



# Updating the European Union's regulation on classification, labelling and packaging of substances and mixtures (CLP): A key opportunity for consumers, workers and stakeholders with interests in the legislation and toxicology of hazardous chemicals

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## ABSTRACT

Recent advancements in toxicology and the European Union's Green Deal, with its Chemicals Strategy for Sustainability, have paved the way for major changes in EU legislation on the control of environmental chemicals for a cleaner and safer environment. Another substantial legislative advancement underway is the update of the "Regulation on Classification, Labelling and Packaging of Substances and Mixtures (CLP)," an ambitious piece of EU legislation with exceptional scientific toxicological background in identifying a hazard, aiming at better protecting its citizens and the environment from the risk of chemical substances and products, the occupational settings included. Update of CLP legislation additionally aims at facilitating the free exchange of chemicals in the European Internal Market, provided that proper labelling and packaging processes are implemented. Participation in the ongoing online public consultation on these issues, ending on November 15, 2021, is of key relevance to ensure a transparent and effective definition of such an important piece of legislation, fully compliant with current EU priorities in terms of human and environmental protection and animal welfare.

## 1. Introduction

An effective assessment, control, and surveillance of the chemicals that are released in the environment within industrial and professional settings, as well as in everyday life, is a major concern not only of the European Union but of every modern political entity. To achieve this goal, most countries have resorted to the implementation of adequate toxicological hazard identification and risk assessment, as well as of a comprehensive and effective body of legislation, mainly belonging to the public law domain [1]. With regard to the manufacturing, import, and distribution of chemical substances in industry and their exchange through commerce, the first prominent example of relevant and generally effective legislation in industrialized countries is the Toxic Substances Control Act (TSCA) in the United States [2], a body of rules established in 1976 that enabled the US Environmental Protection Agency to "require reporting, record-keeping and testing requirements,

and restrictions relating to chemical substances and/or mixtures" [3]. Not all substances were put under the control of TSCA, with food, drugs, cosmetics and pesticides being exempted as already regulated by stricter rules. Concerning the European Union, the key legislation was approved by the European Parliament and the Council in late 2006 and become effective in 2007 under the acronym "REACH" for "Registration, Evaluation, Authorisation and Restriction of Chemicals" [2,4–8]. With the same Regulation, it was decided to establish a new Agency located in Helsinki, the European Chemicals Agency (ECHA). The main characteristics of REACH have been already explained in detail, and such regulatory legislation entails human and environmental health protection from potentially hazardous chemicals, requiring producers to provide (thermo)physical, thermochemical, and toxicological data for the regulated chemicals to allow their marketing [9,10], and also introducing the use of the Precautionary Principle [11]. The main reasons for adopting REACH Regulation were the large amounts of chemicals

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manufactured and placed on the market for years and the scarce information on their hazard for the environment and human health—a situation that for a long time prevented the industry from applying effective measures for risk assessment and protection of workers, professional users, citizens and the environment [11].

The Regulation on the classification, labelling, and packaging of chemical substances and mixtures (CLP Regulation) amended the Dangerous Substances Directive (67/548/EEC (DSD)), the Dangerous Preparations Directive (1999/45/EC (DPD)) and Regulation (EC) No. 1907/2006 (REACH), and since 1 June 2015, is the only legislation in force in the EU for classification and labelling of substances and mixtures. Differently from REACH, which has the task of regulating chemical manufacture and supply (including their import), and eventually safe use of chemical substances, the CLP legislation is aimed at providing a classification, labelling, and packaging of individual chemicals and their mixtures [12]. The basis of CLP regulation is the United Nations' Globally Harmonised System (GHS). The CLP Regulation requires manufacturers, importers or downstream users of substances or mixtures to classify (i.e. identify inherent properties of a substance or a mixture that lead to the manifestation of toxic/ detrimental effects), label and package their hazardous chemicals appropriately before placing them on the market. Classification is the starting point for hazard communication. When relevant information (e.g. toxicological data) on a substance or mixture meets the classification criteria in the CLP Regulation, the hazards of a substance or mixture are identified by assigning a certain hazard class and category, covering mainly physical, health, and environmental hazards. Following classification of a substance or mixture, the identified hazards must be communicated to consumers, workers, professional users and other actors in the supply chain, in order to alert them about the presence of a hazard and the need to manage the associated risks. Labelling elements set by CLP, such as pictograms, signal words and standard statements for hazard, prevention, response, storage and disposal, for every hazard class and category, along with the safety data sheets, specified by REACH, serve this purpose. CLP is also the basis for many legislative provisions on the risk management of chemicals. This legislation has therefore a central role in chemical classification and risk communication to both consumers and workers, in addition to a number of additional tasks less known but still very important including the requirement for suppliers of hazardous chemicals to inform national poison centres for emergency health responses [13].

## 2. Revision of CLP Regulation

From January 2009, when first entered into force, the technical annexes and certain articles of the CLP Regulation have been periodically updated. The amendments of the CLP Regulation are named “adaptations to technical progress” (ATPs) to the Regulation and to date there are seventeen adopted ATPs, the last being published in May 2021 [13].

In August 2021, however, the European Commission has launched a public consultation on the revision of the CLP Regulation, open online for contribution by single scientists or institutions interested in the field until November 15, 2021 [14]. The relevance of this public consultation and the related legislation under both public law and public health perspectives is strong. The key goals in this update of the CLP legislation are: to adequately address a well-known hazard class (and mode of action) of chemical contaminants, endocrine disruptors [15–17]; to take into account the effects of mixtures of chemicals [18–21]; to account for reduced use of animals in laboratory toxicological testing; and to expand the criteria for toxicological risk assessment and legal control of chemicals, i.e. their environmental persistency, bioaccumulation, and toxicity. Some of these goals have already been outlined by some investigators [5,22–24].

At the same time, it should not be lost sight of other key issues in updating the CLP Regulation. For example, more and more studies show that in some particular cases, (e.g. glyphosate and glyphosate-based

herbicides) commercial formulations that contain an active compound along with other considered inert ingredients can be more toxic compared with the active compound alone that is used for classification [25–27]. In addition, hazards not properly described under CLP are constantly being identified, as for example cardiotoxicity, with considerable latency in manifesting adverse effects that bear a long-lasting risk to public health [28–30]. With regard to risk communication, effective labelling provisions of CLP must be enhanced, as users' awareness has proven to be limited in the past and this aspect has to be somehow addressed by the revised Regulation [31–34].

At a general level, it is important to emphasize that the CLP Regulation is appropriately linked to (and to some extent embedded in) two major legislations of the European Union, the “European Green Deal” [35] and the “Chemicals Strategy for Sustainability” [36]. The underlying approach of the latter legislation as well as of the CLP update process is the awareness that chemicals are frequently ubiquitous in the environment and “needed” in our daily life, but that some of them (also based on their amounts, but frequently even at low doses) may pose a risk to the human health, to living organisms overall and to the environment, and thus need to be identified and tightly regulated [37,38]. Admittedly, this update of the CLP Regulation also aims at fostering change in the production process of chemicals by the European suppliers, thus favoring the transition towards safer and more sustainable chemicals in terms of environmental pollution, climate change, and human health risks [39,40].

The public consultation, which has been preceded by another consultation to provide indications for the roadmap, is available until November 15, 2021 [39]. Such consultation can become of key relevance to help the EU Commission in the update process, providing specific feedback useful to identify the most appropriate way forward for CLP Regulation update “taking into account scientific and technical progress”. By accessing the website, not only stakeholders but also investigators, individuals, and organizations are asked to provide a reply to a set of general questions, and some additional more specific questions requiring specific expertise. More specifically, the questions requested in the first part of the CLP update public consultation refer to almost all chemicals and the products containing them, namely industrial chemicals as well as household chemicals, including (among others) fuels, solvents, and detergents as well as both individual substances and their mixtures (all considered to be “chemicals”). All toxic properties of such substances are potentially considered in the update, including cancer, allergy, and disruption of aquatic life. In addition, the most adequate procedures to label toxic products following their content of toxic chemicals before placing them on the market are considered in this process of legislation update. Advice on how to reduce exposure and deal with acute overexposure is also envisaged in this CLP Legislation consultation process, including strengthening the capacity of EU poison centres to counteract the health risks of the single hazardous chemicals [41]. Overall, a key aim of the CLP Regulation is to protect citizens and workers, as well as more generally the environment, from the risks associated with hazardous substances and their mixtures. A second aim is to facilitate the intra-EU exchange of chemicals which can circulate freely within the European Internal Market, if properly labelled and packaged according to the CLP criteria.

The questionnaire for the public consultation includes two parts, the first of which contains questions for all respondents. This section highlights that the European Commission during the preliminary CLP revision process has scrutinized the most recent scientific evidence. Following this, the European Commission has come to the preliminary intention to introduce new categories of hazards in the CLP Regulation, being currently not covered by it, to more adequately protect humans, all living organisms, and the environment. These categories of chemicals are: the “endocrine disruptors,” a wide group of substances able to interfere with the metabolic and endocrine system in humans (particularly in their early life) and wildlife; “Persistent, bio-accumulative and toxic chemicals” substances that accumulate in plants and animals may

harm both humans and the other living organisms”; and finally “persistent, mobile and toxic chemicals,” another class of chemicals not easily metabolized and degraded in the environment and that due to their persistency and mobility may migrate in the environment and pollute water bodies (and drinking water as well) and foods. Still, in the first part of the questionnaire, questions are reported about the real need to use laboratory animals for toxicologic risk assessment of chemicals, and the feasibility and preference for alternatives to the use of animals for this purpose. Other questions refer to the need to improve clarity and completeness of the labelling of hazardous substances and products (also including products bought online), to add to the CLP legislation products not currently covered by CLP such as medicines and medical devices, foods, and cosmetics.

The second section of the questionnaire administered in the public consultation focuses on more technical points of the CLP Regulation that requires prior knowledge and expertise. They include: the need to use the already existing definition for endocrine disruption, such as the WHO one, or to define in a different and up-to-date way these toxic properties; how to adequately label and how to update REACH legislation for toxic chemicals being persistent, bioaccumulative, and/or mobile; if to add “environmental toxicity” among the criteria to define and label toxicity; if to introduce separate and specific hazard classes and criteria for immunotoxicity and neurotoxicity when defining and labelling a potentially hazardous substance or product. The final sets of questions of the public consultation questionnaire include several specific and relevant topics, among which: the need for a more in-depth assessment of the toxic or potentially chemicals to be classified and labelled under the CLP update (e.g. endocrine disruptors, etc.); the impact of the CLP update on the current classifications of chemicals and on the other laws and regulations of the EU; the need to expand the amount of information provided to the EU Poison Centers; more adequate regulations of control and labelling of chemicals sold online; the timeline of the CLP update and its adequate integration within the entire EU legislation; the conflicts between the CLP-regulated labelling and other labelling options and regulations. Overall, these issues address key points of the current laws and regulations in the field of chemical control in the EU, as well as relevant toxicological issues in risk assessment and chemical labelling. This further warrants the need and the relevance of updating CLP and of carrying out the ongoing public consultation.

Finally, among the several important aspects to consider in updating the CLP Regulation, it should not be lost sight of the need of improving legal simplification without sacrificing high standards of environmental and human health protection. In fact, one of CLP most frequently decried shortcomings is its complexity, which seems to hinder both compliance and enforcement, as lengthy and convoluted legal procedures make it difficult for manufacturers to be certain about their legal obligations, and for the enforcement agency to apply the law given its manpower shortage [42]. The European policymaker seems, however, aware of the issue: in the General Report of 2018, the European Commission stressed the need for reducing legal complexity in the REACH area [43]. More recently, on March 15, 2021, the Council of the European Union approved its conclusions on the Sustainable Chemicals Strategy, where it is explicitly mentioned “the need to simplify, strengthen and secure a greater cohesion between the policies and the legal framework for chemicals to accelerate procedures and avoid an unnecessary administrative burden, and create more predictability and transparency” [44]. With specific regard to CLP Regulation, it bears noting that on July 14, 2021, the European Commission launched a stakeholder consultation on the topic of “Simplification and digitalisation of labelling requirements” [45]. After receiving the qualified feedbacks from stakeholders of different countries, the Inception Impact Assessments now schedules a 12-weeks public consultation where European citizens are asked to provide valuable feedback on the ensuing reform of chemical products’ labelling, with the European Commission expected to eventually adopt the Regulation proposal in the fourth quarter of 2022.

### 3. Conclusions

Overall, it appears that the opportunity to provide feedback at the ongoing CLP update consultation should not be missed by scientists and regulators in the fields of public and environmental law, public health, and toxicology, as well as stakeholders from industry, non-profit organizations, workers and citizens. Among the different issues, awareness has recently grown about the relevance of chemical mixtures and the challenges they pose to both risk assessors and risk managers, i.e. to both toxicology and public law. In fact, interactions between multiple substances may increase or decrease – or simply modify – the toxic properties of the single compounds and their effects on living organisms and in the environment. In addition, there are three basic domains that are intended to be covered by this update: a general decrease in environmental contamination for both human health and the environment under the Green Deal EU perspective, the need to decrease the use of laboratory animals for toxicity testing and risk assessment, and the awareness that neurotoxicity due to even low-dose contaminant exposures is a major issue that has been not adequately considered in classification and labelling of chemicals. In this context, other “hidden” health hazards, such as cardiotoxicity, are equally relevant. At present, these goals are pursued by the European Commission through a public consultation on the update of the CLP Regulation, thus providing an important opportunity to all parties having an interest in the field of public law and public policy, public health, toxicology, chemical production, and marketing to intervene, interact and contribute.

### Disclaimer

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### Declaration of Competing Interest

The authors declare no conflict of interest.

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