on 08 December 2016.

Following the implementation of the method in the various sectors of activity, the methodological document of December 2017 has been revised to take into account the adjustments that have been implemented throughout the work and has been submitted for this purpose for validation to the CES on “Health reference values” on 11 December 2020.

It is important to specify that the methodology developed is intended to shed light on the identification of potential alternatives to formaldehyde, first of all to the public authorities, in sectors where co-exist:

- on the one hand part, a regulatory standard or a marketing authorisation issued by the European or French authorities governing these uses of formaldehyde;
- on the other hand, the obligations of the Labor Code which, following the classification of formaldehyde, indicate that the first action to be taken is substitution.

Thus, the identification of alternatives carried out *a priori* within the framework of this expertise cannot predict the results of the assessment procedures to be carried out for use or marketing

authorisations; these procedures are the responsibility of entities mandated for this purpose and may lead to conduct a more in-depth assessment of the effectiveness of the products and/or fall within profit/risk procedures. Besides, the method developed is also a tool that can be used by employers to better exercise their responsibility with regard to the obligations of the Labor Code regarding substitution.

This review was therefore issued by groups of experts with complementary skills.

The expert appraisal was carried out in accordance with French Standard NF X 50-110 “Quality in Expert Appraisals – General Requirements of Competence for Expert Appraisals (May 2003)”.

1.4 Scope of the appraisal

Before answering to the questions of the request, the WG first developed a method to compare and evaluate the substitutes.

The experts in the WG analysed the scientific literature on the subject in order to define their own working method to be applied subsequently in the various sectors of activity targeted by the request.

This report describes the methodological part of request No 2014-SA-0236.

1.5 Prevention of conflicts of interest

ANSES analyses the links of interest declared by the experts prior to their appointment and throughout the work, in order to avoid potential conflicts of interest with regard to the matters dealt with as part of the expert appraisal.

The experts’ declarations of interests are made public via the ANSES website (www.anses.fr).

2 Review of the main assessment methods for existing substitutes

2.1 Methods for comparing substitutes

2.1.1 Literature search strategy

The ANSES experts first searched for available methods in the scientific literature enabling:

- assessment of substitutes compared to a hazardous substance of concern;
- selection of the best substitute possible among the list of potential substitutes.

In the remainder of this report, the term “substitute” is used to refer to a substance, mixture or process to consider as a replacement for the chemical of concern. The term “alternative” covers two notions: both the substitute itself and the changes to make to the working process as part of implementation.

The appraisal started with analysis of a recent literature review on the subject. The review in question was carried out by Molly M. Jacobs and her team at the University of Massachusetts, USA (Jacobs *et al.* 2016), and is entitled “Alternatives Assessment Frameworks: Research Needs for the Informed Substitution of Hazardous Chemicals”.

This literature review identified and compared 20 frameworks for evaluating the use of substitutes for a hazardous substance. The frameworks are all multi-criteria and included at least the following six groups of criteria to compare: (1) hazard assessment, (2) exposure characterisation, (3) life-cycle impacts, (4) technical feasibility evaluation, (5) economic feasibility assessment, and (6) decision making (i.e. how trade-offs among alternatives are evaluated and resolved). This review considered articles, reports, and web-based documents identified using a large variety of search tools such as EBSCO’s Discovery Service, which aggregates several literature databases or indexes, Medline, several Google search engines, and conversations with experts in the field.

The search terms used by the authors of the review to identify bibliographic references included: “alternatives analysis,” “alternatives assessment,” “chemical alternatives assessment,” “chemical alternatives analysis,” “chemical substitution,” “chemical substitution assessment”, and “technology options assessment.”

The search was limited to literature published between January 1990 and December 2014.

The literature eligible for review included 200 articles and reports. Only articles outlining a multi-step process based on a comparison of the six retained criteria groups and enabling identification, assessment and implementation of alternative solutions were retained. Documents and reports that addressed only policy aspects of alternatives assessment were excluded. Papers that simply described an alternatives assessment case study were also excluded.

To supplement this literature review, a bibliographic search profile was developed at ANSES to continue identifying new methods published between January and December 2015 on SCOPUS and Medline. This profile was based on the same terms as those used by the authors to index the methods described in the literature review by Jacobs *et al*.

Ultimately, 21 methods were identified in the scientific literature and examined by the ANSES experts:

Table 1: Methods examined by the ANSES experts

Names and authors of the examined methods	Publication date	References	Annex
Toxic Use Reduction Institute (TURI), University of Massachusetts	2006	(Eliason and Morose 2011, TURI 2006)	2
Royal Society of Chemistry (RSC) method, learned society in the United Kingdom	2007	(RCS 2007)	3
Technical Rules for Hazardous Substances (TRGS) method developed by the German Committee on Hazardous Substances (AGS), German Federal Institute for Occupational Safety and Health (BAuA)	2008	(BAuA 2008)	4
Significant New Alternatives Policy (SNAP) programme, available on the website of the United States Environmental Protection Agency (US EPA)	Updated in 2016	(US EPA 2016)	5
Method developed by the National Research Council (NRC), a body of the American Academy of Sciences	2014	(NRC 2014)	6
Cleaner Technologies Substitutes Assessment (CTSA) method, developed by the United States Environmental Protection Agency (US EPA)	1996	(US EPA 1996)	7
Pollution Prevention - Occupational Safety and Health (P2OSH) Assessment method developed by a team from the Lowell Center for Sustainable Production, University of Massachusetts and the Boston Medical Center (Massachusetts)	2006	(Quinn *et al*. 2006)	8
Method developed by BizNGO, a collaborative network of business leaders, representatives of environmental protection organisations, government agencies, and universities	2012	(Rossi, Peele, and Thorpe 2012)	9
Method developed by the Ministry of the Environment, Government of Ontario (Canada)	2012	(Ontario Toxics Reduction Program 2012)	10
The European Chemicals Agency (ECHA) Guidance on the preparation of an application for authorisation	2011	(ECHA 2011)	11
Method developed by the Directorate General for Employment, Social Affairs and Inclusion at the European Commission	2012	(European Commission 2012)	12
Method developed by Goldschmidt	1993	(Goldschmid 1993)	13
Method developed by Rosenberg	2001	(Rosenberg *et al.* 2001)	14
Method developed by the Lowell Center for Sustainable Production, University of Massachusetts	2006	(Rossi, Tickner, and Geiser 2006)	15
Method developed by the persistent organic pollutants (POP) Review Committee of the Stockholm Convention	2009	(UNEP 2009)	16

Guide on sustainable chemicals method developed by the German Federal Agency for the environment (Umweltbundesamt – for our environment).	2011	(Umweltbundesamt 2011)	17
Method developed by the United States Occupational Safety and Health Administration (US OSHA)	2013	(OSHA 2013)	18
Design for the Environment (DfE) programme, United States Environmental Protection Agency (US EPA)	Updated in 2011	(Lavoie *et al*. 2011, US EPA 2011)	19
Method developed by the Interstate Chemicals Clearinghouse (IC2), an association of departments responsible for health and/or the environment in 10 US States and 3 local governments.	2013	(IC2 2013)	20
Method developed by the University of California, Los Angeles (UCLA)	2011	(UCLA 2011, Malloy *et al*. 2013)	21
Method developed by Subsport	Updated in 2013	(SUBSPORT 2013, SUBSPORT)	22

A summary of each of these 21 methods is presented in individual annexes to this report. Each summary contains details concerning the method: author, objective, scope, description of the main steps, advantages and disadvantages regarding the issues raised in Request No 2014-SA-0236.

2.1.2 Summary of the examined methods

2.1.2.1 Primary limitations of the available methods

Complex methods

Certain methods appear to be very complex making them difficult to apply within a company or laboratory.

In fact, some of them require more than 10 consecutive steps in order to select a substitute. In addition to the length of the process, the boundaries of the various modules and their interactions can sometimes be poorly structured, making the method difficult to understand.

Some have substantial time requirements. As an example, one of the methods indicates a very long expected time frame to carry out a relatively simple substitution, i.e. dichloromethane in paint strippers, and estimates that 40 weeks are needed purely for the step involving assessment of the alternative solution.

Lastly, when examining the various methods, it appears that a large number of them require significant expertise to collect and summarise all the defined parameters, or use of complex calculation software to carry out the substitution process.

Highly general methods

Many methods ultimately proved to be too general.

Some of them, for instance, focus exclusively on defining the basis for an ideal substitution, rather than defining actual comparison criteria.

The lack of a precise description of the steps and parameters to be compared makes the method in question difficult to apply. A number of methods do not describe the parameters to be compared and sometimes even leave this choice to the user's discretion, while others

describe the parameters precisely but do not provide information on how to perform the comparison.
Moreover, some documents do not put forward their own comparison method but rather list several existing methods without necessarily indicating which one of them should be given priority over the others.

Methods developed in highly specific contexts
Some methods were designed to meet highly specific objectives (examples: method developed to reduce exposure to pesticides, method to take into account POP substitutes, alternatives assessment method for occupational health and safety and prevention of pollution in hospitals, etc.), which makes them difficult to transpose to the sectors of activity targeted by the expert appraisal.

Conclusions
On the basis of the review of the various risk comparison or assessment methods for available substitutes, it became clear that none of these methods were suitable to directly address the issue raised in the framework of this request.
However, even though strict application of these methods does not precisely meet all the requirements, some of the methodological concepts, tools and comparison criteria proposed are relevant and could be integrated after adjustment to produce a method suitable for ANSES's work.

2.1.2.2 Relevant methodological concepts retained

A pragmatic method
Certain methods are directly intended for small and medium-sized enterprises. Since they have just a few steps (maximum of five), they are directly applicable in the occupational setting.

The need to develop a pragmatic method with six to seven steps at the most was recognised so that the method can be understood by all those involved and be reused and adapted for other industrial sectors. To avoid excess steps in the method, it was considered relevant to set up a module for "other impacts" at the end of the approach to provide a space where environmental concerns or possible risk-shifting can be addressed, without including additional complex modules to the method.

Involvement of the stakeholders
Some methods highlight the need to involve the stakeholders in the process of implementing substitution. Including professional employer or trade union federations, key leaders in the target industrial sectors, and simply the personnel directly affected by the substitution process is a key aspect to understanding the sector and identifying realistic substitution solutions, but also to achieving acceptance by the profession.

The working method therefore included the idea of carrying out interviews with competent professionals in each of the sectors of activity to better define the issues involved in substitution in these sectors and to better identify potential substitutes.

A method documenting realistic alternatives

All the methods examine alternative solutions on the basis of several groups of criteria: hazards, technical performance, economic performance, exposure data, etc., and therefore require a large amount of data on each of the alternatives. Several methods point out this issue and suggest initial identification of the most viable substitutes before they are studied in detail. It was decided to break the method down into two steps, with a preliminary step used to rule out non-relevant alternatives, and a second step to examine only those that warrant closer attention.

The question that arises is then to determine which criteria can be used to rule out non-relevant alternatives during the preliminary step. Certain methods place the greatest emphasis on the functional requirements of the substitute by focusing from the start on the function and usage of the chemical of concern. In other words, the following questions are the first that need to be addressed when a substitution process is required in a company: “Why do you use the substance (what does it do?)” and “How do you use it”?

The question of the technical performance of the substance was retained as an essential criterion because a substitute must also fulfil the function of the original substance in an equivalent or sufficiently similar manner. Identifying the technical criteria of performance was considered essential for the success of the approach. This is why, for each of the sectors of activity studied, it was decided to define the expected technical criteria upstream of any assessment, in order to select substitutes that are in principle technically effective from the very start.

Beyond the identification of technical criteria, certain methods emphasise the need to rapidly identify the substances that are as hazardous or even more hazardous than the chemical of concern. These types of substances would not be suitable substitutes since they would not reduce the hazard posed to exposed populations.

The principle retained was to first select the most viable alternatives on the basis of technical criteria, followed by hazards.

A method to assist in decision-making

Almost all the methods are intended for industrial users who make the final choice of the substitute depending on their priorities and their investment potential in the best alternative solution.

The most evolved methods to guide the choice of a substitute are those that rely on a comparative approach. These methods compare the various alternatives on the basis of quantitative criteria and sometimes even qualitatively using symbols such as “+”, “-” or “=” if numerical data are not available. All the criteria for each substitution solution are thereby assessed individually by comparing them with the chemical of concern. It is thus the difference between the two that is evaluated for each criterion. This comparative approach enables the decision-maker to examine the best possible alternative on the basis of an overall view of the substitution solution for a given use.

It was therefore decided that the second step of the method should involve a comparison, with the aim of obtaining an overview of the possible alternative solutions and all the information concerning them, to help the decision-maker compare the different substitutes with each other.

Comparison of the hazards using available tools

Concerning the comparison of hazards related to the substitutes, many methods refer to existing tools from the scientific literature or from industrial practice.

Since there are already many broadly accepted tools to compare substitutes on the basis of hazard criteria for human health and the environment, it was decided to examine them in detail to identify those that could be used directly.

2.2 Tools for comparing the hazards related to substitutes

2.2.1 Literature search strategy

The Organisation for Economic Co-operation and Development (OECD) published and released the first version of its Substitution and Alternatives Assessment Toolbox (SAAT) in January 2015: this is a toolbox designed for the substitution of chemical substances. The SAAT identifies all the existing relevant tools that can be used in substitution processes or within the framework of alternatives assessment. One of the spaces in this toolbox shows the practical assessment tools for the chemical risks of substances and for the comparison of alternatives on the basis of the hazard criteria of the substances. By selecting the “compare alternatives” and “free of charge” filters, the toolbox proposes a list of 10 cost-free tools that can be used to compare substitutes among themselves with regard to various attributes, such as the hazards associated with the physico-chemical properties and the hazards to human health or the environment (OCDE 2015).

An additional search was performed using the first part “Tools for selecting less hazardous chemicals” of the book entitled “Chemical Alternatives Assessment” (Whittaker and Heine 2013), which describes the tools enabling comparisons of substitutes with each other in view of their hazards. In this part, 10 tools were identified.

After removing redundant tools between those identified in the OECD toolbox and in the above-mentioned book, a total of 16 practical tools enabling comparisons of hazard criteria were identified:

Table 2: Tools for hazard comparisons identified by the ANSES experts

Names and authors of the identified tools	Publication date	References	Annex
GreenScreen® for Safer Chemicals developed by Clean Production Action (CPA), a consulting firm based in the United States and Canada.	Updated in 2016	(CPA 2016a, c, OCDE 2015, Whittaker and Heine 2013)	
GreenScreen® List Translator (GSLT) developed by Clean Production Action (CPA), a consulting firm based in the United States and Canada	2011	(OCDE 2015, CPA 2016b)	23
Quick Chemical Assessment Tool (QCAT) developed by the Washington State Department of Ecology	2012 Updated in 2015	(OCDE 2015, Department of Ecology State of washington 2016)	
Quick Scan developed by the Dutch Ministry of Housing, Spatial Planning and the Environment	Not documented	(Whittaker and Heine 2013)	

Column Model developed by the Institute for Occupational Safety and Health (IFA) of the German Social Accident Insurance	Updated in 2014	(OCDE 2015, Whittaker and Heine 2013)	
Evaluation Matrix developed by the German Federal Environmental Agency	2003	(Whittaker and Heine 2013)	
Pollution Prevention Options Analysis System (P2OASys) developed by the Toxic Use Reduction Institute (TURI)	2013	(OCDE 2015, Whittaker and Heine 2013)	
Program for Assisting the Replacement of Industrial Solvents (PARIS) III developed by the United States Environmental Protection Agency (US EPA)	1995	(OCDE 2015)	
ISUSTAIN™ Green Chemistry Index developed by Cytec Industries Inc., Sopheon (international software publisher in product life-cycle management) and the Beyond Benign Foundation	Not documented	(OCDE 2015)	
The Chemical Scoring and Ranking Assessment Model (SCRAM) developed by Snyder *et al*.	1999	(Whittaker and Heine 2013)	
Keml PRIO developed by the Swedish Chemicals Inspectorate (KemI), monitoring authority und+er the Ministry for the Environment	Updated in 2015	(OCDE 2015, Whittaker and Heine 2013)	
SIN List and SINimilarity developed by ChemSec, a non-governmental organisation founded in 2002 by 4 environmental organisations	Updated in 2015	(OCDE 2015)	
Chemicals Assessment and Ranking System (CARS) developed by the Zero Waste Alliance (Portland, Oregon, USA)	Not documented	(Whittaker and Heine 2013)	
Safer Chemical Ingredients List (SCIL) developed by the United States Environmental Protection Agency (US EPA)	Updated in 2015	(OCDE 2015)	
SC Johnson & Son's Greenlist developed by the American Company SC Johnson & Son (SCJ)	2001	(Whittaker and Heine 2013)	
Cradle to Cradle (C2C) created by Michael Braungart and William McDonough, maintained and administered by "the Cradle to Cradle Products Innovation Institute" (C2CPII)	Not documented	(Whittaker and Heine 2013)	

Through the analysis of these tools, other tools, which require payment and originate from the private sector, were also identified. Since these tools are not open-access, they were not retained in the framework of this appraisal.

2.2.2 Examination of the tools

Most of the identified tools have common features. Some tools are occasionally incomplete but very easy to use, while others are complex and require months of training to learn how to use them. Certain tools have not been updated and still refer to former classifications of

chemical substances and not to the CLP Regulation. Others still are described as accessible but are not, in fact, in practice.

Ultimately, only the Quick Chemical Assessment Tool (called QCAT hereafter), GreenScreen® for Safer Chemicals (called GreenScreen hereafter) and GreenScreen List Translator (called GSLT hereafter) were examined in this appraisal because they were considered easily accessible, easy to implement, and comprehensive, and can be used to generate a final list of substances by comparison of hazards.

2.2.3 Selection of tools

It was considered beneficial to have two additional tools for hazard comparisons:

- a first, rapid and easy-to-use tool that can quickly exclude from the list of potential substitutes any substances that are as hazardous as or more hazardous than the chemical of concern;
- a second tool that can be used to carry out a deeper analysis of hazard assessment for a limited number of substances.

After evaluating the tools available in the literature, it was decided to retain the following two tools: GreenScreen and QCAT. GSLT, described in Annex 23, was not retained because it enables identification of the most hazardous substances but does not propose a readily usable final ranking.

Importantly, the tools GreenScreen and QCAT are based on the same overall approach, i.e. the Design for the Environment (DfE) programme of the US EPA. This general approach was used to make available several tools for the comparison of hazards related to substitutes: GreenScreen and QCAT.

2.2.4 The GreenScreen tool

(CPA 2016a, c)

This tool can be used to assess the intrinsic hazards associated with chemical substances in a transparent manner for a wide range of effects and then to generate an interpretation of this information that is helpful to industries and risk managers by categorising these substances into four hazard classes that include recommendations for use.

Since the tool was designed to produce summarised results of the hazard analysis by substance, it is intended to compare several specific chemical substances to classify the substitutes based on results. This tool may be subjected to updates that should require attention.

2.2.4.1 Scope

This tool can be used for chemical substances and mixtures.

The types of hazards addressed are those affecting humans (health effects and physico-chemical properties), as well as environmental hazards (ecotoxicity and aspects related to the fate of the substance in the environment).

2.2.4.2 Operating principles

The process follows four successive steps.

1) Identification and classification of hazards

The first of these steps is to determine hazard levels for each of the 18 effects of interest from among the six proposed levels: very high (vH), high (H), moderate (M), low (L), very low (vL) or data gap (DG).

The list of the 18 effects is described in the following table.

Table 3: Types of hazards analysed by substance within the GreenScreen tool

Human toxicity (group I)	Human toxicity (group II)	Environmental health and environmental fate	Physical hazards
• carcinogenicity (C) • mutagenicity and genotoxicity (M) • reproductive toxicity (R) • developmental toxicity (D) • endocrine activity (E)	• acute mammalian toxicity (AT) • systemic toxicity and organ effects (ST) • neurotoxicity (N) • skin sensitisation (SnS) • respiratory sensitisation (SnR) • skin irritation (IrS) • eye irritation (IrE)	• acute aquatic toxicity (AA) • chronic aquatic toxicity (CA) other ecotoxicity studies (when available) • persistence (P) • bioaccumulation (B)	• reactivity (Rx) • flammability (F)

To be able to attribute a hazard level to each effect, information must first be collected. The GreenScreen tool describes 4 distinct types of sources to collect this information. It can come from:

1. a search of toxicological data in a list of websites or toxicological databases described in a document entitled “Informations sources” available on the GreenScreen website (CPA 2016d);
2. a search among 42 specific lists which propose a classification of substances. These lists are described in a document entitled “GreenScreen translator” available on the GreenScreen website (CPA 2016b);
3. a search of measured toxicological data for a relevant structural analogue of the substance of interest;
4. a data modelling in order to complete missing measured data.

The GreenScreen tool leaves the choice to the user to rank its search in these 4 types of sources according to its preferences.

Regarding the 42 specific lists proposing classifications of substances, the GreenScreen tool classifies them in 2 categories:

- the lists considered to be “authoritative” (Authoritative lists) which are often created as part of regulatory processes to identify hazardous substances;

- the “selection” lists (Screening lists) which are developed on the basis of a less comprehensive review of the scientific literature or which are compiled by organisms not considered to be authoritative in the field.

Each of these 2 lists can be classified in the sub-category A or B:

- the sub-category A corresponds to a list associating data with a single hazard level;
- the sub-category B corresponds to a list which leaves the choice to the user to attribute a hazard level among several proposals for the same data.

The GreenScreen tool also allows to assign a level of confidence to each assigned hazard level. Thus, the hazard levels coming from information sources with a high level of confidence will be highlighted in bold capital whereas those coming from information sources with a lower level of confidence will be highlighted in italics.

This information is then summed up in one line per substance as presented in the figure below for a chemical substance:

Group I Human					Group II and II* Human									Ecotex		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						SINGLE	REPEATED*	SINGLE	REPEATED*										
DG	*L*	*L*	M	M	DG	*L*	*L*	M	M	L	L	L	L	*L*	*L*	*vH*	*M*	*L*	*L*

Figure 1: Example of grading and hazard comparison for a chemical substance in GreenScreen

Hazard levels assigned by effect: very low (vL), low (L), moderate (M), high (H), very high (vH), data gap (DG)

(CPA 2016a)

2) Assigning the initial hazard class

The user is then invited to assign one of four hazard classes (benchmark scores) to the substance based on the hazard categories obtained for each of the effects considered in the previous step. To start, this benchmark score is considered preliminary and does not take into account possible data gaps associated with the effects. A very general management recommendation is associated with each of these classes.

As described in the table below, the hazard levels obtained for the substance will be used to classify the compound as Benchmark 4 (Prefer – safer chemical), 3 (Use but still opportunity for improvement), 2 (Use but search for safer substitutes), 1 (Avoid – chemical of high concern), or U (Unspecified due to insufficient data). The terminology listed here is that defined and used in the GreenScreen tool.

Table 4: Assigning a GreenScreen hazard class

Benchmark 1	Avoid – chemical of high concern
Benchmark 2	Use but search for safer substitutes
Benchmark 3	Use but still opportunity for improvement
Benchmark 4	Prefer – safer chemical
Benchmark U	Unspecified due to insufficient data

As shown in the figure below, the assessor must begin with Benchmark 1. If one of the class 1 statements applies to the substance, the substance will be graded Benchmark 1. If this is not the case, the assessor can pass on to Benchmark 2. Likewise, the substance will be graded Benchmark 2 if one of the class 2 statements applies to the data on the compound. If not, the assessor can move onto Benchmark 3 and so on, up to Benchmark 4.

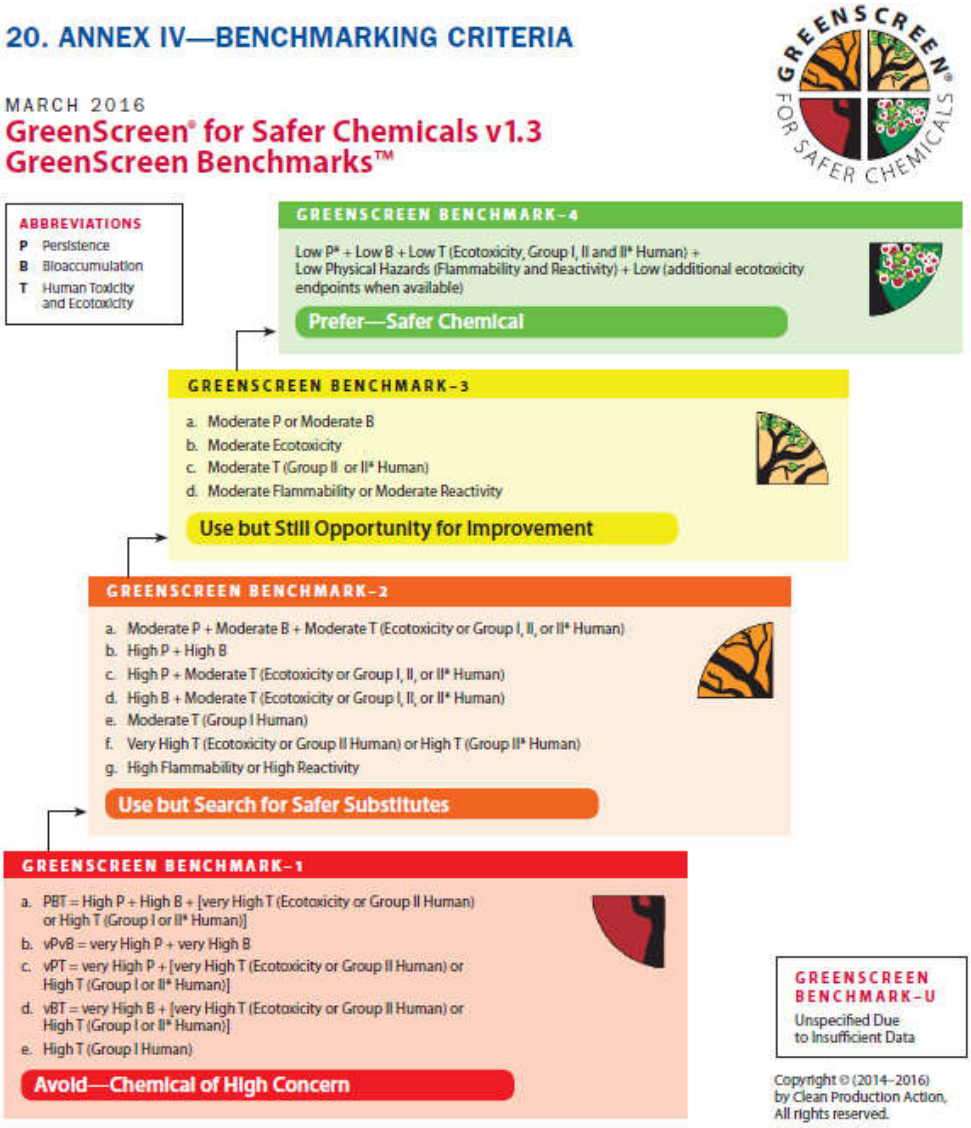


Figure 2: Assigning a GreenScreen benchmark hazard class

3) Assigning the final hazard class

The tool then offers an analysis of missing data in order to attribute a final hazard class to the substance. This analysis takes into consideration the quantity of missing data and the effects for which data are missing.

Assigning a final hazard class is based on the following approach:

- If the substance is graded class 1, it remains in class 1.

- If the substance is graded class 2, it remains in class 2, if the following conditions have all been met:
  - data are available for at least three of the five effects concerning human health (group I). Data may be missing for reproductive toxicity (R), developmental toxicity (D), or for endocrine activity (E);
  - data are available for at least four of the seven effects concerning human health

(group II). Data may be missing for either skin sensitisation (SnS) or respiratory sensitisation (SnR); for either skin irritation (IrS) or eye irritation (IrE); or for a single other effect;
- data are available for at least three of the four effects concerning environmental health and environmental fate. Data may be missing either for acute aquatic toxicity (AA) or for chronic aquatic toxicity (CA);
- all data must be available for physical hazards.

If these conditions are not met, the final class U (unspecified due to insufficient data) will be assigned to the substance.

- If the substance is graded class 3, it remains in class 3, if the following conditions have all been met:
  - data are available for at least four of the five effects concerning human health (group I). Data may be missing for endocrine activity (E);
  - data are available for at least five of the seven effects concerning human health (group II). Data may be missing for either skin sensitisation (SnS) or respiratory sensitisation (SnR); for either skin irritation (IrS) or eye irritation (IrE); or for a single other effect;
  - all data must be available for environmental health and environmental fate;
  - all data must be available for physical hazards.

If these conditions are not met, the substance will be graded class $2_{DG.}$
If the substance does not meet the conditions required for class 2, it will be graded class U.

- If the substance is graded class 4, it remains in class 4 if all the data for the 18 effects are available, i.e. there are no missing data.

If this condition is not met, the substance will be graded class $3_{DG.}$
If the substance does not meet the conditions required for class 3, it will be graded class 2_{DG}.
If the substance does not meet the conditions required for class 2, it will be graded class U.

4) Characterisation of the results and decision-making

This last step consists in processing and analysing the data obtained based on the specific objective of the study, in order to guide management decisions. A few suggestions are put forward including grouping the various substances analysed by hazard class in an effect analysis table, or identification of gaps in existing knowledge.

2.2.5 The QCAT tool

(Washington State Department of Ecology, 2016)

QCAT is a simplified tool originating directly from the GreenScreen tool (see previous section). GreenScreen aims to establish hazard levels for 18 effects, while QCAT studies only nine.

Due to the smaller amount of data evaluated by QCAT, the tool cannot be used to identify possible alternatives to a chemical product to be substituted because it does not address a certain number of important hazards (explosivity, flammability, sensitisation, irritation, etc.).

However, the tool can be used to rapidly identify the most toxic chemical products. This tool may be subjected to updates that should require attention.

2.2.5.1 Scope

This tool can be used for chemical substances and mixtures.

The types of hazards addressed are those affecting humans (health effects), as well as environmental hazards (ecotoxicity and aspects related to the fate of the substance in the environment).

2.2.5.2 Operating principles

The process follows four successive steps.

1) Identification and classification of hazards

The first of these steps is to determine hazard levels for each of the nine effects of interest from among the six levels to assign to each effect: very high (vH), high (H), moderate (M), low (L) and very low (vL), or data gap (DG). This classification depends on the available data. Data collection is guided entirely by a simplified table listing the information sources to consult. This list of information sources is limited in comparison with the list in the GreenScreen tool.

This collection of data on the hazards of the substances may require two successive steps. Irrespective of the substance, step I of the search is mandatory.

The sources in step I are mainly lists considered to be authoritative. Assessment of the substance depends on its inclusion in a list. These sources are divided into two categories: priority sources and secondary sources. Priority sources are lists issued by recognised European or international organisations that have examined all the data on the substance. Secondary sources are lists from governments and other organisations that may not have studied all the data available on the substance.

If the data are incomplete after step I, the QCAT tool then proposes to search for data in a list of additional sources indicated in Appendix 2 of the method. This is step II of data collection. The sources in step II refer to measured or modelled data on the substance.

The priority sources in step I are considered authoritative and can be used directly in the classification process with no further examination or search for additional information. The secondary sources in step I can also be used with no further examination unless the assessor decides to examine the sources in step II to obtain additional data.

Following these two steps, an initial hazard class is assigned to the compound on the basis of the hazard levels. Each of the nine effects is presented in the table below. Appendix 8 of the QCAT tool is used to assign the hazard level to retain based on the available data (classification or literature data).

Table 5: Types of hazards analysed by chemical substance within the QCAT tool

Human toxicity (group I)	Human toxicity (group II)	Environmental health and environmental fate	Physical hazards
• carcinogenicity (C) • mutagenicity and genotoxicity (M) • reproductive	• acute mammalian toxicity (AT)	• acute aquatic toxicity (AA) other ecotoxicity studies (when available) • persistence (P)	none

toxicity (R) • developmental toxicity (D) • endocrine activity (E)		• bioaccumulation (B)	

The results are then presented in a table identical to that used in GreenScreen, except that the nine columns corresponding to the nine non-assessed endpoints are not filled in.

A colour code is used to facilitate interpretation of the table: dark red is used for a “very high (vH) level”, red for a “high (H)” level, yellow for a “moderate (M)” level, green for a “low (L)” level, and dark green for a “very low (vL)” level.

Human Health Group 1 (HH1)					Human Health Group 2 (HH2)							Env. Health			Fate		Physical	
C	M	R	D	E	AT	ST	N	SnS	SnR	Irs	IrE	AA	CA	Eo	P	B	Ex	F
H	M	H	H	DG	vH							H			L	vL		

Figure 3: Example of grading and hazard comparison for a chemical substance in QCAT

Key:

Hazard level assigned by effect: very low (vL), low (L), moderate (M), high (H), very high (vH), data gap (DG), not studied in the QCAT tool (X)

(Washington State Department of Ecology, 2016)

2) Assigning the initial grade

As described in the table below, the hazard levels obtained for the substance will be used to grade the compound as Grade A (Prefer – safer chemical), B (Use but still opportunity for improvement), C (Use but search for safer substitutes), or F (Avoid – chemical of high concern). The terminology listed here is that defined and used in the QCAT tool.

Table 6: Assigning a QCAT hazard class

Grade F	Avoid – chemical of high concern
Grade C	Use but search for safer substitutes
Grade B	Use but still opportunity for improvement
Grade A	Prefer – safer chemical

To do this, the assessor must start with Grade F. If one of the Grade F statements applies to the substance, the substance is graded Grade F. If this is not the case, the assessor can move on to Grade C. Likewise, the substance will be graded C if one of the Grade C statements applies to the data obtained for the substance, and so on, up to Grade A.

Grade A	1. Low P + Low T (AA, AT and all HH1 endpoints)
Grade B	1. Moderate P; or 2. Moderate B; or 3. Moderate AA; or 4. Moderate AT or one or more HH1 endpoints
Grade C	1. Moderate P + Moderate B + Moderate T (AA, AT, or any HH1 endpoint); or 2. High P + High B; or 3. High P + Moderate T (AA, AT, or any HH1 endpoint); or 4. High B + Moderate T (AA, AT, or any HH1 endpoint); or 5. Very High T (AA or AT).
Grade F	1. PBT = High P + High B + [Very High T (AA or AT) or High T (HH1)]; or 2. vPvB = very High P + very High B; or 3. vPT = very High P + [very High T (AA or AT) or High T (HH1)]; or 4. vBT = very High B + [very High T (AA or AT) or High T (HH1)]; or 5. CMR = High T (HH1).

Figure 4: Assigning the grade

Key:

AA = acute aquatic toxicity; AT = acute mammalian toxicity; B = bioaccumulation; C = carcinogenicity; D = developmental toxicity; E = endocrine activity; G = genotoxicity; HH1 = human health, group I (C, M/G, R, D and E); M = mutagenicity; P = persistence; R = reproductive toxicity; T = human and environmental toxicity

(Washington State Department of Ecology, 2016)

3) Assigning the final hazard grade

Some of the nine hazard endpoints in the QCAT tool may not be filled in using the data sources in steps I and II. In this case, the QCAT tool suggests assigning a final hazard grade to the substance based on the type of missing data. This grade is called X_{DG} where X is the hazard grade (B, C, or F) and DG indicates a data gap.

Assigning a final hazard grade is based on the following approach:

- If the substance is assigned Grade F, it remains in Grade F;
- If the substance is assigned Grade C, it will be graded F_{DG} if at least one of the following three hypotheses applies:
  - Hypothesis 1: data are missing for at least three effects concerning human health;
  - Hypothesis 2: data are missing for one of the following effects: persistence, bioaccumulation, acute mammalian toxicity or acute aquatic toxicity;
  - Hypothesis 3: data are missing for two effects concerning human health from among carcinogenicity, reproductive toxicity or developmental toxicity.
- If the substance is assigned Grade B, it will then be:
  - assigned Grade F_{DG} if hypothesis 1, 2 or 3 applies;
  - assigned Grade C_{DG} if hypothesis 4 applies, i.e. data are missing for an effect concerning human health other than endocrine activity.
- If the substance is assigned Grade B, it will then be:
  - assigned Grade F_{DG} if hypothesis 1, 2 or 3 applies;
  - assigned Grade C_{DG} if hypothesis 4 applies;
  - assigned Grade B_{DG} if missing data concern endocrine activity.

4) Characterisation of the results and decision-making

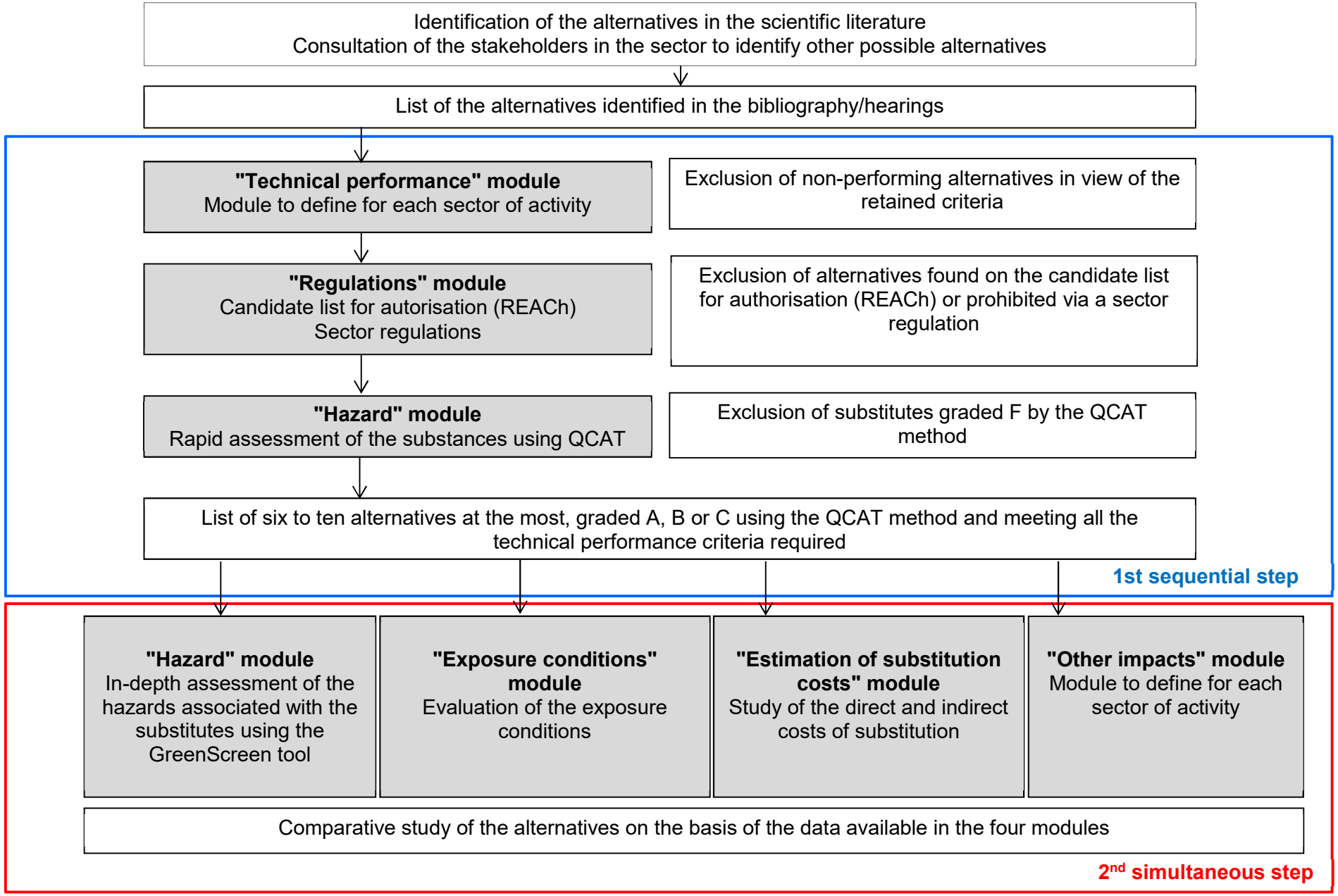
This last step consists in processing and analysing the data generated based on the specific objective of the study.

QCAT enables rapid identification of the most hazardous substances graded F. This is, in fact, why this tool was retained as part of the appraisal because it can be used at a preliminary stage to rule out substitutes that are more hazardous than the chemical of concern.

QCAT also makes it possible to identify and prioritise substances to assess with GreenScreen.

3 Design of the comparison method for alternatives

3.1 General description


Identification of the alternatives in the scientific literature
Consultation of the stakeholders in the sector to identify other possible alternatives
List of the alternatives identified in the bibliography/hearings
"Technical performance" module
Module to define for each sector of activity
Exclusion of non-performing alternatives in view of the retained criteria
"Regulations" module
Candidate list for autorisation (REACh)
Sector regulations
Exclusion of alternatives found on the candidate list for authorisation (REACh) or prohibited via a sector regulation
"Hazard" module
Rapid assessment of the substances using QCAT
Exclusion of substitutes graded F by the QCAT method
List of six to ten alternatives at the most, graded A, B or C using the QCAT method and meeting all the technical performance criteria required
1st sequential step
"Hazard" module
In-depth assessment of the hazards associated with the substitutes using the GreenScreen tool
"Exposure conditions" module
Evaluation of the exposure conditions
"Estimation of substitution costs" module
Study of the direct and indirect costs of substitution
"Other impacts" module
Module to define for each sector of activity
Comparative study of the alternatives on the basis of the data available in the four modules
2nd simultaneous step

The method retained by the WG is **general** and will be applied and adapted if necessary to the various sectors of activity studied.

The method follows a **multi-criteria** approach since it is not aimed solely at assessing the hazards of alternatives but also at studying issues around their technical performance, the estimated costs of substitution, and the conditions of exposure of workers to the alternative solutions identified.

The method is considered to be **"mixed"** because it is divided into two broad steps: the first, which is **sequential**, and the second, which is **simultaneous**:

- The first sequential step involves studying the various alternatives through three successive modules, each containing exclusion criteria.
- The second simultaneous step takes a comparative approach. The remaining alternatives are then studied in parallel through four modules. This second step is a comparison of the selected alternatives and is used to determine their substitution abilities.

To summarise, the method retained is able to rule out potential alternatives in the first step, thereby enabling more detailed data collection on a smaller number of alternatives with the aim of comparing them in the second step.

3.2 Detailed description of the method developed to compare the alternatives

To illustrate use of the method developed to compare alternatives, a fictitious example assessing six different alternatives for a hazardous substance is described below.

3.2.1 Initial list of alternatives

The method requires a preliminary compilation of the possible alternatives that is as exhaustive as possible. These alternatives must be identified on the basis of a bibliographic search, supplemented by hearings with professionals, unions or associations in the sector of interest. Any alternative identified and used in combination with the substance to be substituted is excluded.

3.2.2 The three modules of the sequential step

3.2.2.1 "Technical performance" module

The purpose of this module is to rule out any alternatives that do not offer the essential functions that must be fulfilled by use of the chemical of concern.

This module involves determining a maximum of six criteria considered necessary for use in the sector of interest.

Each of these criteria will be examined by comparison with the substance routinely used and allocated to one of five categories: superior (sup), equivalent (eq), inferior (inf), insufficient (insuff) or "yes" (when a criterion is favourably assessed but without any comparison with that of the substance to be substituted).

Importantly, only the criteria considered essential for the alternative to fulfil are retained. An insufficiency regarding one of these criteria necessarily entails lower effectiveness, and no offsetting between essential criteria is possible.

The ultimate aim is to assign one of the following classes to each alternative:

Table 7: Assigning classes in the "Technical performance" module

Class 1	Insufficient technical performance
Class 2	Inferior technical performance
Class 3	Equivalent technical performance
Class 4	Superior technical performance
Not assigned	Not assigned due to insufficient data

The results will be presented in a table of the following type:

Table 8: Example of a comparison of technical performance criteria

Assessment criteria for "technical performance"	Hazardous chemical of concern	Alternatives							
		No. 1	No. 2	No. 3	No. 4	No. 5	No. 6	No. 7	No. 8
Criterion 1		eq	sup	eq	sup	sup	inf	yes	sup
Criterion 2		eq	sup	eq	eq	inf	inf	yes	insuff
Criterion 3		eq	sup	eq	sup	eq	inf	yes	eq
Criterion 4		eq	eq	eq	eq	eq	inf	yes	eq
"Technical performance" classes	Class 3	Class 3	Class 4	Class 3	Class 4	Class 2	Class 1	Class 3	Class 1

All the criteria for each alternative are thereby assessed individually by comparing them with the chemical of concern. It is thus the difference between the two that is evaluated for each criterion.

An examination of the quality of sources and of the quality of the assessment method used to obtain the data on the technical performance of the alternatives is taken into account to assign categories to each technical criterion identified.

The rules of allocation of the final classes will be defined specifically for each sector of activity based on experts judgment.

As a result, it is recommended that only alternatives in Classes 2, 3 and 4 be retained.

In the example shown here, only alternatives Nos. 1 to 5 and alternative No. 7 would be selected for study in the next module of the sequential step.

3.2.2.2 "Regulations" module

The purpose of this module is to identify alternatives that are prohibited for health/safety/environmental concerns by a sector regulation applicable to the sector of activity in which the alternatives assessment is taking place. In this way, any alternative that is prohibited by regulations for health and safety reasons will be excluded from the method.

Likewise, a substitute that is included in the candidate list for authorisation of the REACh Regulation will be excluded from the method. The substances on this list are to be included in the list of substances requiring authorisation, and thus ultimately to be banned in Europe, unless an authorisation is granted by the European Chemicals Agency (ECHA).

In our example, alternative No. 5 is included in the candidate list for authorisation and will therefore not be studied in the last sequential step module, the “hazard” module.

3.2.2.3 “Hazard” module

The purpose of this third module is to exclude from the method any substitutes that are as hazardous as or more hazardous than the chemical of concern.

Principles of the QCAT tool

This module involves studying the substitute using the QCAT tool and assigning one of the seven hazard grades A, B B_{DG}, C, C_{DG}, F or “not assigned”. The experts from ANSES decided to change the category “F_{DG}” described in the QCAT tool into “Not assigned”, as they prefer to highlight the absence of data that characterizes this category, rather than keeping the letter F, which is assigned to extremely hazardous chemical substances.

The purpose of this module is to exclude substances graded F. All the other grades, including ”Not assigned”, allow study of the substitute in the four modules of the simultaneous step.

All substances present at a concentration of more than 0.1% in a mixture are assessed using QCAT, and the grade of the most restrictive substance will be assigned to the mixture under study.

When using the QCAT tool, the sources used to collect data on the hazards associated with the substitutes will be described. The terminology defined and used by this tool (management measures for the risks accompanying each grade) is not reflected in this method. The ANSES experts have retained only the distributions of products in the various grades in order to compare the different alternatives with each other and have defined the terminology to associate with each of them.

Table 9: Assigning a grade in the “Hazard” module using the QCAT tool

Hazard grade F	Extremely hazardous chemical substance
Grade C Grade C_{DG}	Very hazardous chemical substance Very hazardous chemical substance due to missing data
Grade B Grade B_{DG}	Hazardous chemical substance Hazardous chemical substance due to missing data
Grade A	Low hazard chemical substance
Not assigned	Not assigned due to insufficient data

Adjustment of the QCAT tool by the experts of ANSES

In order to assign the different hazard levels to the effects, the experts of ANSES followed the rules of the QCAT tool with some adjustments related to some situations described below.

Data reported in a priority source in step I is used to directly assign a hazard level to the effect.

Data reported in a secondary source in step I is used to directly assign a hazard level to the effect. However, the QCAT tool leaves the choice to the experts to consult the other sources of the tool if wanted. Thus, the experts directly assign a hazard level to the effects when information is found in the secondary sources in step I, except in 2 situations. Namely, the experts of ANSES considered that the classifications from Japan (GHS) and the presence of the substance on the Domestic Substance List (DSL List) of Environment and Climate Change Canada are two penalising sources. These sources may, in fact, lead to high hazard levels for some effects for a large number of substances. In these 2 cases, the experts preferred to complete their analyses by studying experimental data reported in the sources of step II in order to confirm or adjust the hazard level assigned to the effects in question.

When no information is found in the priority or secondary sources of step I, the experts analyse all bibliographic sources of step II. The experts assign a hazard level to an effect by using first of all experimental data. The experts give priority to experimental data described in literature and use as the last resort experimental data reported by industries in substance registration dossiers available on the ECHA website. When no experimental data is available, the experts refer to modelled or estimated data described in literature. When no information is available, the experts refer to modelled data they generate themselves by tools such as PBT Profiler or the Danish QSAR database.

The ANSES experts also wanted to modify the allocation of some hazard levels as initialy intended by the QCAT tool.

A substance on the TEDX List (one of the lists of potential endocrine disruptors) leads, according to the QCAT tool, to a high hazard level (H) for endocrine activity. Yet, the purpose of this list is to present chemical substances for which at least one study showing an effect on the endocrine system has been published in order to improve the information of scientists, risk managers and the public. In June 2015, nearly 1,000 substances were listed as ED on the TEDX List. In this list, no ED classification is proposed. Therefore, the experts of ANSES preferred to assign the moderate hazard level (M) for endocrine activity when a substance is included in this list, rather than the high hazard level (H) which will be retained for substances that are present on lists proposing ED classification, such as the European Union lists for instance.

A substance classified by the MAK Commission (Maximale Arbeitsplatz-Konzentration) of the DFG (Deutsche Forschungsgemeinschaft) in group 5 for carcinogenicity (MAK Carcinogen Group 5 - Genotoxic carcinogen with very slight risk under MAK/BAT levels); or in group 5 for mutagenicity or genotoxicity (Germ Cell Mutagen 5) or in group C for developmental toxicity (Pregnancy Risk Group C) is assigned in each case a moderate hazard level (M) according to the QCAT tool. The experts of ANSES considered that these allocations are too strict in view of the definition of each of the 3 groups. Therefore, the experts preferred to assign the low hazard level (L) for each of the 3 effects when the substance is classified in the 3 groups previously described.

A substance classified by IARC (International Agency for Research on Cancer) in group 3 (the agent is not classifiable as to its carcinogenicity to humans) is assigned a moderate hazard level (M) for carcinogenicity according to the QCAT tool. The experts of ANSES considered that this allocation is too strict in view of the definition of this group. Therefore, the experts preferred to assign the low hazard level (L) to this effect when the substance is classified in group 3 by IARC. Nevertheless, when IARC classification is old, the experts prefer to check studies on which this classification in group 3 is based in order to guarantee that a low hazard

level (L) can actually be assigned and that this classification is not exclusively due to missing data to characterise carcinogenicity.

A substance with the note “Some Evidence of no Adverse Effects - Reproductive Toxicity” in a US NIH (National Institutes of Health) monography is assigned a moderate hazard level (M) according to the QCAT tool. The experts of ANSES considered that this allocation is too strict in view of the definition of this note. Therefore, the experts preferred to assign the low hazard level (L) for reproductive toxicity when the substance is assigned this note.

A substance listed on the DSL List of Environment and Climate Change Canada leads, according to the QCAT tool, to a very high hazard level (vH) for persistence. The experts of ANSES considered this hazard level too high and preferred to assign a moderate hazard level (M) for persistence when the substance is included in this list.

Thus, all alternatives not graded F by the QCAT tool can be studied during the second simultaneous step.

3.2.3 The four modules of the simultaneous step

3.2.3.1 Hazard module

Principles of the GreenScreen tool

The purpose of this “hazard” module is to assign a final hazard class (among the following classes: 1, 2, 2_{DG}, 3, 3_{DG}, 4, or not assigned) by applying the GreenScreen tool to each of the identified alternatives, i.e. to the alternative substance or to each of the substances present in the alternative mixture.

All substances present at a concentration of more than 0.1% in a mixture are assessed using GreenScreen, and the grade of the most restrictive substance will be assigned to the mixture under study.

This module involves studying the substitute using the QCAT tool and assigning one of the seven hazard grades A, B B_{DG}, C, $C_{DG,}$ F or “not assigned”. The experts from ANSES decided to change the category “F_{DG}” described in the QCAT tool into “Not assigned”, as they prefer to highlight the absence of data that characterizes this category, rather than keeping the letter F, which is assigned to extremely hazardous chemical substances.

Table 10: Assigning a hazard class in the "Hazard" module using the GreenScreen tool

Hazard class 1	Extremely hazardous chemical substance
Hazard class 2 Hazard class 2_{DG}	Very hazardous chemical substance Very hazardous chemical substance due to missing data
Hazard class 3 Hazard class 3_{DG}	Hazardous chemical substance Hazardous chemical substance due to missing data
Hazard class 4	Low hazard chemical substance
Not assigned	Not assigned due to insufficient data

The results will be presented in a table of the following type:

Table 11: Example of assigning hazard classes using GreenScreen

Assessment criteria for hazards	Hazardous chemical of concern	Alternatives			
		No. 1	No. 2	No. 3	No. 4
Hazard classes according to GreenScreen	Class 1	Class 2	Class 2	Class 3	Class 4

Adjustment of the GreenScreen tool by the ANSES experts

Taking into account the assessments according to the QCAT tool

The substances analysed by the GreenScreen tool have already been analysed by the QCAT tool.

The 9 new effects, not assessed by the QCAT tool, are assessed using the GreenScreen tool.

For the effects already assessed by the QCAT tool, the experts adopted the following approach:

1. check that data used to assign a hazard level according to the QCAT tool enables to assign the same hazard level according to the GreenScreen tool. If this is not the case, the experts then modifiy the hazard level according to the GreenScreen tool so that it corresponds to the assessment criteria of the GreenScreen tool;
2. for effects for which hazard levels have been assigned according to QCAT from secondary sources in step I or sources in step II, the experts allow themselves reassessing this effect by seeking additional information in the sources of the GreenScreen tool;
3. the effects whose assessment according to the QCAT tool concluded that there is a lack of data (DG) are systematically reassessed using the GreenScreen tool.

Hierarchisation of information sources

The GreenScreen tool leaves the choice to the user to rank information sources for data collection. Thus, the experts of ANSES adopted a 5-step approach. Each step refers to information sources to be consulted. The experts start by seeking information in the sources described in step I. If information is collected at this step, it is then used to assign a hazard level to the effect under study. Otherwise, the experts look for information in sources of step II. So on, the experts continue to search for information step by step until they find information about the effect under consideration. In general, when information is found in one of the sources described in a step, it can be used to assign a hazard level to the effect under study without seeking additional information in sources described in the next step(s).

The experts adopted the following 5-step approach:

The step 1 consists in collecting information about classification in “authoritative” lists in the sub-category A or B. The experts used the document entitled “GreenScreen translator” (CPA 2016b) to identify these lists.

The step 2 consists in collecting measured data in guides and toxicological databases described in the document entitled “Information sources” (CPA 2016d).

The step 3 consists in collecting information about classification in “selection” lists in the sub-category A or B. The experts used the document entitled “GreenScreen translator” (CPA 2016b) to identify these lists.

The step 4 consists in collecting estimated or modelled data in guides and toxicological databases described in the document entitled “Information sources” (CPA 2016d).

The step 5 consists in collecting information about one or several relevant structural analogs of the substance of interest in order to assign a hazard level to the effect under consideration.

If no information is found at the end of this last step, the experts then undertake a broader literature review in order to identify information on the substance.

If no information is found, the experts then assign “data gap” to the effect under consideration.

Attributing levels of confidence to hazard levels

The experts of ANSES decide to assign:

- a high level of confidence to the hazard level when the data retained to assign a hazard level comes from a source in step 1 or when the data is measured and accessible in a source in step 2;
- a low level of confidence to the hazard level when the data retained to assign a hazard level comes from a source in step 3, 4 or 5.

Special case: The reliability of the data available in registration dossiers on the ECHA website is assessed by the Klimisch score. The scale consists of 4 grades: 1 (reliable without restriction), 2 (reliable with restriction), 3 (not reliable) and 4 (not assignable). Although the measured data available on the ECHA website belong to a source from step 2, the experts of ANSES did not want to systematically assign a high level of confidence to the available data. The experts wanted to take into account the Klimisch score related to the data in order to be able to assign a level of confidence to the hazard levels. Thus, data with a Klimisch score of 1 are linked to a high level of confidence whereas data for which the registrant assigned a Klimisch score of 2, 3 or 4 in the registration dossier are linked to a low level of confidence. Nevertheless, if the experts themselves assess the Klimisch score of a study, the allocation of the low level of confidence linked to a Klimisch score of 2 could be revised to a high level of confidence if deemed relevant.

3.2.3.2 “Exposure conditions” module

The purpose of this module is to determine the exposure conditions to the substitutes.

The aim is to assign one of the following five classes to each alternative.

Table 12: Assigning classes in the “Exposure conditions” module

Class 1	High exposure conditions
Class 2	Moderate exposure conditions
Class 3	Low exposure conditions
Class 4	Exposure conditions considered negligible
Not assigned	Not assigned due to insufficient data

The criteria are detailed in the table below:

Table 13: Assessment criteria for “Exposure conditions”

Criterion				
Vapour pressure	0 – 5 Pa Low volatility	5 – 1000 Pa Moderate volatility	1000 – 5000 Pa Volatile	> 5000 Pa High volatility
Flammability (flash point noted *fp* and boiling temperature noted *bt*)	fp > 60°C Non-flammable liquids and vapours	23°C ≤ fp ≤ 60°C Flammable liquids and vapours	fp < 23°C bt > 35°C Highly flammable liquids and vapours	fp < 23°C bt ≤ 35°C Extremely flammable liquids and vapours
Process	Closed	Closed but regularly opened	Open	Dispersive
Frequency of use	Occasional	Intermittent	Frequent	Constant
Quantity used	Very low	Low	Intermediate	High

The “vapour pressure” and “flammability” criteria reported in the table above are applied to substances and mixtures in liquid form. In the case of substances in other forms (solids, gases or emitted during processes…), these criteria are assessed case-by-case with the possiblity to be filled with the note “non applicable”.

The “process” criterion is applied as a general rule.

The scale of the “frequency of use” and “quantity used” criteria need to be defined case-by-case by sector of activity.

Depending on the data collected, the experts could discuss and rank the criteria, and assign a final class to the alternative further to their evaluation. If data are lacking for certain criteria, the experts can assign the final class “Not assigned” to the alternative.

The results are described and presented in the following table, which continues the example developed in this section:

Table 14: Example of a comparison of “exposure conditions” criteria

Assessment criteria for “exposure conditions”	Hazardous chemical of concern	Alternatives			
		No. 1	No. 2	No. 3	No. 4
Vapour pressure (Pa)	6000	4	No numerical data	No numerical data	1200
Flammability (°C)	fp = 85°C	fp = 120°C	fp = 65°C	fp = 75°C	fp = 85°C
Process used	Closed but regularly opened	Closed	Closed	Dispersive	Open
Frequency of use	Constant	Constant	Constant	Constant	Constant
Quantity used	High	Low	Very low	High	High
Classes for exposure conditions	Class 2	Class 4	Class 4	Class 1	Class 2

3.2.3.3 Estimation of substitution costs' module

This module concerns the financial costs of substitution and assesses the level of economic resources required.

Two types of costs are taken into account:

- Direct costs incurred by purchasing the substitute in the case of substitution by changing a chemical product, or by possibly adjusting or even changing the process when the substitution does not involve replacing one chemical product by another;
- Indirect costs related to peripheral expenses as part of substitution. For example, they may include R&D expenses, licence acquisition, and training of staff concerning changes to their working procedures. They can take into consideration costs related to testing requirements or auxiliary equipment, etc.

The aim is to assign one of the following five classes to each alternative:

Table 15: Assigning classes in the "Estimation of substitution costs" module

Class 1	Highest related costs
Class 2	Moderate related costs
Class 3	Low related costs
Class 4	Lowest related costs
Not assigned	Not assigned due to insufficient data

The alternatives are divided into four classes depending on their quartiles in the breakdown of substitution costs.

The alternatives for which the cost of substitution is between 75% and 100% of the maximum cost observed across all the alternatives are assigned to Class 1.

The alternatives for which the cost of substitution is between 50% and 75% of the maximum cost observed across all the alternatives are assigned to Class 2.

The alternatives for which the cost of substitution is between 25% and 50% of the maximum cost observed across all the alternatives are assigned to Class 3.

The alternatives for which the cost of substitution is between 0% and 25% of the maximum cost observed across all the alternatives are assigned to Class 4.

If data are lacking to generate the economic scenarios, the alternative will be considered "not assigned".

The acceptability of these substitution costs (a factor that can prove to be critical in actual adoption of substitution solutions) is therefore not taken into account in the method because it is not necessary in order to compare the alternatives, and because of absence of the necessary data and the difficulty in gauging the ability of the affected economic players to absorb the costs of substitution.

An acceptability criterion could be taken into account by the decision-makers at the time of selecting and recommending a substitution solution.

The results are described and presented in the following table:

Table 16: Example of assigning classes in the "Estimation of substitution costs" module

	Hazardous chemical of concern	Alternatives			
		No. 1	No. 2	No. 3	No. 4
Class in the "Estimation of substitution costs" module	Class 4	Class 3	Class 3	Class 4	Class 1

3.2.3.4 "Other impacts" module

This module provides additional information to compare the alternatives with each other.

It does not need to be completed systematically but the experts would like to have the option of using it to take into account other types of information that they may have.

Therefore, this module may include aspects related to the availability of alternatives, risk shifting, the life-cycle, organisational constraints, or the societal dimension associated with use of the substitute.

Availability entails examining whether a proposed alternative in a given sector is produced in sufficient quantities on the market to meet the needs in the sector. Market projections can be generated to estimate the time needed to produce estimated sufficient quantities.

Risk shifting: implementing a substitution may for instance remove the carcinogenic risk of the hazardous substance but increase or reveal other risks such as the risk of musculoskeletal disorders (MSDs) or generate new risks in terms of safety.

Analysis of the life-cycle enables evaluation of the overall environmental impact of the substance (consumption of energy, water and other resources), and helps to address the synthesis by-products (both regarding their recovery and their elimination as waste produced), or the processing of toxic waste for example.

The purpose of this module is to identify other impacts regarding substitution and to illustrate them as far as possible through tangible examples in view of professional practices.

3.3 Final presentation of the results

The results are presented in two tables covering all the conclusions of the various modules.

Table 17: Example of final presentation of the results

Conclusion of the modules	Hazardous chemical of concern	Alternatives			
		No. 1	No. 2	No. 3	No. 4
Final class in the "Technical performance" module	Class 3	Class 3	Class 4	Class 3	Class 4
Final class in the "Hazards" module (GreenScreen)	Class 1	Class 2	Class 2	Class 3	Class 4
Final class in the "Exposure conditions" module	Class 2	Class 4	Class 4	Class 1	Class 2
Final class of the module "Estimation of substitution costs"	Class 4	Class 2	Class 2	Class 3	Class 1

Conclusion of the modules	Hazardous chemical of concern	Alternatives			
		No. 1	No. 2	No. 3	No. 4
Identification of “other impacts”	Other impacts identified	Other impacts identified	Other impacts identified	Other impacts identified	Other impacts identified

The results and conclusions are presented in the form of these final tables showing the various alternatives with their advantages and disadvantages to enable the decision-makers to retain the best option, with full knowledge of the facts, in view of the criteria they consider high-priority and acceptable.

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ANNEXES

Annex 1: Request letter

2014 -SA- 0 2 3 6

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RÉPUBLIQUE FRANÇAISE

MINISTERE DU TRAVAIL, DE L'EMPLOI, DE LA FORMATION PROFESSIONNELLE ET DU DIALOGUE SOCIAL

MINISTERE DES AFFAIRES SOCIALES, DE LA SANTE ET DES DROITS DES FEMMES

MINISTERE DE L'ECOLOGIE, DU DEVELOPPEMENT DURABLE ET DE L'ENERGIE

MINISTERE DE L'ECONOMIE, DE L'INDUSTRIE ET DU NUMERIQUE

COURRIER ARRIVE
22 JAN. 2015
DIRECTION GENERALE

Paris le 09 OCT. 2014

Le Directeur général du travail

Le Directeur général de la santé

La Directrice générale de la concurrence de la consommation et de la répression des fraudes

La Directrice générale de la prévention des risques

à

Monsieur le Directeur général
de l'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail
27-31 avenue du Général Leclerc
94701 Maisons-Alfort cedex

Objet : Utilisation de substituts au formaldéhyde dans différents domaines

Contexte de la demande

Le formaldéhyde a été classé en 2004 par le Centre international de recherche sur le cancer (CIRC) dans le groupe 1 des cancérogènes avérés pour l'espèce humaine, sur la base d'études épidémiologiques en milieu de travail portant sur la survenue de cancer du nasopharynx par inhalation. En outre, au niveau européen, une évolution du classement de cancérogène de catégorie 2 à cancérogène de catégorie 1B a été adoptée par le règlement (UE) N° 605/2014 de la Commission du 5 juin 2014 modifiant aux fins de son adaptation au progrès scientifique et technique le règlement CLP.

Les mesures de prévention des risques professionnels liés aux agents chimiques dangereux (ACD) CMR[1] de catégorie 1A ou 1B sont précisées aux articles R. 4412-1 à R. 4412-93 du code du travail qui visent à systématiser - sous la responsabilité de chaque employeur - l'évaluation du risque chimique, en vue de permettre la mise en place de mesures de prévention adaptées à chaque situation de travail et au niveau des risques constatés. Elles prévoient éventuellement une

[1] Cancérogènes Mutagènes, toxiques pour la Reproduction.

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obligation de substitution des ACD par des substances, préparations ou procédés non dangereux ou moins dangereux. Cette obligation est plus affirmée encore pour les agents CMR de catégorie 1A ou 1B pour lesquels la substitution est impérative lorsque cela est techniquement possible.

Lorsque l'application du principe de substitution s'avère impossible, l'employeur doit mettre en œuvre tous les moyens permettant de réduire l'exposition en utilisant des mesures de prévention et de protection adaptées (système clos, ventilation générale, autres moyens de protection collective, puis moyens de protection individuelle, formation et information du personnel, surveillance médicale).

Compte-tenu de ces nouvelles informations sur les propriétés dangereuses du formaldéhyde et de la hiérarchie des mesures de gestion des risques y afférant, il est demandé à l'Anses d'éclairer les pouvoirs publics sur les risques pour les travailleurs et la population générale de l'utilisation du formaldéhyde dans les trois domaines ci-après, où il parait être d'utilité fondamentale.

Activité d'anatomie et cytologie pathologiques

Les médecins spécialisés en anatomie et cytologie pathologiques (ACP) ont alerté nos services sur les difficultés qu'ils rencontrent à appliquer la réglementation française issue du code du travail en matière d'utilisation du formaldéhyde (« formol ») dans les laboratoires d'anatomie et cytologie pathologiques, et notamment l'obligation de substitution.

Le formaldéhyde est le fixateur chimique de référence utilisé en anatomie et cytologie pathologiques notamment à l'étranger. Ces travaux exposant au formaldéhyde étant classés dans la liste des procédés cancérogènes, ils sont soumis à ce titre, aux mesures particulières de prévention des risques cancérogènes, mutagènes ou toxiques pour la reproduction (CMR) de catégorie 1A et 1B.

Les conditions de préservation des tissus constituent une étape critique conditionnant la qualité des résultats des techniques et des diagnostics.

Les publications les plus récentes, qu'elles soient françaises, européennes ou nord-américaines, considèrent en effet le formol comme le fixateur de référence. Le développement des techniques d'immunohistochimie, puis de biologie moléculaire depuis le milieu des années 80, ont conduit à un processus de standardisation des pratiques de fixation en faveur du formaldéhyde, avec l'abandon progressif d'autres fixateurs traditionnels (liquide de Bouin, AFA, etc.) et la mise sur le marché de réactifs de biologie moléculaire adaptés aux tissus fixés au formol.

Le pathologiste français s'estime ainsi soumis à une double obligation contradictoire : assurer une activité d'anatomie et cytologie pathologiques en lien avec les publications scientifiques internationales qui crédibilisent l'utilisation du formol et, en tant qu'employeur, protéger ses collaborateurs des risques liés au formol en le substituant par un autre produit.

Activité de thanatopraxie

La thanatopraxie consiste aux soins de conservation pratiqués sur le corps des personnes défuntes, ayant pour finalité de retarder la thanatomorphose et la dégradation du corps.
Les thanatopracteurs sont amenés à manipuler du formol et il importe ainsi que ces professionnels disposent de l'ensemble des informations nécessaires à l'utilisation de cette substance et qu'il puisse leur être apporté des réponses en termes de solutions alternatives.
L'exposition éventuelle des familles est également à prendre en compte.

Activité de production et d'utilisation de produits alimentaires

En alimentation animale

Le formaldéhyde est à l'heure actuelle utilisé en alimentation animale pour les usages suivants :

1) En tant qu'auxiliaire technologique pour le procédé de « protection contre la dégradation ruminale » (tannage des tourteaux) :

Cet usage est autorisé par le règlement (CE) n°68/2013 de la Commission du 16 janvier 2013 relatif au catalogue des matières premières pour aliments des animaux. Ce règlement fixe une teneur en aldéhydes libres inférieure ou égale à 0,12%
Lors des négociations précédant le vote du règlement (CE) n°68/2013, les professionnels ont indiqué ne pas disposer de produits de substitution au formaldéhyde pour cet usage.

2) En tant qu'additif technologique (ensilage et conservateur) :

Le formaldéhyde est par ailleurs également autorisé comme additif pour l'alimentation animale pour deux usages : en tant qu'agent d'ensilage et comme conservateur pour les porcs de moins de 6 mois et pour le lait écrémé avec une teneur maximale de 600 mg/kg.
Il a fait l'objet d'une demande de réautorisation comme additif conservateur pour toutes les espèces. L'Agence Européenne de la Sécurité Alimentaire (AESA) a émis un avis sur cette demande le 18 février 2014. Dans son avis, l'AESA considère que des mesures devraient être prises pour éviter que le système respiratoire, la peau et les yeux de toute personne manipulant le produit ne soit pas exposé à toute forme de poussière ou vapeur générée par l'utilisation du formaldéhyde (« *Formaldehyde is a strong irritant, a potent skin and respiratory sensitiser. Measures should be taken to ensure that the respiratory tract, skin and eyes of any person handling the product are not exposed to any dust, mist or vapour generated by the use of formaldehyde* ») mais ne s'oppose pas formellement à l'autorisation du formaldehyde en raison d'un risque pour la santé du travailleur.

Enfin, une demande pour un nouvel usage du formaldéhyde en tant qu'additif technologique ayant une fonction de réduction de la charge microbienne des organismes pathogènes ("*feed hygiene*") a par ailleurs été déposée. Elle est en cours d'évaluation auprès de l'AESA. L'utilisation est demandée pour toutes les espèces animales, avec une teneur maximale de 1000 mg/kg pour les aliments composés et 2000 mg/kg pour les matières premières. Cette autorisation nécessiterait au préalable la création d'un nouveau groupe fonctionnel d'additif par règlement, suivant la procédure de règlement avec contrôle (PRAC).

Dans son rapport de mai 2009 sur les risques sanitaires liés à la présence de formaldéhyde, l'Afsset n'a pas relevé de données spécifiques relatives aux possibilités de substitution pour le secteur de l'alimentation animale lors de ses recherches.

En alimentation humaine :

Le formaldéhyde est actuellement autorisé comme auxiliaire technologique pour la fabrication de certains alginates.
Par ailleurs, les professionnels du secteur du sucre ont demandé le maintien de l'utilisation du formaldéhyde (autorisé jusqu'au 31 décembre 2014). Cette requête a reçu un avis favorable de l'Anses le 21 novembre 2013. Le formaldéhyde a été présenté par ces professionnels comme le « bactériostatique universel utilisé en sucrerie ». Néanmoins, l'arrêté du 19 octobre 2006 relatif à l'emploi d'auxiliaires technologiques dans la fabrication de certaines denrées alimentaires autorise également les extraits de houblon comme produit de substitution du formol pour cet usage.

Objet de la demande

Au regard de ces éléments, nous souhaitons donc recueillir votre avis :

1- Sur l'intérêt du formol par rapport aux autres substituts pour le diagnostic en matière d'anatomie et cytologie pathologiques dans les situations de routine et dans des situations particulières pour lesquelles le formol reste indispensable et qu'il conviendra de préciser ;
2- Sur l'intérêt du formol par rapport aux autres substituts pour les actes de thanatopraxie Aussi, nous souhaitons également disposer d'un l'état des lieux sur les travaux en cours au niveau européen dans le cadre du règlement biocides en matière d'évaluation de la substance active formaldéhyde (TP 2, 3, 20 et 22). Par ailleurs, nous souhaiterions disposer, dans le cadre des travaux menés sur les substituts au formol en anatomie et cytologie pathologique, d'une analyse sur les possibilités d'utilisation de ces substituts dans certains types de produits biocides, et notamment en TP22, et sur les conséquences éventuelles en termes de toxicité et d'écotoxicité.
3- Sur l'intérêt du formol par rapport aux autres substituts pour l'utilisation en alimentation animale en tant qu'auxiliaire technologique pour la protection contre la dégradation ruminale, en tant qu'additif conservateur, en tant qu'additif d'ensilage et en tant qu'additif visant à limiter ou à réduire la charge microbienne des organismes pathogènes présents dans les aliments pour animaux.
4- Sur l'intérêt du formol par rapport aux autres substituts pour l'utilisation en alimentation humaine en tant qu'auxiliaire technologique pour d'une part la fabrication de certains alginates et d'autre part l'utilisation comme bactériostatique dans la filière du secteur du sucre.
5- Si des substituts au formol peuvent être utilisés, nous souhaitons que vous étudiiez leur toxicité pour les professionnels et la population générale.

Nos services sont à votre disposition pour tout renseignement complémentaire.

En ce qui concerne l'évaluation de l'intérêt du formol par rapport aux autres substituts pour une utilisation en tant qu'additif pour l'alimentation animale, compte tenu des demandes d'autorisation actuellement en cours, il serait souhaitable que l'Anses puisse se prononcer rapidement (d'ici fin novembre 2014). Pour les autres questions, l'avis est attendu dans un délai de 6 mois.

Le Directeur général de la santé

Benoît VALLET

La Directrice générale de la consommation, de la concurrence et de la répression des fraudes

P.O.

Nathalie HOMOBONO

La Directrice générale de la prévention des risques

Patricia BLANC

Le Directeur général du travail

Yves STRUILLOU

Copie : Direction générale de l'alimentation (DGAL)

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Annex 2: The Toxic Use Reduction Institute (TURI) method

(Eliason and Morose 2011, TURI 2006)

General description

The Toxic Use Reduction Institute of the University of Massachusetts published an article in June 2006 evaluating the substitution of five chemical products.

Objective of the method

The method evaluates the alternative solutions by involving the stakeholders in the sectors of interest to determine priorities and successfully evaluate the alternatives, specifically concerning technical and economic feasibility, environmental impact, and health and safety aspects.
The method also features an economic impact study for the company.

Scope

The method applies to chemical substances. It was tested on the following five products or product groups: lead and lead compounds, formaldehyde, perchloroethylene, chromium (VI), and bis(2-ethylhexyl) phthalate (or DEHP).

Description of the method

This method has three steps.

Step 1: Use and impacts of chemical products.

The first step involves compiling basic information about the substance of interest. Data on health, the environment and safety are compiled and are then compared with the various possible alternatives. The main uses of the substance are identified (main suppliers, consumers), and the question of why the product is used is asked. Lastly, the uses are ranked based on the quantities used or produced, the availability of alternative solutions, and the possible exposures (for the environment, health of workers, health of consumers).

Step 2: Alternative solutions

The second step first consists in identifying the possible alternative solutions: whether this involves substitutions by chemical products, substitutions by materials, or changes in processes. The sources of information include for example industry, research, published literature, or internet searches.
Preliminary screening of these alternatives helps to rule out those that present a risk for health or the environment, i.e. substances fulfilling PBT or CMR criteria are eliminated immediately. This is an environmental and health/safety filter used to reduce the alternatives to study in more depth to a maximum of six substances.
The alternatives are ranked on the basis of various criteria to select.
The alternative solutions are studied by assessing several criteria:

- the performance of the alternative solution
- the availability of the new products: number of manufacturers and quantities produced
- the place of production: giving priority to local production

- environmental aspects, health and safety
- market effects: possible restrictions
- the availability of similar alternative solutions: in this case, only one type is chosen for the remainder of the study
- cost aspects: comparison of the cost of the initial solution with the possibilities of reducing costs by including the cost of raw materials, storage, production, and auxiliary costs.
- priority is given to solutions that integrate development of local activity

Step 3: Assessment

Technical, environmental, health/safety, and economic data are collected for each alternative. Each parameter is assessed as better (+), equivalent (=), or worse (-). If no data are available, a "?" is indicated. These assessments are based on personal or institutional values, on priorities, or on acceptability levels.

Technical feasibility is first studied among industrial stakeholders, those that have experience with chemical products and their substitutes.

Economic feasibility is studied for all the alternatives. Attention is given to the fact that costs today can change tomorrow: economies of scale that reduce costs. The method emphasises the importance of taking into account: investments, the costs of waste, energy, labour, and all peripheral costs related to the life of the product. This assessment is simple for substitutions by products, but it is more complex for changes in processes.

Health and environmental aspects must be based on recent data, taking into account several available sources (official and bibliographic).

Advantages and disadvantages of the method

Advantages

The main advantage of this method is that it performs a pre-selection from a list of potential substitutes, providing six substances that are then studied in a more in-depth manner.
The method gives the user, in particular, the option of selecting the criteria related to technical feasibility depending on the usage of the substance.
This is a complete method assessing many criteria and guides the user through the various steps.

Disadvantages

The main disadvantage is the very large quantity of data to collect, and much of this data is not accessible, making application of the method less relevant.

Annex 3: The method of the Royal Society of Chemistry (RSC)

(RCS 2007)

General description

This method was developed in 2007 by a working group of the Environment, Health and Safety Committee of the Royal Society of Chemistry (RSC). The RSC is a learned society in the United Kingdom that aims to promote, support and encourage the growth and application of chemistry.

Objective of the method

Substitution is defined here as a complex process that should aim to reduce the risk. This method establishes the principles of a comparative assessment of risks in order to provide objective data that can be used for decision-making to implement substitution.

The main objectives of comparative risk assessment are to optimise the choice of substances for a specific use, taking into account the potential risks for health, fauna and the environment, and the advantages for society as a whole, and to facilitate the development of rankings that place "risk profiles" of chemical substances on a structured scale to reduce the overall risk based on their intended use.

For each chemical of concern, the method aims to establish:

- its usefulness;
- the availability of substitution substances;
- the risks for humans and the environment of chemical substances;
- the effectiveness (advantages) of the alternatives;
- the socio-economic impact of the proposed substitutions.

The method emphasises that the stakeholders must be consulted during the design of the substitution criteria.

Scope

This method can be applied to all chemical products of any kind, but also to industrial processes and materials.

Description of the method

This method consists of four main steps.

Step 1: Identification

As a first step, it is necessary to identify the substances to compare, their properties (intended effects), and their intrinsic hazards. After this identification process, the assessor evaluates exposure to these substances and determines the extent of the adverse effects. This step must conclude on whether or not there are harmful effects on health or on the environment.

Step 2: Definition of the key impacts to take into consideration

Once the list of chemical substances to replace has been drawn up, the next phase of the process aims to specify and quantify the "risk profiles" of the substitution substances. These profiles are generated by determining the expected impact caused by a probable range of

exposures. The process adopted is essentially that described in the document of the International Programme on Chemical Safety (Environmental Health Criteria 170 / 210 WHO). Initially, a limited range of effects is addressed: PBT, vPvB and endocrine disruptor.

Step 3: Description of impacts

Each “risk profile” is examined by a group of experts and stakeholders.
Ideally, the conclusion of this step should be a table presenting each substitution substance and its characteristics for each criterion. This would facilitate comparison of the alternatives.
In addition to the hazard and exposure aspects, the impacts must also take into account socio-economic factors such as the availability of effective national and global alternatives, the impact of the loss of goods and services if the substances is withdrawn, the effectiveness of the reformulated products, and the costs of reformulating products that contain the withdrawn active substances.

Step 4: Ranking the alternatives

The experts note and rank individually the impacts of each effect for each chemical substance according to: the severity of the effects (irreversibility); the probability of an effect (use/exposure); the groups of concern (vulnerable groups, young and elderly people); the affected environment (aquatic, terrestrial or atmospheric); the longevity (and thus an analysis of the life-cycle), and the societal attitudes toward the various risk classes (“intentional”/”non-intentional”, “feared”, etc.). A consensus should be sought among the experts and stakeholders for one or more substances.

Advantages and disadvantages of the method

Advantages

The method is very general and is therefore suitable for many situations. It can be used to define an overall strategy and can cover a wide range of parameters.

Disadvantages

The method is not particularly substantive and can become rather complex to implement depending on the criteria defined initially. It can require significant expertise to collect and summarise all the parameters.

Annex 4: Method developed for the "Technical Rules for Hazardous Substances" – substitution (TRGS 600)

(BAuA 2008)

General description

This substitution method was developed by the German Committee on Hazardous Substances (*Ausschuss für Gefahrstoffe*, AGS) at the Federal Institute for Occupational Safety and Health (BAuA) in August 2008.
It was designed to guide employers in complying with their substitution obligations within the framework of the occupational health and safety regulations.
In accordance with the German Hazardous Substances Ordinance (GefStoffV), employers are required to search for and examine substitution possibilities, decide on their implementation, and document their findings and/or decisions.

Objective of the method

TRGS 600 provides an up-to-date overview of requirements concerning substitution. This overview includes examples of criteria to take into account to make decisions on aspects such as technical feasibility, protection of health, and the physico-chemical risks of the substitution solutions.

Scope

The method applies to substances and mixtures.

Description of the method

General recommendations

To begin, the TRGS establishes general principles to help compare the risks of a substance in use with those of a substitution substance. The risks associated with a substance can be assessed in consideration of criteria for hazards to health, physico-chemical hazards, and hazardous emissions.
In the case of activities involving hazardous substances that are toxic, highly toxic, carcinogenic, mutagenic, or toxic to fertility (classified in categories 1 and 2 in accordance with Council Directive 67/548/EEC), substitution is required if alternatives are technically possible and lead to a lower risk. In the other cases, the employer must include economic aspects in the decision.
If it is not possible to decide on the relevance of a substitution solution using the general recommendations or if the risk assessment is not particularly simple to perform, it is recommended that estimation methods be used: the column model and the effect factor model. Both models are based on use of the risk phrases indicated on the safety data sheets.

Column model

Using the column model, a rapid comparison of the substances and preparations can be performed.
A comparative assessment of a product and its potential substitute is carried out in five columns, separately for the two solutions:

- Acute and chronic health risks (columns for “acute health hazards” and “chronic health hazards” as a single column),
- Environmental risks,
- Fire and explosion risks,
- Potential emission risks,
- Process-related risks.

The information sources used to fill in the column model are essentially based on the safety data sheets (SDSs).

Effect factor model

The effect factor model enables the assessor to apply a proportionate approach using the risk phrases in order to compare different substances, including when few data are available.

The effect factor model concerns the toxic properties. When decisions are required on the implementation of substitution substances, the physico-chemical properties, environmental risks, and conditions of exposure and application must be assessed separately.

In the case of mixtures, the various weights of the constituents are added depending on the proportion of the preparation they represent.

Advantages and disadvantages of the method

Advantages

In addition to risk assessment and the performance of the substitution solution, the impact related to the social and economic environment on the full life-cycle of the product is important. This method, intended for companies (SMEs, SMIs) appears to be simple and rapid to implement. It requires little specialised knowledge because it is based on easily accessible risk phrases and does not require specific training. However, the reliability and exhaustivity of SDSs are broadly called into question.

Disadvantages

Implementation is limited to comparison of one product with another, in isolated cases of substitution. It is not possible to compare products with substitution procedures or technologies.

The method should be updated to take into account the CLP Regulation.

Annex 5: Significant New Alternatives Policy (SNAP) programme

(US EPA 2016)

General description

The method is available on the website of the United States Environmental Protection Agency (US EPA). It was last updated in 2016.

Historically, the aim of the programme was to identify and assess substitutes to chemical substances damaging the ozone layer.

The current programme analyses the risks to human health and the environment of older and newer substitutes and publishes a list of substitutes considered “acceptable” or “unacceptable”, thus providing the public with information on the potential impacts of the substitutes examined by the US agency.

Objective of the method

The programme classifies the substitutes into four groups: "acceptable"; "acceptable subject to use conditions"; "acceptable subject to narrowed use limits" and "unacceptable alternatives".

The programme generates a public list of acceptable or unacceptable substitutes for the largest industrial sectors.

Scope

This method applies to chemical substances.

Description of the method

The method generates a list of substitutes by assessing several parameters:

- Ozone depletion potential (ODP);
- Global warming potential (GWP);
- Toxicity;
- Flammability;
- Occupational and consumer health/safety;
- Local air quality;
- Ecosystem effects.

Advantages and disadvantages of the method

Advantages

A public list of “acceptable” substitutes according to the criteria of the US EPA is given by sector of activity.

Disadvantages

The parameters are clearly compared but there is no information on the details of this comparison. The method is more geared towards environmental protection than protection of occupational health.

Annex 6: National Research Council (NRC) method

(NRC 2014)

General description

The method was developed in August 2014 by the US National Research Council (NRC), a body of the American Academy of Sciences.

The method describes itself as a literature review of existing resources for the analysis of alternatives to a chemical substance.

Objective of the method

The report provides a description of an assessment method in 13 steps to help in selecting an alternative to a chemical substance.

Each of the steps described refers to existing tools or methods that can be used to meet the objective of each step.

Scope

The method applies to chemical substances.

Description of the method

The method follows 13 steps.

Step 1: Identify chemical of concern

Step 2: Scoping and problem formulation (principles, aims, etc.)

Step 3: Identify potential alternatives

Step 4: Determine if alternatives are available

Step 5: Assess physico-chemical properties

Step 6: Assess human health, ecotoxicity, and comparative exposure

Step 7: Integration of information to identify safer alternatives

Step 8: Life-cycle thinking

Step 9: Optional assessments: Assessment of technical and economic performances

Step 10: Identify acceptable alternatives and refer cases with no alternatives to research and development

Step 11: Compare or rank alternatives

Step 12: Implement alternatives

Step 13: Research, if necessary

Advantages and disadvantages of the method

Advantages

The method is multi-step and comprehensive. It takes into account the essential modules required to implement substitution.

Disadvantages

The document proposes a very general method in 13 steps but does not indicate how to address each step. The document simply highlights several existing methods that can address the questions raised in each step. As such, for each step, the method refers systematically to methods of the following types: Design for the Environment (DfE), Interstate Chemicals Clearinghouse (IC2), BizNGO, Registration, evaluation, authorisation and restriction of chemicals (REACh), University of California Los Angeles (UCLA), Toxic Use Reduction Institute (TURI), etc. which are already all described in this report. The document cites these methods without necessarily indicating one as a preferred method over the others for a specific step.

The study of performance takes place late in the method (Step 9). The method requires a very in-depth assessment of the hazards associated with the substances even though they may not be technically appropriate for the given case.

The GreenScreen method is cited several times to compare al the hazards (health, environment, etc.).

Annex 7: Cleaner Technologies Substitutes Assessment method

(US EPA 1996)

General description

The method known as the "Cleaner Technologies Substitutes Assessment" (CTSA) is a method to assess risks, performances, costs, and protection of resources for alternatives identified compared with those of the chemical products currently in use by specific industrial sectors.

This method was developed in 1996 by the United States Environmental Protection Agency (US EPA), the Design for the Environment (DfE) programme, the Center for Clean Products and Clean Technologies at the University of Tennessee, and other partners, public interest groups, professional federations, and various industries, including SMEs.

The method is intended for professional federations, industries, government agencies, or any other interested parties wishing to initiate or take part in a CTSA.

In 1991, the Office of Pollution Prevention and Toxics (OPPT) of the US EPA created the DfE programme in order to help industry integrate environmental considerations into their product design, processes and techniques, as well as in their management systems. The CTSA method thus originates from the DfE programmes that brought together companies, professional federations, and institutions to help companies in certain sectors to select the most ecological products, processes and technologies.

Objective of the method

A CTSA aims to promote informed decision-making among companies that are taking into account the various concerns (risks, performance, cost) by providing them with easily accessible information.

The document entitled: "Cleaner Technologies Substitutes Assessment – a Methodology & Resource Guide" presents the method to draft a CTSA report. This report is a reference document summarising technical information (products, manufacturing methods and technologies), economic data, and information on the hazards and environmental performances of the chemical products in use and the identified alternatives, for a specific use or sector of activity. A CTSA is not aimed at recommending alternatives or reaching conclusions about a substitute. The data in the CTSA are used to draft summary information sheets or reports intended for suppliers or users who do not have sufficient resources to find this information themselves. The information is then used by the companies or professional federations to carry out their comparative assessment: products currently in use versus substitutes.

Scope

The method applies both to products (substance/mixture) and processes.

Description of the method

The method defines a "**use cluster**" as a product- or process-specific use or application in which a set of chemical products, technologies, or processes can substitute for one another to perform a particular function.

The method follows a module approach in order to collect a set of data and thus provide a "standard" information basis for alternatives assessment.

The method follows ten steps.

Step 1: Set up a multidisciplinary working group

Step 2: Prepare scoping documents

Step 3: Select a use or specific application for a product or process in which a group of chemical products, technologies, or processes can substitute for one another to perform a particular function (use cluster)

Step 4: Identify potential substitutes

Step 5: Select a subset of substitutes for assessment

Step 6: Establish the project baseline

Step 7: Set the boundaries of the evaluation

Step 8: Perform CTSA

Step 9: Develop information products

Step 10: Disseminate results

Advantages and disadvantages of the method

Advantages

The method is very detailed and comprehensive, and deals with many parameters. For each module, the objective, the competence needed for implementation, the definitions of the characteristics or information to collect, the method, and the sources of information are cited.
Implementing the method calls on a multidisciplinary working group (multiple stakeholders: companies, public interest groups, institutions, professional federations) open to interested parties other than industry.

The method provides tools, questionnaires to collect information, and examples for certain sectors of activity (lithography, screen printing).

Disadvantages

The method is not current and dates from 1996; it does not cite recent references or sources of information (such as databases).

Annex 8: Pollution Prevention–Occupational Safety and Health (P2OSH) Assessment method

(Quinn *et al*. 2006)

General description

The Pollution Prevention–Occupational Safety and Health (P2OSH) Assessment method aims to develop an integrated strategy for the assessment of alternatives or substitutes in terms of occupational health and safety, and pollution prevention in hospitals. This method was developed in 2006 by a team from the University of Massachusetts Lowell (Department of Work Environment and the Lowell Center for Sustainable Production) and the Boston Medical Center (Massachusetts).

In the United States, the activities of hospitals have a significant impact on the environment (waste produced, emission into the air and water, consumption of raw materials and energy). In this context, the government and safety agencies have encouraged hospitals and healthcare establishments to implement measures for pollution prevention. Since the sources of hazards for the environment also affect occupational health, a substitution method incorporating both these issues was developed.

Objective of the method

This method aims to develop an integrated assessment strategy for alternatives or substitutes in terms of occupational health and safety, and pollution prevention in hospitals.

The purpose of this method is to:

- Develop a participatory method that integrates the working practices and materials that are specific to the procedures of the hospital sector;
- Develop P2OSH assessment tools to evaluate the impacts of substitutes on the environment and on the health of workers;
- Implement and assess substitutes on site, using integrated assessment methods.

Scope

This method applies to substances, mixtures, or processes **implemented in hospitals**.

Description of the method

The method follows eight steps.

Step 1: Set up the P2OSH team within the hospital to determine alternatives.

The first step is to set up a multidisciplinary team (P2OSH team) within each hospital taking part in the study. This team includes administrators, managers and personnel implementing the potential substitutes. Different departments are represented in the team (upstream of implementation: purchasing, logistics; downstream: cleaning, waste management). The P2OSH team generally has five or six members.

Step 2: Identify processes, materials or products to be substituted;

In order to characterise the existing process, a large amount of information is collected via a questionnaire. This information concerns specifically: the process, the working environment,

the tasks performed, the frequency and duration of exposure, and the hazards the personnel may be exposed to: chemical, biological, physical, and ergonomic.

Step 3: Assess the work site concerned before implementation of the potential substitute.

Step 4: Identify and select potential substitutes;

The hazards associated with the potential substitutes are examined at this stage.

The hazards related to the physico-chemical properties are also examined: vapour pressure, flammability, odour, as well as other physical properties linked to safety, storage, handling, and disposal requirements.

The data identified on health hazards concern toxicity, sensitising and irritant properties, skin absorption, headache, postural constraints (repetitive movements, musculo-skeletal constraints), screen work, and infectious potential.

The environmental hazards examined include biopersistence, air and water pollution, production of chemical waste, plastics, and water consumption.

The technical feasibility is examined firstly during the search for potential substitutes, then during implementation of the substitute. However, the publication provides little information on the criteria retained to assess technical feasibility.

The direct and indirect costs of implementing the substitute are assessed:

- direct costs: for example the cost of acquiring materials and equipment;
- indirect costs: worker training, communication on hazards, protection equipment, installation, maintenance and verification of equipment, measurement of air and water emissions, incidents, management of hazardous materials and storage, handling and disposal of waste, medical follow-up, preparation of emergency interventions, and penalties for non-compliance with regulations.

Step 5: Implement potential substitutes – test phases;

Step 6: Assess the work site concerned after implementation of the potential substitute;

Step 7: Assess the potential substitute;

Step 8: Implement the retained substitution.

Advantages and disadvantages of the method

Advantages

The method applies to a specific sector of activity: healthcare facilities.
This approach is participatory, directly involving hospital activities (in particular, this promotes acceptance of the substitution solution by the personnel).

Disadvantages

The study targets a specific sector and is not, in principle, transposable as-is to the sectors of interest in this appraisal.

The study provides few details on the various steps and the different parameters observed (for example: criteria for technical feasibility) through the method.

Annex 9: Method developed by BizNGO

(Rossi, Peele, and Thorpe 2012)

General description

BizNGO is a collaborative network of company directors, representatives of organisations for environmental protection, government agencies, and universities, established in 2006.

The method developed by this network of international experts was published in April 2012. The network's aim is to promote research and development for the least hazardous, environment-friendly chemical products/materials/processes, with a focus on sustainable development.

The objective is to support a transition programme towards "clean" production for economic health that integrates environmental protection and the health of the population. It is intended for company and government decision-makers, and for environmental protection associations or consumers.

Objective of the method

The method was developed as an aid to decision-making. It describes a chemical risk assessment method that aims to reduce the inherent risk related to the use of chemical products by drawing on the principles of innovation and "clean" production. Reducing the dependence of industry on hazardous products/materials/processes is a public health challenge, along with reducing the environmental impact, which must be integrated into the strategic choices of industrial manufacturers and users of these types of products, materials and processes.

This approach first involves a risk assessment for human health and the environment, without neglecting a subsequent assessment of the technical feasibility and economic performance of the proposed alternatives.

Scope

This method applies to products, materials and processes.

Description of the method

The method follows seven steps:

Step 1: Identify the hazardous chemical of concern

Chemical products of concern are the starting point of the assessment protocol for identifying alternatives. Government legislation, market requirements, user/client requirements, and the analysis of internal practices in the area of the search for alternatives to reduce the chemical risk are the triggers initiating the assessment protocol.

Step 2: Characterise the final uses of the products and their functions

Companies need to characterise the uses and functions of chemical products found in a material or a manufacturing process.

Step 3: Identify alternatives

The search for alternatives complies with the principles of green chemistry.

The method supports the implementation of practices that favour a reduction in exposure of workers and of the general population.

Step 4: Assess the hazards of the substitutes

The chemical hazards of the substitutes for human health and the environment are described.

The method cites the example of the GreenScreen method to compare the hazards of the substitutes.

The most hazardous potential substitutes are eliminated from the method.

The potential exposures (workers, general population) and the environmental impacts are described. The most hazardous potential substitutes with the highest exposure are eliminated from the method.

Step 5: Assess the technical feasibility and economic performance of the retained option.

Step 6: Examine the life-cycle

The remaining alternatives are examined in view of the hazards for human health and the environment at each step of the life-cycle of the chemical product, material, or process of interest.

The aim is to identify any significant repercussions that could result from opting to use the alternative to ultimately avoid an unfavourable solution in terms of chemical risk assessment or risk shifting.

Step 7: Select the alternative

The most favourable alternative in view of the criteria for the protection of human health and the environment, and economic efficiency is selected and implemented.

Advantages and disadvantages of the method

Advantages

The method is simple and accessible in terms of the substitution strategy. The target audience could be either companies, government agencies, or consumer associations.

The method is based on the main principles of clean, environment-friendly chemistry which aim to reduce the impacts on human health and the environment.

On the basis of a multi-criteria analysis upstream of any new industrial choice, BizNGO defines a comprehensive substitution strategy from identification of the substance/material/process to be substituted through to the final decision, while addressing issues around technical feasibility and economic performance.

Disadvantages

The method requires some expertise to collect the data, particularly concerning the step in which hazards for human health and the environment are identified.

The criteria to assess technical feasibility and performance are not stipulated or are left to the discretion of the companies.

Although reference is made to lists of hazardous substances (the Restriction of Hazardous Substances (RoHS) list for electric and electronic equipment, the list of candidate substances for assessment under the REACh Regulation, etc.), and to validated assessment methods (Design for the Environment (DfE)), the lack of criteria to rank the alternatives in a clear and

precise way makes the assessment results for a single product/material/process of interest less reliable and not comparable.

Annex 10: Method of the Ministry of the Environment, Government of Ontario (Canada)

(Ontario Toxics Reduction Program 2012)

General description

The Ministry of the Environment, Government of Ontario (Canada), public information centre, promotes an overall and very detailed decision-support method for the use of substitutes for hazardous chemical substances on the basis of the principles of green chemistry and corporate social responsibility (CSR).

Published in 2012, the method is intended for decision-makers in companies and government, but also for consumer associations and unions.

Objective of the method

The method proposes a chemical risk assessment upstream of any industry choice to use chemical products to reduce the inherent risk of a product/material/process.

The search for a safer alternative is one of the main prevention principles developed in the method.

Scope

This method applies to products, materials and processes.

Description of the method

The method follows five steps:

Step 1: Survey current conditions

The method invites the user to define:

- the process flow-chart and the mass balance (input/output) of the products/materials/processes
- the problem and identify the target
- the functional requirements of the manufacturing process

Step 2: Identify the possible alternatives

Step 3: Carry out a preliminary assessment of the alternatives

- concerning technical feasibility
- concerning economic performance
- check the presence/absence of the substitution product/material/process on regulatory and non-regulatory lists

Step 4: Perform a detailed evaluation of the remaining alternatives

- identify the hazards (impact on the environment, human health, and occupational health and safety)
- evaluate the technical feasibility: optimisation of the planned manufacturing process, evaluation of the risks for occupational health and safety

- evaluate the economic feasibility: detailed mass balance (input of raw materials/waste generated, etc.), costs (research and development, production chain, raw materials, etc.), and analysis of the financial benefit/technological risk ratio
- evaluate the social impact: analysis of supply and demand, loss or creation of employment, effects on the local economy, etc.
- evaluate the life-cycle of the product/material/process of interest

Step 5: Select and implement the chosen alternative.

Advantages and disadvantages of the method

Advantages

The method is based on the main principles of clean and environment-friendly chemistry which aim to reduce the impacts on human health and the environment.

The method proposes a multi-criteria analysis upstream of any new industrial choice, defines a substitution strategy that addresses technical feasibility, economic performance, and the socio-economic impacts of the planned alternatives after ruling out the most hazardous industrial processes.

The method facilitates an understanding of the principles behind the search for alternatives from identification of the hazards of the substance/material/process to be substituted through to the final decision on and implementation of the substitution.

The method enables regulation of supply and demand on the market by integrating the principle of safety in industrial choices and prevention policies to protect the population and the environment.

The method offers two types of assessment: a preliminary assessment to rule out non-relevant substitution candidates and a detailed one to compare the remaining alternatives in order to ultimately select a single solution.

Disadvantages

The method requires some expertise to collect the data, particularly concerning the step in which hazards for human health and the environment are identified.

Annex 11: The ECHA guidance on the preparation of an application for authorisation

(ECHA 2011)

General description

The guidance was drafted by the European Chemicals Agency (ECHA) in 2011 and is intended for companies preparing an authorisation application in order to continue using substances included in Annex XIV of the REACh Regulation (SVHC – Substances of very high concern). The purpose of the REACh authorisation procedure is the substitution of these substances of very high concern. As a result, in addition to the presentation of the way in which the company uses this substance and the way the risks inherent to its use are controlled, an authorisation application under REACh must necessarily include a robust analysis of the alternatives to this substance: chemical and/or technical alternatives (process, equipment, etc.). The guidance therefore indicates what this type of analysis should contain, including:

- identification of the alternatives
- characterisation of their hazards and risks for human health and/or the environment
- analysis of their technical feasibility
- analysis of their economic feasibility
- analysis of their availability

If an alternative meets all these criteria, it is considered feasible (suitable) for the applicant. Importantly, however, it may not be suitable for the applicant's clients/users downstream.

The guidance describes the steps that the company must follow on the basis of certain criteria defined below.

Objective of the method

The objective of this method is for the company to be able to identify and characterise the possible and feasible alternatives in the dossier on the basis of risk and feasibility criteria so as to rule out certain alternatives if they prove not to meet the required criteria, and to compare the others that are potentially eligible for substitution. The approach is considered to be mixed because it contains a simultaneous part and a sequential one. An approach is "sequential" when it follows a series of steps and is considered "simultaneous" when several steps are to be performed in parallel to have a full overview of all the alternatives identified, even those that do not seem to meet the criteria in the first steps of the method.

In the case of an alternative meeting all the criteria but not immediately applicable, the company must present a substitution plan aimed at adopting it, including the R&D efforts to achieve this and the intended time scale (Chapter 4 of the guidance).

If no alternative seems feasible, the company must indicate the R&D efforts planned to further investigate the issue of substitution.

Scope

This method applies to all authorisation applications under REACh, i.e. to all the substances within the scope of the REACh Regulation and included in Annex XIV – Authorisation.

Description of the method

The method follows three steps.

Step 1: Identify alternatives

The identification of alternatives is based on the fact that the (chemical) alternative must perform the same function as that for which the substance in the application is used. A combination of alternatives may be needed to reach this equivalent function.

The criteria to define the function are as follows:

- the exact usage of the substance in the process and the specific physico-chemical properties that ensure the intended function
- the conditions of use of the substance: physical, chemical and temporal
- the impact on the quality of the final product (durability, resistance, ability to be recycled, etc.).

Step 2: Assess alternatives

Assessment of alternatives begins with the collection of data on the hazards, exposure levels, and if possible characterisation of the risks on the basis of use of the alternative. These criteria are to be compared for the substance concerned and the alternative in order to determine the health and/or environmental impacts.

An analysis of the technical feasibility can be used to gauge the relative performance of the alternative compared to the substance of concern. The functional and performance criteria are not defined exhaustively in the guidance because they are use-specific. Nonetheless, certain criteria and indicators to evaluate them are provided for information:

- **Ability of the alternative to reach the same level of functionality** (speed, cleaning, required degree of purity, yield, etc.)
- **Ease of use** (specific constraints: frequency of refilling, quantities to use, etc.)
- **Adjustment of the process** (higher energy requirement, adjusted design of certain parts, reformulation of certain mixtures, etc.)
- **Additional equipment** (capital, training, specific maintenance)
- **Other requirements** (product safety, consumer demands, certification, tests, and R&D)

An analysis of economic feasibility is used to gauge the economic viability of use of the alternative compared to the substance of concern. This analysis focuses on changes in costs and revenues for the applicant, including the possibility the applicant has to pass on all or part of the potential additional costs to the supply chain up to the consumer. The assessment of economic feasibility in this case also focuses on the applicant and does not take into account the overall impact on society or the economy as a whole.

The assessment criteria and measurement indicators for these criteria are as follows:

- **Investment costs** and **ongoing operating costs** (and associated revenues): measurement of the cost differential between the substance of concern and its substitute, as well as the expected variation over time (direct costs: capital, production costs, maintenance, waste management; indirect costs: costs related to the specific use of a substance)

- **Other substitution costs**: costs of additional equipment, training, energy requirements, regulatory costs, machine standing time, etc.
- **R&D costs** including tests
- **Time** and **cost** impact for users downstream to adjust to the substitute
- **Possible market distortions** (redistribution of market share, for example in the case of a monopoly or oligopoly)

Lastly, the availability of the alternative is also taken into account. The availability or non-availability of an alternative will depend on the various players involved in the authorisation procedure.

Step 3: Compare the alternatives

Advantages and disadvantages of the method

Advantages

This method is comprehensive because it includes both identification criteria and assessment criteria. These assessment criteria include hazard criteria, exposure criteria, risks, technical feasibility, economic feasibility, and the availability of substitutes.

Disadvantages

Although the proposed indicators to measure each criteria are listed and explained in detail, the final comparison of the substitutes remains partly qualitative (especially when access to the data is partial) and involves a degree of uncertainty and subjectivity regarding ranking of substitutes.

Annex 12: European Commission method

(European Commission 2012)

General description

The Directorate General for Employment, Social Affairs and Inclusion at the European Commission published a method in 2012 to analyse and assess the practical implementation of the substitution principle for hazardous chemical substances that workers are exposed to.

Objective of the method

The purpose is to further increase worker protection (health and safety) by putting forward a common EU approach to substitution, on the one hand, and guiding companies in their substitution activities, while facilitating the decision-making process, on the other.

Substitution in this context is considered a risk management measure.

The report contains two parts:

1. practical guidance: the target for this guidance is companies that have limited knowledge of substitution, such as SMEs. The purpose is to make scientific knowledge on the hazards and risks accessible and understandable to these companies.
2. a study report on identifying a viable risk management measure with a focus on substitution. This study report shows that the main drivers of substitution are legislation and pressure within the supply chain or within a single company. It focuses on the practical implementation of chemical substance substitution in companies across Europe via a four-step process: plan - do - check - act. It provides a decision-making framework for substitution based on a rather general multidisciplinary approach. It also examines the players and institutions involved in implementation or promotion of substitution at the national and European levels. The guidance documents produced in certain EU countries are examined in view of their way of addressing risk assessment or technical or economic considerations.

Scope

The approach developed aims to be systematic but flexible to identify chemical substances that should be substituted and to assess the possible alternatives in view of their own risks.

The method applies to any type of process and any type of chemical substance/mixture.

Description of the method in the guidance part

The guidance part proposes a sequential approach first to determine whether the target companies (SMEs) are concerned by a need for substitution, and if they are, provides information on how they should carry out the process.

The method follows seven steps.

Step 1: Assess the current level of risk

Step 2: Decide on risk reduction needs

Step 3: Assess margins for change

Step 4: Look for alternatives

The requirement to substitute becomes effective once the need to reduce the risks of a substance in use is identified. The alternatives that meet the specific requirements of the use in question may be chemical, non-chemical or technical.

Once a risk related to a substance and a need to substitute are identified, this step involves:

- **Making a list of potential alternatives**: identifying alternatives includes discussions with the supply chain to collect information on the needs and practices of each party and should also be based on publicly available data and an exchange with the competent authorities.
- **Checking that the identified alternatives meet requirements** for the use of interest: legal obligations, technical, quality and standard requirements. No criteria are specified to assist in this selection.
- **Finding the alternatives that best meet the requirements.** No criteria are specified to assist in this selection.
- **Performing testing and piloting to measure the performances of the alternatives in the existing process**
- **Choosing the most satisfactory alternative.** If none are satisfactory, considering the possibility of accepting certain technical compromises.

Step 5: Check the consequences of a change

After having identified and selected alternatives, this step involves:

- **Calculating the impacts (costs and benefits)** of adopting each alternative: the impacts to take into account include the cost differential regarding use (tasks), the purchase of the alternative or any required control measures regarding this alternative (management of associated waste, emissions, etc.), the cost of personnel training, and also the possible savings made in terms of personal protection equipment (PPE) or any type of investment.
- **Assessing and comparing the risks** (to workers and others) for each alternative given their hazards. The guidance part indicates that both acute and chronic adverse effects for human health, safety, and environmental hazards must be considered. Risks related to technical performance, risks regarding the supply chain, indirect, cumulative and long-term effects on the entire life-cycle of the substances are also to be taken into account. To characterise the hazards, the guidance part recommends first focusing on the reference data in the safety data sheets (SDSs) and the CLP classification. It also proposes a multiple-dimension risk comparison matrix with colour codes. If the risks prove to be too high, the guidance recommends returning to Step 4 and, if possible, looking for other alternatives; if this is not possible, other ways of increasing safety and reducing the risks of the substance in use should be examined, for example through alternative processes or technologies (automation, etc.).
- **Assessing other potential relevant benefits** such as waste reduction, recycling, emissions, improved company image, technological modernisation, environmental footprints, potential market benefits, etc.
- **Carrying out an overall comparison** of all the alternatives assessed with each other and with the substance currently in use in view of the evaluated impacts. The guidance proposes an overall comparison matrix with colour codes modelled on the risk matrix and the qualitative annotations.

Step 6: Decide on change

In view of all the impacts assessed above, the guidance part then recommends:

- **Ranking the alternatives** on the basis of criteria specific to company policy in order to opt for or against substitution
- **Conducting a field testing programme** once the ranking is complete
- Deciding

Step 7: Implement, monitor and evaluate

Advantages and disadvantages of the method

Advantages

This report has the advantage of proposing guidance for assessment and for decision-making concerning the substitution.

Disadvantages

The approach presented in the guidance part and in the study report remains rather general and lacks precise criteria to enable application. Moreover, the methodological aspects and diagrams are spread between the guidance (first part of the document) and the study report (second part), making understanding of the general approach difficult.

Annex 13: Method developed by Goldschmidt

(Goldschmid 1993)

General description

The method was developed by Goldschmidt at the Technical University of Denmark using data regarding substitution of chemical agents. The purpose of this method is to facilitate the substitution process recommended by the Danish authorities in a regulatory text on the workplace.

Objective of the method

The aim of the method is to reduce the risks for the health of workers.

Scope

The method applies to any chemical agent (compound, product) and to processes.
Three examples illustrate this approach:

- Replacement of a lacquer containing a chromate pigment by a lacquer containing an organic pigment without a change to the process;
- Replacement of paints containing organic solvents by water-based paints in the building sector. This substitution involved a change in the application tools (paintbrushes, etc.);
- Process change for the watertighting of electrical wiring connections: substitution of an acrylic monomer by a mechanical process.

Description of the method

An iterative method including seven steps.

Step 1: Characterise the problem
This step involves a functional analysis and aims to indicate the reasons for use of the product in as comprehensive a way as possible, along with the conditions of implementation and the requirements of the “finished product”. Ideally, this step should include the product users. In addition to this approach, the author proposes a substitution assistance tool for solvents with a view to qualifying the solubility parameters of the substance or the product (HSPs).

Step 2: Identify a range of alternative solutions
The approach implemented is identical to that in the first step.

Step 3: Characterise the consequences related to each alternative solution
At this stage, the intrinsic hazards of the product, the economic aspects, technical considerations, and the effect on occupational exposure must be addressed. The other risks associated with the workplace must also be assessed: physical and postural issues, etc.

Step 4: Compare the retained solutions
The various solutions are then compared in order to select the most suitable one, taking into account the different impacts on the risks and the technical and economic consequences. At

this stage, calculation tools can be used to assess the health risks considering the volatility and the OELs.

Step 5: Decide on implementation of the chosen solution

Step 6: Implementation

Step 7: Assessment of the substitution solution
Assessment of the various effects on: health risks, economic and technical aspects.

Advantages and disadvantages of the method

Advantages

The method describes the decision-making process while insisting on the need to include all the parties concerned by the substitution. The most important steps are defining the context (purpose and conditions of use of the product) and identifying alternative solutions. These steps are carried out as brain-storming exercises and should in principle rule out none of the ideas expressed by the players. Tools can assist in the decision-making process when comparing alternative solutions.

Disadvantages

The method does not fix precise limits in terms of functional analysis but implementation probably takes a long time: identification of the players involved, organisation of meetings, summaries, etc.

Annex 14: Method developed by Rosenberg

(Rosenberg *et al*. 2001)

General description

The method is intended to assess the effects of product substitution on workers' health. The authors are affiliated with university departments in family medicine, community health and occupational health. The method is not aimed at selecting an alternative solution but rather involves a successive approach for functional analysis that is illustrated by a practical case concerning substitution of a pesticide in agriculture.

Objective of the method

The purpose of the method is to assess expected and unexpected consequences on the work environment following substitution of a chemical product.

Scope

The method applies to any chemical agent (compound, product) and to any process.
An example concerning the replacement of a pesticide (Alar (daminozide)) illustrates the approach.

Description of the method

A method including four steps.

Step 1: Characterise the objective and the function of the chemical product.
For example, in the case of the pesticide Alar, the objective is in particular to decrease the crackling of fruit, improve colour, and above all to prevent fruit from falling before harvest.
Alar was used to make apple trees more resistant to parasitic infestation.

Step 2: Identify a range of alternative solutions.
According to the authors, searching for alternative solutions essentially focusing on the identification of substitution products is a "limited" approach. All technological solutions must be considered to reach the usage objective.

Step 3: Assess the effects of the alternative solution on workers' health in the workplace.
The objective is to check that the alternative solution does not create a risk that is higher than that generated by the substituted product. In this case, the intrinsic hazards of the substitution product are addressed: toxicity, flammability. The presence of physical risks (heat, noise, radiation, etc.), and ergonomic and psychosocial risks related to the alternative solution are also assessed.

Step 4: Assess the other risks induced by the alternative solution.
During this step, impacts on the following are examined:

- production of the substituted product;
- employment and occupational organisation;
- public health;

- international uses;
- economic aspects (cost)

Advantages and disadvantages of the method

Advantages

The method describes the assessment approach implemented for an alternative solution taking into account all the positive and negative effects associated with substitution.

The authors' priority was to make available a decision-making process that would provide the best available alternatives. The method provides a list of actions to undertake for a critical analysis bringing together all the stakeholders, including workers. The authors indicate that this approach is not a universal solution to address the impacts related to substitution.

Disadvantages

Implementing this approach while including all the stakeholders also involves an investment and a relatively long-term time frame before the alternative solution can be assessed in all its aspects.

Annex 15: Method developed by the Lowell Center

(Rossi, Tickner, and Geiser 2006)

General description

The Lowell Center for Sustainable Production, University of Massachusetts drafted a guide in 2006 with the following objectives: to significantly advance dialogue on reforms in chemicals policy in the United States, to help develop ustainable chemicals management outside the United States, to encourage the development and use of safer alternatives by creating and promoting a comprehensive framework for the assessment of alternative solutions, and to identify tools and the appropriate ways of assisting innovation in green chemistry and safer management of the supply chain for chemical products.

Objective of the method

The Lowell Center developed a framework for the assessment of alternative solutions concerning chemical products. This open-source framework aims to rapidly assess safer and more socially just alternatives concerning the substitution of chemical products, materials, and associated products.
Open-source refers to collaborative development, sharing and development of methods, tools and databases that facilitate decision-making.
Rapid assessment means that the decision-making process yields robust decisions underpinned by the best available scientific data, while avoiding the “paralysis” of analysis.

Scope

The method applies to any chemical agent (compound, product) and to any process. Various case studies on a dedicated website illustrate the method applied in different sectors of activity: clothing, furniture, chemistry, etc. (www. Bizngo.org).
The approach can be implemented during the development of new products.

Description of the method

The document presents an approach and tools that can be used specifically during the assessment phase of alternative solutions.
The approach has three main steps for which the document provides references of tools to distinguish products on the basis of their hazards. The document concerns directly the assessment of alternative solutions, without providing details on the search for substitution solutions for chemical products, for example.

Step 1: Define the basis for alternatives assessment
This step has three main components:

- Identification of the aims and objectives: each organisation must indicate the reason for wishing to assess the alternatives;
- The guiding principles: each organisation must define the guiding principles that it will follow when carrying out the approach. For example, the organisation may decide to follow the 12 principles of green chemistry, the nine general principles of prevention, etc.

- Decision-making rules: each organisation must establish decision-making rules for selecting the alternative solutions to compare and assess.

Step 2: Identify the alternatives
This step is used to identify the chemical of concern and to document its final uses and functions to identify alternatives.

Step 3: Assess alternatives
The alternatives are assessed based on the impact on human health, the environment, social and economic aspects, and technical performance.
The choice is then made once this analysis is completed.

Since the publication of this document, a website has been set up (bizngo.org) which contains documentary and methodological resources specifically to assess the hazard level of an alternative solution taking into account the impacts on human health and the environment, using benchmark methods that enable the various alternatives to be separated. The guide cites the hazard classes developed in the GreenScreen method.

Advantages and disadvantages of the method

Advantages

The method describes the assessment approach implemented for an alternative solution taking into account all the positive and negative effects associated with substitution. It is consistent with a functional analysis.

There is a dedicated website (www.bizngo.org) that explains the approach and presents a certain number of case studies in different sectors: clothing, furniture, paint stripping, etc. In this last case, the report indicates a duration of 40 weeks only to assess the alternative solutions.

Disadvantages

Implementing this approach while including all the stakeholders also involves an investment and a very long time frame before the alternative solution can be assessed in all its aspects.

Annex 16: Method developed by the POP Review Committee of the Stockholm Convention

(UNEP 2009)

General description

The method was developed by the persistent organic pollutants (POP) Review Committee of the Stockholm Convention in 2009.

Objective of the method

The purpose of the method is to establish general guidance to evaluate alternatives and substitutes to POPs and candidate chemical products.
No decision-making approach is put forward.

Scope

The scope essentially covers alternatives (materials, systems, processes, strategies) and substitute chemical substances to POPs.

Description of the method

The method has five steps

Step 1: Collect use and emission information
From this first step, exposure data are described by collecting information on environmental releases and their management (including during waste processing and recycling).

Step 2: Identify potential alternatives
In this step, the availability, technical feasibility, accessibility, and efficacy of the alternatives are examined.

Step 3: Assess risks related to alternatives and substances
The hazards related to the physico-chemical properties are determined simply by applying the POP screening criteria. Those that concern human health are determined by applying two criteria: hazard and exposure conditions. A comparison of the toxicity data based on the behaviour of the substances during transport in the environment is also carried out. The method also provides for an evaluation of the potential for harm in real conditions of use.
The environmental hazards are determined on the basis of a comparison of the levels of ecotoxicity of the substances depending on their transport in the environment.

Step 4: Assess social and economic impacts

Step 5: Perform an overall assessment of the alternatives

Advantages and disadvantages of the method

Advantages

The method is very logical, well organised, and has the advantage of relying on many study results concerning POPs. It also proposes an indicative table to assess alternatives that is easily transposable to the search for other substitutes or alternatives.

The method involves a preliminary selection of alternatives based on the availability of the substance on the market and on the question of technical feasibility.

Disadvantages

The method is general, not very detailed, and was designed for a single category of pollutants: POPs.

Annex 17: German Guide on sustainable chemicals

(Umweltbundesamt 2011)

General description

The method was developed by the German Federal Agency for the environment (*Umweltbundesamt* – for our environment) in 2011.

Objective of the method

The purpose of the method is to propose guidance on the use of substances from sustainable chemistry instead of more hazardous comparable products. It does not propose a decision-making approach. The method helps in selecting sustainable products or more sustainable uses through criteria to distinguish between sustainable and non-sustainable substances.

Scope

The scope is very wide. The criteria proposed can be used in all sectors of activity.

Description of the method

The method has two steps to assess “sustainability”.

Each of the described criteria is assessed and ranked in one of four levels: green – no hazardous properties; yellow – some properties of concern; red – substance of concern; and white – insufficient data.

Step 1: The first step addresses 8 substance-specific criteria:

- included or not on a list of substances of concern;
- physico-chemical properties;
- human toxicity;
- properties indicating an environmental hazard;
- mobility (emission potential, persistence);
- origin of raw materials;
- greenhouse gas emission potential;
- assessment of resource use (energy, water, etc.)

Step 2: The second step takes into account 7 use-specific criteria of the substance:

- emission potential;
- user groups (possible identification of susceptible populations);
- used amount;
- waste stage;
- substitution alternatives;
- quality of finished products;
- innovation potential.

The technical and economic feasibilities are only mentioned in the chapter on the substitution potential where it is indicated that one can use replacement substances if this is “economically and technically” feasible.

Advantages and disadvantages of the method

Advantages

One of the main advantages of the method is that it addresses both the substance and its uses. As a result, it can be used in all sectors of activity.

Disadvantages

The major drawback is that the method is too focused on identifying substances from sustainable chemistry.

Annex 18: Method developed by the United States Occupational Safety and Health Administration (US OSHA)

(OSHA 2013)

General description

The United States Occupational Safety and Health Administration (US OSHA) published this method in 2013.

Objective of the method

The purpose of the method is to establish a management system for chemical products to reduce or eliminate chemical hazards at the source, thanks to substitution processes. To do this, the method aims to provide a tool to assist employers and workers, and to guide them on the best way to use these substitutions.

Scope

The scope is vast as the tool can be used by:

- companies using chemistry in their processes and all those using chemistry in their daily tasks;
- workers in their workplace, to better understand the uses of products, use safer products, and with their employers, discuss processes to follow to identify safer alternatives.

Description of the method

The tool has seven steps:

Step 1: Set up teams to establish a work programme and fix objectives

Step 2: Examine the use of chemical products and associated hazards
In this step, information on the workers potentially exposed to the chemical substances is collected.

Step 3: Identify the alternatives

Step 4: Assess and compare the alternatives
The method recommends systematic comparison of hazards (without other details).

Step 5: Select a safer alternative
The guide insists on weighting to establish for the various criteria and impacts to protect worker health as best as possible.

Step 6: Implement the alternative (pilot stage) to become aware of the changes made and the problems related to practical implementation.

Step 7: Execute the change and assess the alternative.

The programme provides no technical details on the description of hazards related to the physico-chemical properties of the products, nor those for the environment. Technical feasibility and economic feasibility are not mentioned as such; the first is considered one of the economic factors and the costs are only cited in a few steps.

Advantages and disadvantages of the method

Advantages

The advantages of the method are only company-related: enable “employer-worker” dialogue on examination of problems related to use of chemical products.

Disadvantages

The main disadvantages are the absence of scientific and technical considerations. This is a very general method that refers mainly to the REACh Regulation or other directives or regulations.

Annex 19: Design for the Environment (DfE) programme of the United States Environmental Protection Agency (US EPA)

(Lavoie *et al*. 2011, US EPA 2011)

General description

The United States Environmental Protection Agency (US EPA) developed a programme in 2004, updated in 2011, called “Design for the Environment (DfE)”.
This programme develops a method and lists assessment criteria to conduct an alternatives assessment for hazardous substances.

Objective of the method

The purpose of the tool is to define an overall method from identification of the chemical of concern through to the final decision.
The programme encourages substitution with less hazardous alternatives.

Scope

The method applies to conventional chemical substances and mixtures.

Description of the method

The method follows seven steps.
The method provides its most important contributions in steps 1 to 5 and gives more general information for steps 6 and 7.

Step 1: Determine feasibility

The programme considers above all that the alternatives must: be available on the market, profitable, able to improve health and the environment, and able to generate sustainable change.

Step 2: Collect data on the alternatives

Before including the stakeholders in the discussions, the method recommends collection of data on the alternatives (processes, uses, etc.)

Step 3: Invite the stakeholders to become involved in defining the scope of the project

Step 4: Identify the alternatives that can effectively replace the substance

The hazard analysis will be conducted on the retained alternatives.

Step 5: Perform the hazard analysis

The types of hazards addressed are those affecting humans (health effects and physico-chemical properties), as well as environmental hazards (ecotoxicity and aspects related to the fate of the substance in the environment). To do this, the guide proposes allocation of a hazard level to each of the 18 effects of interest from among the five proposed levels: very high, high, moderate, low or unknown. This category determination is guided entirely by a table providing the information sources to consult and indicating the types of hazards depending on the collected data.

Step 6: Address the economic context and the product life-cycle

The economic feasibility must contain a description of the costs incurred by substitution.

Step 7: Make a decision on use of a safer substitute.

Advantages and disadvantages of the method

Advantages

The overall approach is very interesting in terms of the method because it first proposes selection of a list of substances based on criteria of availability and profitability on which a full hazard analysis will then be carried out. The hazard analysis is thus carried out on a list of pre-selected substances.

The method is very precise and comprehensive concerning the hazard assessment of substitution substances and mixtures. The hazard criteria are presented in a comprehensive way with solid bibliographic references (CLP Regulation, etc.).

Disadvantages

The non-availability of an alternative on the market is considered one of the first exclusion criteria, which appears to be illogical since substitution may prompt the development of an alternative on the market.

The exhaustive nature of information sources to characterise the hazards of a substitute is not associated with a ranking of their relevance and their reliability. The tool recommends several sources without recommending a specific one for the studied effects.

Annex 20: Method developed by Interstate Chemicals Clearinghouse (IC2)

(IC2 2013)

General description

In the United States, IC2 is an association of departments responsible for health and/or the environment in 10 US States and 3 local governments.

The IC2 published a guide on alternatives assessment for chemical substances in 2013.

Objective of the method

The method was developed to provide a common framework for substitution work carried out by the various authorities, thereby sharing efforts in terms of studies and assessments of substitutes as well as their results.

The aim is also to assist all interested parties: small and medium-sized enterprises in particular, and public departments.

The objective is to offer a guide covering all the aspects related to alternatives assessment: hazards, exposure, performance, costs, availability, etc. with priority given to hazard reduction over the other criteria.

Scope

The method applies primarily to substances but also addresses the question of non-chemical alternatives as a precondition or addition to the search for a chemical alternative.

Description of the method

The method provides three specific frameworks to assist decision-making:

- Firstly, a sequential framework in which the alternatives that do not meet the criteria of a module are ruled out of the method.
- Secondly, a simultaneous framework in which the alternatives are compared on the basis of data collected in each module.
- Thirdly, a hybrid framework in which some steps are sequential and others simultaneous.

Each framework contains five modules:

- Assessment of hazards and performances

This preliminary module analyses whether a substance is truly useful/intentional and the possibility of eliminating it ahead of any analysis of alternatives.

- Hazard
- Performance

The assessment of technical feasibility is based on the approach in the REACh guide for the analysis of alternatives.

- Cost and availability

This module should be viewed as equivalent to the assessment of the socio-economic impact of a chemical product and its alternatives as defined in the REACh Regulation.

The module is based on the life-cycle costing method but includes aspects that are more closely related to socio-economic analysis. Ultimately, the module appears to mix aspects that are somewhat foreign to the concept of economic cost for those involved in a substitution process.

- Exposure assessment

The exposure assessment module offers several approaches of increasing complexity to address this topic. However, it appears that the issue that is actually dealt with in this module is rather the combination between hazard and exposure, i.e. risk. The analyses are either qualitative or involve an actual quantitative assessment of the ultimate risks. This module is useful and goes beyond the usual few criteria by proposing an actual reasoning framework to characterise exposure.

For each of these modules, there are several procedures: an initial screening approach and approaches of increasing complexity (with increasing data requirements). These modules often refer to other detailed methods (available in the form of software): QCAT and GreenScreen for hazards, life-cycle assessment, cost/benefit analysis, etc. Among the "satellite" methods to use, some are documented as "cradle to cradle" for example.

Advantages and disadvantages of the method

Advantages

The method is comprehensive, instructional and precise (with "algorithms" to follow and cross-references to practical methods).

One good idea is to perform an initial screening with a preliminary assessment of hazards and technical performances to immediately rule out certain alternatives that are not particularly realistic, and then to focus the analysis on a smaller number of alternatives; this reflects the approach adopted by industry.

Considerable attention is paid to the validation processes for the technical performance of alternatives.

Disadvantages

If implemented completely, the method is complex and cumbersome. Although the method is clear and operational as a whole, specifically concerning the more technical modules (hazards, exposure, feasibility), it is less transparent in the economic area in which it tends to mix different tools in several modules with poorly structured interactions and boundaries. For example, the documentation of social, economic and life-cycle assessment aspects is consistent more with an inventory than actual ranking. In particular, the "life-cycle" module appears to be rather redundant in view of the other modules and largely optional, and the "social" module is too ambitious and not particularly in line with the actual issues that arise in substitution processes.

Annex 21: Method developed by the University of California, Los Angeles (UCLA)

(UCLA 2011, Malloy *et al*. 2013)

General description

The University of California, Los Angeles (UCLA) developed this method of analysis in 2011.

Objective of the method

The purpose is to propose an alternatives assessment method to assist in application of the Californian law on risk management for chemical substances.

The aim is to rank alternatives (by scores or by order of preference) by means of three case studies and to evaluate the ranking's stability if changes are made in various ways (simplification of the criteria, change in the decision-making method). The methods prove to be insensitive to the changes made for the test cases.

The document is in fact less a tool and more a study to explore the use of multi-criteria methods in order to rank or select alternatives, and test their feasibility and their robustness to missing data or methodological variations.

Scope

The method is in principle more focused on alternatives for chemical products but could be considered for other cases (technology comparisons).

Description of the method

The method involves a multi-criteria analysis and thus follows the conventional thinking of these methods: definition of the criteria, choice of the respective weight of the various criteria, ranking of the alternatives, and calculation of the ranks or scores of the different alternatives. The choice of criteria and weighting may require methods developed to consult and include the stakeholders.

The method involves the study of six successive modules:

- Module on hazards associated with the physico-chemical properties

The following criteria are assessed: oxidising properties, flammability, flash point, and self-ignition temperature.

- Human health impact module

The following criteria are assessed: acute toxicity, carcinogenicity, mutagenicity, genotoxicity, endocrine disruption, reproductive toxicity, developmental toxicity, epigenetic toxicity, other toxicity (for an organ, tissue or cellular toxicity)

- Ecological impacts module

The adverse impacts (species, ecosystems, protected species, protected habitats) and exposure criteria (volume in manufacture or in use, dispersive use, sensitive populations, persistence and bioaccumulation) are assessed.

- Environmental impacts module

Life-cycle assessment criteria for each compartment (air, water, soil) and consumption of natural resources (non-renewable, renewable, water, energy, waste, recycling potential) are assessed.

- Technical feasibility module

The assessed criteria include functionality, reliability, usability, maintainability and efficiency.

- Economic feasibility module

Economic feasibility is not described with precision; only impacts on manufacturers and on consumers are assessed.

Advantages and disadvantages of the method

Advantages

The report is a well-structured, easily accessible source on multi-criteria methods and presents the method in an instructive manner, giving tangible examples.

Disadvantages

The document does not provide a tool; to implement the method one needs to refer to sophisticated multi-criteria methods and to their associated software and be familiar with how they work.

The results of the case studies, which show an insensitivity of the choice of alternatives to the methods used, does not in principle favour deepening of these choices in the practical cases.

Annex 22: Method developed by Subsport

(SUBSPORT 2013, SUBSPORT)

General description

The website www.subsport.eu is a free, open-access web portal to assist in the substitution of hazardous substances. This website was funded by a LIFE programme contract (European Union) and by the German Federal Institute for Occupational Safety and Health (BauA) and the Austrian Ministry of Labour.

This tool is aimed at helping companies implement substitution projects for hazardous substances, by communicating information on replacement products, in order to meet the objectives of the REACh Regulation.

The Subsport website publishes feedback on substitution projects from either the scientific and technical literature or from experiences shared by companies.

Objective of the method

The method developed by Subsport and updated in 2013 is aimed at selecting substitution examples for publication on the website.

Scope

The method applies to hazardous chemical substances.

Description of the method

The method follows six steps.

Step 1: Characterise the hazards of substances

The first step consists in collecting information on the physical hazards, human health hazards, and environmental hazards of the chemical of concern. The guide provides a list of bibliographic sources to find this information. It also highlights the need to have a minimum amount of information on the substance for comparison of the alternatives to be possible.

Step 2: Identify and rank the uses of the substance

The guide provides links to databases, and examples from the scientific and technical literature to document the uses of the substance.

The guide then proposes to rank the uses on the basis of criteria such as the volume of substance used, the exposure data, and the type of population (susceptible, etc...).

Step 3: Identify potential substitutes

The guide provides a list of references to find information on possible substitutes. At this stage, technical feasibility and costs do not limit the search.

Step 4: Rule out the hazardous alternatives

An alternative that is either carcinogenic, mutagenic, reprotoxic, endocrine disruptive, highly persistent or highly bioaccumulative, neurotoxic or sensitising will be excluded from the method and will not be published on the Subsport website.

Step 5: Characterise the alternatives

Information on the environment, health, safety, technical performance, availability, cost and life-cycle impact will be collected.

Step 6: Compare the alternatives

The alternatives are compared on the basis of the data collected in the previous step.

Advantages and disadvantages of the method

Advantages

The method is simple and instructive. It is designed in a rather logical way, starting with a broad search of all possible alternatives. The most hazardous are then excluded from the method and lastly, additional information is collected on all the other alternatives.

Disadvantages

The method is very general. Only the hazard criteria are named specifically. There are no defined criteria to assess costs, availability or technical performance.

The method may generate time losses inasmuch as it is exclusively comparative. The method recommends collecting large amounts of data on all the alternatives provided that they are not hazardous. As a result, it is probable that hazards will be documented for a substance that will ultimately not be technically effective as a substitute.

Annex 23: GreenScreen List Translator (GSLT)

(CPA 2016b)

General description

Clean Production Action (CPA) is an expert consulting firm based in the United States and Canada that developed a simplified tool to compare the hazards of substances in 2011, using a simplified version of the GreenScreen for Safer Chemicals method.

Objective of the method

GreenScreen List Translator (GSLT) is a tool used to rapidly identify the most hazardous substitutes (and thus directly rank them in hazard class 1) without it being necessary to apply the GreenScreen for Safer Chemicals method in its entirety.

Scope

The method applies to chemical substances.

Description of the method

The tool follows three steps.

Step 1: Select the substances to assess

Step 2: Collect data on the hazards

The types of hazards addressed are those affecting humans (health effects and physico-chemical properties), as well as environmental hazards (ecotoxicity and aspects related to the fate of the substance in the environment).

The second step is to determine hazard levels for each of the effects of interest from among the proposed levels: very high, high, moderate, low, etc. This classification is guided entirely by a simplified table providing the information sources to consult and indicating the hazard classes depending on the collected data.

Step 3: Rank the substances

The tool is used to rank the substances in one of three levels:

- LT-1: Hazard class 1 (benchmark 1)
- LT-P1: Possible hazard class 1 (possible benchmark 1)
- LT-U: Not specified (unspecified benchmark)

The tool thus enables rapid identification of substances in hazard classes 1 or U (unspecified) on the basis of the GreenScreen for Safer Chemicals method and for which it will therefore not be necessary to apply the entire GreenScreen method to assign a ranking.

Advantages and disadvantages of the method

Advantages

Applying the GreenScreen List Translator (GSLT) is very useful before implementing the demanding GreenScreen for Safer Chemicals method. This is because the classification of certain types of hazards will directly assign a substance to hazard class 1 (benchmark 1) and thus place it directly in the category of highly hazardous substances, irrespective of the classifications of the other types of hazards.

The method avoids time being wasted documenting all the hazards of highly hazardous substances.

Disadvantages

The tool enables identification of the most hazardous substances but does not put forward a clear ranking system of substances based on their hazards. To do this, one needs to apply the GreenScreen method.

The types of hazards addressed are very broad in view of substitution of a carcinogen.

Annex 24: Public consultation

This report was made available for public consultation on the ANSES website from 08 August 2016 to 30 September 2016.

The following persons or organisations forwarded their comments during the consultation phase:

- EIHF-isofroid

Annex 25: Report updates

Date	Version	Description of change
07/07/2016	01	Validation by the CES before consultation
08/12/2016	02	Final version (addition to indicate the consultation procedure; inclusion of the update of the QCAT tool in 2016 and semantic adjustments)
04/12/2017	03	Semantic adjustments following the translation of the method into English
11/12/2020	04	Addition of adjustments of the QCAT and GreenScreen tools implemented while applying the methodological document in the different sectors of activity and of details on the objectives of this methodological document.

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