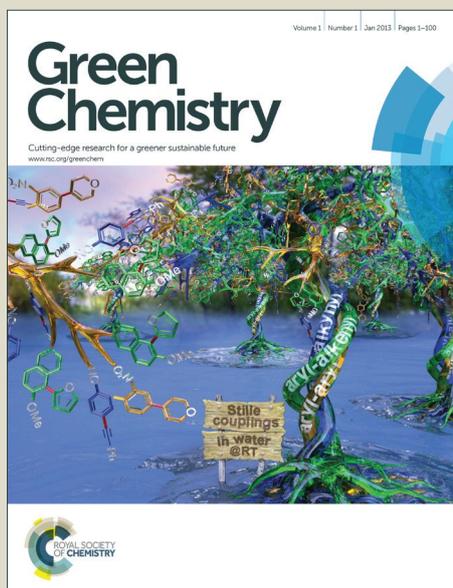


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ARTICLE

Simplified early stage assessment of process intensification: glycidol as value-added product from epichlorohydrin industry wastes

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The present work deals with the production of glycidol through a new synthetic approach based on the conversion of 2-chloro-1,3-propanediol (β -MCH), a by-product in the epichlorohydrin production plant. β -MCH was converted with high yield (90%) and selectivity (99%) to glycidol using an alcoholic solution of KOH at room temperature in only 30 minutes. A simplified early stage assessment based on the use of the green metrics and a life cycle analysis was adopted in order to evaluate the environmental feasibility of this innovative route if compared with the traditional chain to epichlorohydrin. The waste recovery and the maximization of the overall process efficiency leads to sensible reductions per each indicator considered in the assessment, suggesting the possibility of developing on a full industrial scale. In addition, in order to verify the potentialities behind the substitution of the fossil-based glycidol with the product resulted from the recovery of the β -MCH a cradle-to-gate analysis and the GREENMOTION[®] tool were adopted.

Introduction

The real meaning of the Anastas and Warner principles,¹ which is usually enclosed in the concept of *green*, could be summarized by the expression "more with less". This means applying the PREVENTION strategy to avoid fighting with the consequences of our mistakes. The word prevention and its meaning characterized the decade during which the principles were released. The 1990 is well recognized as the year when the US environmental protection strategy moved away from the "command and control" approach to a more innovative plan aimed to pollution prevention (Pollution Prevention Act).² Indeed, while the first was based on the application of the set of strategies so-called *end-of-pipe*, which include all technologies able to reduce or neutralize the pollutants before their release into the environment, the new plan focused on the *front-of-pipe* approach, mainly developed to prevent the burdens on environment. Several areas were involved in this radical change. Chemistry, in particular, saw the origin of a new class of scientist called *the green chemist*, i.e. a researcher aimed to prevent environmental concerns within the chemical industry (e.g. waste, hazardous and non-renewable substances, pollution, energy depletion, non degradability, etc.). However, years before the release of the Sustainable Development concept³ and the Green

Chemistry principles,¹ the 20th century philosophy has already dealt with the issue of *prevention for environment*. Hans Jonas in his work "*Das Prinzip Verantwortung: Versuch einer Ethik für die technologische Zivilisation*" (The imperative of responsibility: in search of an ethics for the technological age)⁴ declared his vision of sustenance: humanity must consider the consequences of his actions and choices to allow the development of future generations. Therefore, it looks evident that the same philosophy should become part of the entire productive sector, in particular in the areas with higher concerns such as chemistry: the chemical and petrochemical industry contributes for the emission of the 7% worldwide Greenhouse gases (GHG, 1.24Gt of CO₂ eq.) and for the consumption of the 10% of the global primary energy (15EJ).⁵ Moreover its spread in our everyday life makes it essential to think about prevention: everything we touch and we work with implies at least a chemical material or reaction. Therefore, before allowing the development of a new product or route on industrial scale, it is appropriate to evaluate its environmental effect, together with the economic feasibility. This kind of evaluation called *at early stage* (AES) and its application to the industrial chemical sector was already proposed by researchers. Patel et al.^{6,7} suggested the AES approach to assess opportunities behind the use of bio-based feedstock in the commodities manufacturing, starting from limited lab-scale data. Zheng et al.⁸ published an approach based on thermodynamic parameters in order to develop *benign by design chemicals*.⁹ Governmental agencies as well are looking for more green processes from the beginning. The US Environmental Protection Agency (EPA) and its GREENSCOPE tool (acronym of Gauging Reaction Effectiveness for ENvironmental Sustainability of Chemistries with a multi-Objective Process Evaluator), released by Gonzalez and Smith in 2003,¹⁰ laid the basis for the development of more sustainable processes combing 8 economic, environmental and efficiency indicators into an unique analysis methodology.

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The important role given by the research community for the use of AES-based methodologies is also confirmed by the publications trend: according with Scopus® database,¹¹ from 1991, the year in which the term Green Chemistry was first coined,¹² since 2013 there was a sensible increase in the number of publications which enclose the AES approaches. However, not only public institutions are interested in this kind of approach; private sector as well has developed several screening tools. BASF SE,^{13,14} GlaxoSmithKline plc.,^{15,16} Chimex¹⁷ and MANE¹⁸ just represent few examples of companies involved in the adoption of the AES approaches to promote the inclusion of the green chemistry principles within their business. Therefore, it looks evident that when innovations are proposed their feasibility should be always evaluated before concentrating a huge amount of time and efforts on them. In this paper we propose a simplified AES evaluation of a new route aimed to enhance the process efficiency in the synthesis of the chlorohydrins. The innovative pathway, fully developed on a laboratory scale, was thought to enclose the green chemistry principles. In particular, the waste minimization (1st), the increase of the atom economy (2nd) and the use of renewable raw materials (7th) were taken into account during the design stage. The AES assessment was based on the use of the green metrics and a simplified life cycle approach, both able to predict benefits and disadvantages due to the scientific implementations. Below, a description of the chemical background behind the development of the new route is listed in details.

Background

Nowadays with the continuous increase of the biodiesel demand significant amounts of glycerol are put on the market and in 2020 its production is expected to rise to 2.5 Mt.¹⁹ Glycerol (1,2,3-propanetriol) is mainly obtained as the principal by-product from the biodiesel production process by transesterification of triglycerides with methanol and the saponification of vegetable oil.²⁰ Furthermore, the glycerol flood and the corresponding reduction in glycerol price has strongly attracted industrial and research interests and a great number of new uses of glycerol have been proposed in the last years.^{21,22,23} As a confirmation of these trend, EU, the major world producer, together with the US production facilities reached in 2013 1.6Mt of biodiesel-based glycerol, respectively 1.04Mt²⁴ and 0.60 Mt.²⁵ Moreover, forecast estimation evaluated the glycerol market for 2018 around 3.1Mt, with an expected income \$2.1 billion.²⁶ Therefore it looks evident that glycerol will represent one of the major worldwide drop-in chemicals for the near future. Among the various possibilities for the production of a wide spectrum of molecules (fine chemicals, commodities, fuel additives, specialities) starting from glycerol, the production of epichlorohydrin (ECH), mostly used in the production of epoxy resins, is an important industrial reality.²⁷ As a matter of fact, Solvay started in 2011 the glycerol-based production of epichlorohydrin, the so-called Epicerol® process that actually supports the traditional process based on the chlorination of propene at elevated temperatures.²⁸

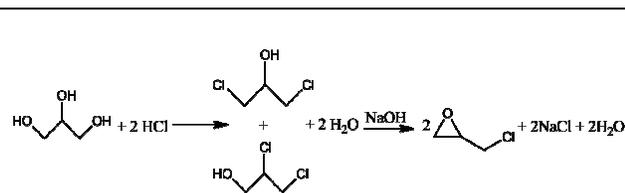


Fig. 1 The Epicerol® process.

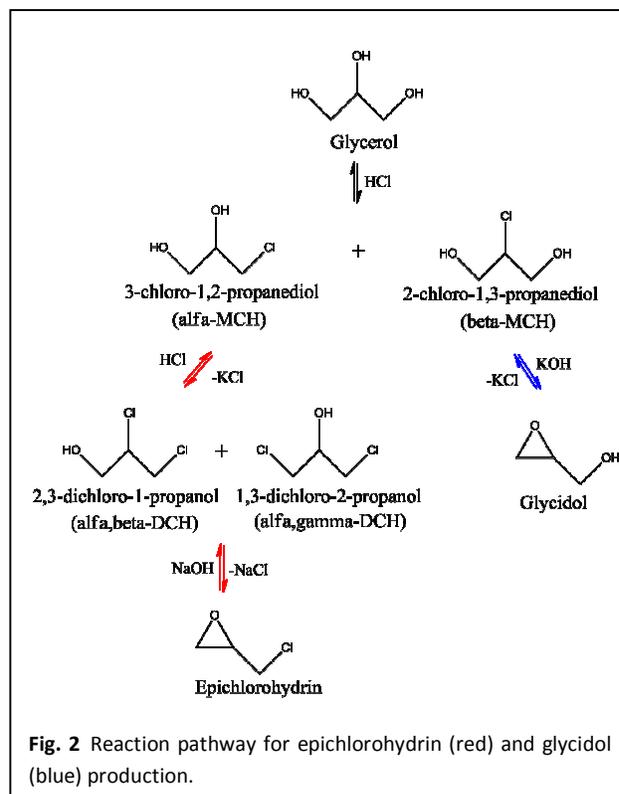


Fig. 2 Reaction pathway for epichlorohydrin (red) and glycidol (blue) production.

The Epicerol® process involves the reaction of glycerol with two moles of gaseous hydrochloric acid in the presence of Lewis acid catalysts (generally carboxylic acid) followed by alkaline hydrolysis as described in Figure 1. Reaction pathway, shown in Figure 2, includes a first chlorination step of glycerol forming 3-chloro-1,2-propanediol (α -MCH) and water with a small amount of 2-chloro-1,3-propanediol (β -MCH) (about 7 % wt. among glycerol).²⁸ 1,3-dichloro-2-propanol (α,γ -DCH) with a small amount of 1,2-dichloropropanol (α,β -DCH), considered as by-product because the reaction rate for obtaining ECH is 20 times slower than from α,γ -DCH, are formed through the α -MCH chlorination reaction.²⁹ Finally, α,γ -DCH is successfully converted in ECH by alkaline hydrolysis. As clearly shown by the reaction scheme, β -MCH does not react to form α,β -DCH because chlorine in the β position inhibits the further chlorination and it must be considered as waste. In order to improve the sustainability of the ECH global process, the search of new synthetic strategies for the transformation of β -MCH into value-added product seems to be very promising. In this scenario, an interesting route is the conversion of the β -MCH into glycidol (Figure 2) integrating the existent epichlorohydrin plant. Glycidol (2,3-epoxy-1-propanol) is a versatile molecule with a high reactivity due to oxiranic and alcoholic functionality and accordingly is an important monomer in the synthesis of polymers and rubbers,³⁰ surface-active agents, varnishes and fabric dyes. Furthermore, glycidol finds application in the synthesis of antiviral

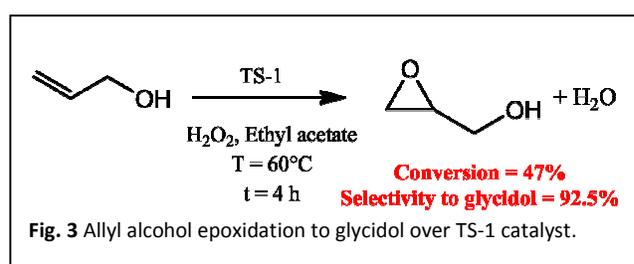


Fig. 3 Allyl alcohol epoxidation to glycidol over TS-1 catalyst.

and analgesic drugs.³¹ Moreover, glycidol can be the starting material for the preparation of other chemicals such as propylene glycol or glycerol carbonate.^{32,33} The first synthetic route to produce glycidol is reported by Rider et al. in 1930 through basic treatment of α -MCH in alcoholic solution with a yield of 64%.³⁴ Nowadays it is mainly produced by allyl alcohol epoxidation with H_2O_2 using titanium silicate (TS-1) as catalyst,³⁵ although several synthetic strategies have been investigated. In this context, glycerol carbonate decarbonation³⁶ and epichlorohydrin treatment with caustic³⁷ produce glycidol with good yields but, at the same time, no industrial applications are based on these reactions because they are both economically disadvantageous. Heterogeneous TS-1 catalyst, introduced by Taramasso et al.,³⁸ is commonly used for its high tolerance to water that allows its use in the presence of an oxidizing agent such as hydrogen peroxide, normally supplied in a 30 wt % aqueous solution. Authors report that a conversion of 47% with a selectivity of 92.5 % toward glycidol (7.5% of impurities are not characterized) is obtained after 4 h of reaction at 60°C in ethyl acetate solution (22.5 mL) using 0.25 g of catalyst, 0.05 mol of allyl alcohol and 5.67 g of H_2O_2 solution. Reaction scheme of allyl alcohol epoxidation by hydrogen peroxide is reported in **Figure 3**. Reaction shows a moderate conversion with a good selectivity to glycidol. On the one hand, the catalyst can be simply recovered by filtration but unfortunately it cannot be reused for several reaction cycles. Furthermore, another critical issue is related to allyl alcohol production from a propylene derivative, which is allyl chloride. In this context, the β -MCH conversion to prepare glycidol can be sustainable if compared with that from allyl alcohol. Glycidol preparation could be integrated in the operative epichlorohydrin plant also to solve the problem of β -MCH waste production. This means that in a common ECH industrial plant of 100000 ton/y, around 7000 ton/y of glycidol could be produced (see **Figure 2**) with a consequential reduction of around 10000 ton/y of β -MCH. In this paper, a green and economic approach to convert 2-chloro-1,3-propanediol to glycidol was investigated. Experiments are carried out using 2-chloro-1,3-propanediol (β -MCH) produced by chlorination of glycerol with gaseous HCl. β -MCH conversion to glycidol is developed using an alcoholic solution of KOH.

Experimental part

- *Materials*

Glycerol, glycidol 96%, 3-chloro-1,2-propanediol (α -MCH), 1,3-dichloro-2-propanediol (α,γ -DCH), potassium hydroxide, sodium hydroxide, acetic acid and ethanol were purchased from Sigma Aldrich. Gaseous hydrochloric acid has been purchased from Air Liquide Italy (99.8%). Glycidol and ethanol were distilled before reactions.

- *Glycerol chlorination in a gas-liquid semi-batch reactor*

Glycerol chlorination was performed as described by Vitiello et al.²⁸ In a typical experiment glycerol (150 g) and acetic acid (7.8 g) are loaded into a 300 cm³ Hastelloy steel reactor equipped with a magnetically driven stirrer, and the temperature is raised to 100°C. Then, HCl is sent to the reactor keeping constant the overall pressure (8 bar). After 4 h of reaction the hydrochloric acid in excess is flushed by N_2 through traps containing NaOH solutions, and the system is brought back to room temperature. About 10 mL of the reaction mixture was neutralized to eliminate the acetic acid and the dissolved

hydrochloric acid. 20 mL of 1.0 M solution of Na_2CO_3 were slowly added to the mixture under stirring keeping the system at 100°C for about 30 min. Then, the solid was removed by centrifugation and the resulting liquid was analyzed by gas chromatographic (GC).

- *Chlorohydrins (α -MCH and β -MCH) conversion to glycidol*

Reaction products of glycerol chlorination obtained as described previously, are distilled in order to separate in the first step the α -MCH and β -MCH from α,β -DCH and α,γ -DCH. Preliminary experiments are performed using a mixture of α -MCH and β -MCH. In a 1 L round bottom flask, one mole of potassium hydroxide was dissolved in 400 mL of distilled EtOH. Afterwards, one mole of chlorohydrins mixture (α -MCH and β -MCH) was dissolved in 200 mL of pure EtOH then added to KOH solution under magnetic stirring (300 rpm). Reaction was carried out for 30 minutes at room temperature after which it was filtered. Ethanol was removed by using a rotary evaporator and used for successive experiments while the product was analyzed by using gas chromatography with flame ionization detector (FID). β -MCH was separated from α -MCH through distillation under vacuum and was converted to glycidol using the same reaction conditions described for the chlorohydrins mixture.

- *Products characterization (GC-FID analysis)*

For the GC analysis, samples were prepared by diluting 0.1 mL of product sample to a final volume of 10 mL with ethanol in a glass vial. Analyses were carried out using a Thermo Trace GC equipped with a 30 m x 0.32 mm (i.d.) polar column Fawemax. The initial oven temperature was 40°C, then programmed to 200°C at 10°C/min and held at 200°C for 5 minutes with the flow rate 1.0 mL/min (splitless injection mode was used). The injection volume was 1 μL . FID temperature was 280°C while 230°C for the inlet. The integrated areas were converted to mole percentages for each component present in the sample using the calibration curves prepared for all the components. The integrated areas were converted to mole percentages for each component present in the sample using the calibration curves prepared for all the components. The data obtained were used to calculate the conversion and selectivity of reactant species. Conversion (C) and selectivity (S) to product *i* were calculated using the following equations:

$$C_i(\%) = \left(\frac{\text{mol}_{i\text{to}} - \text{mol}_{i\text{tn}}}{\text{mol}_{i\text{to}}} \right) * 100 \quad (1)$$

$$S_i(\%) = \left(\frac{\text{mol}_i}{\text{mol of all products formed}} \right) * 100 \quad (2)$$

Methodology

Although the Green Chemistry's aim was well summarized by Sheldon as the discipline which "efficiently utilizes (preferably renewable) raw materials, eliminates waste and avoids the use of toxic and/or hazardous reagents and solvents in the manufacture and application of chemical products",³⁹ sustainability behind the

application of this qualitative approach should be evaluated by the use of more quantitative instruments. Several sets of tools were developed by researchers in order to assess problems and propose alternatives. In this manuscript, we suggest an easy approach based on the use of some environmental/process efficiency indexes and a simplified cradle-to-gate analysis. Therefore, we propose a double objective: *i)* verify the benefits and potential disadvantages (if any) derived from the process intensification in the chlorohydrins synthesis; *ii)* provide a fast set of indicators to evaluate potentialities of new routes under investigation. This approach should emphasize the importance of the AES analysis and encourage its adoption as a support and screening tool of the laboratory experiments.

- *Green chemistry process metrics*, represent a set of indicators useful to assess easily and quickly the process performances in terms of material and energy efficiency, and waste production. Several indexes were included in this definition by the years,^{40,41,42} as a consequence of their common scope: the simple quantification of the process greenness using mass/energetic balances. Among these, three indicators were selected to assess: waste production, raw materials consumption and reaction efficiency.
- *E-factor*, introduced by Sheldon at the beginning of 90s,^{43,44} is an easy way to relate the amount of waste produced per unit of desired product. Although usually the E-factor does not include water fluxes, in this manuscript we decided to make comparisons using the *complete* E-factor (cEF) index.⁴⁵ This choice was done in order avoid objections, since in our opinion the stress on water resources and quality should be always take into consideration. Therefore, cEF was estimated following the equation below (Eq.3), more adequate to evaluate the whole process waste streams.⁴⁶

$$cEF = \frac{\text{total mas of waste}}{\text{mass of desired product}(s)}$$

(3)

- *Process Mass Intensity (PMI)*, represents the total amount of mass (including water) required to synthesize the desired product. The term was first coined by Curzons et al. in the early 2000's⁴⁶ and then proposed as the key index to drive a benign by design drug within the pharmaceutical sector.^{47,48} A similar approach was also suggested later by Andraos,⁴⁹ who referred to the global reaction mass efficiency (RME) to evaluate synthesis sustainability: RME is considered identical to the inverse of PMI.⁵⁰

$$PMI = \frac{\text{total mass of raw materials used}}{\text{mass of desired product}(s)}$$

(4)

- *Atom Economy (AE)*, was first coined by Trost in 1991⁵¹ in order to improve the concept of selectivity as key indicator of the synthesis efficiency.⁵² By introducing AE,

Trost suggested to consider how much of the reagents spent in the reaction end up in the desired product.⁵³ The Eq. 5 shows the process efficiency as a function of the desired product generated by the synthesis, according with literature.⁵³ Optimal AE is 100%.

$$AE = \frac{\text{mass desired product}(s)}{\text{mass of all reaction products}}$$

(5)

- *Life Cycle Assessment (LCA)*, a standardized methodology^{54,55} which provides information about the potential environmental loads within the entire life cycle of a product or process. More comprehensive methodology details can be found in a recently published tutorial review.⁵⁶ Literature⁵⁷ has already shown the increasing trend in the number of the peer-review papers which deal with the LCA issues. This is a further confirmation of the increasing interest of researchers to verify the sustainability considering the all the stages implied within the manufacturing process. The importance of the holistic perspective when the product greenness is under investigation was very well recognized by literature.^{42,58} In particular, just considering the entire chain researchers avoid shifting the environmental burdens from one stage to another, taking into account all the implications which occur within the boundaries considered. This perspective was promoted by the United Nations Division for Sustainable Development since 1992⁵⁹ as the correct strategy to reduce the amount of waste and realize the environmental and economic benefits. In this research, a licensed LCA software (SimaPro, v. 8.0.4.30)⁶⁰ was used to run the *cradle-to-gate* analysis. Ecoinvent database⁶¹ was selected to fill the data gap within the whole system boundaries (in terms of raw material extraction, energy, utilities, etc.). ReCiPe (midpoint and endpoint level, v.1.11)⁶² and cumulative energy demand (CED, v 1.09)⁶³ methods were suggested as comprehensive analysis methodologies able to cover wide range of impact categories. Several environmental scores were already proposed to investigate sustainability within the bio-based industry.⁵⁷ Among these, carbon (CF) and water footprint (WF) were used to address stresses in terms of carbon and water fluxes. On the other hand, the CED was selected as a valuable indicator of the resources (renewable and non-) consumption. Finally, the ReCiPe single-score (SS) was adopted to evaluate the global score reached by each scenario as a result of the combined negative burdens on different receptors. Usually, the *cradle-to-gate* analysis is intended to include each stage which occurs within the synthesis chain: from the raw material extraction up to the production of the desired product(s), including the environmental releases. In this case, the production of the same amount (1kg) of valuable products (intended as the substances with significant relevance from a synthetic and economic point of view) on the laboratory scale was considered as a

functional unit (FU) to refer each input and output of the system under investigation. α,β -DCH and α,γ -DCH are intended as valuable products for the traditional route, because they are commonly used as a feedstock in the ECH synthesis (Figure 2). On the contrary, the innovative pathway includes glycidol from β -MCH in addition to the previous mixture, thanks to the high number of different applications (see Background paragraph). Inventories for both routes are reported in the supporting information (Table S1). They are based on the experimental data already discussed, and LCA software is able to translate them in order to evaluate the potential impacts on the basis of the desired FU (1kg of valuable products). Moreover, the boundaries considered in the cradle-to-gate assessment are explicated by the Figure S1.

As said above, the simplified LCA analysis was carried out using a licensed software. However, in order to promote the AES analysis to new chemical routes and extend its application beyond the community of LCA practitioners (e.g. synthesis chemists), which constitutes one of the purpose of this paper, the assessment could be also completed by the use of open source software tools. Among these, the CCalC2, developed by researchers of the University of Manchester, is a free LCA software which can be used in order to estimate the product carbon footprint.⁶⁴ Moreover, inventory gaps can be filled by the Economic Input-Output LCA released by Carnegie University.⁶⁵ Finally, to manage mass balances and evaluate (eco-)toxicity values the EATOS (*Environmental Assessment Tool for Organic Syntheses*) constitutes a viable solution.⁶⁶

Results and discussion

In this work, the possibility to convert β -MCH, the major by-product in the epichlorohydrin industrial plant, into a value-added product such as glycidol was studied. β -MCH was obtained by glycerol hydrochlorination using acetic acid as catalyst in a gas-liquid semi batch reactor. The production of glycidol using a mixture of α -MCH and β -MCH, which represent the reaction products of the first chlorination of glycerol (Figure 2) has been also investigated. In this way, the distillation step to separate the two isomers (α -MCH and β -MCH) could be removed. According to previously published results by Santacesaria⁶⁷ glycerol was successfully chlorinated with HCl in 4 h at 100°C and quantitatively converted to a mixture of chlorohydrins (Figure 4).

Under these operative conditions, 7.5% in moles of β -MCH was obtained and, at the same time, the major product was the α,γ -DCH (89.5% in moles). Moreover, only a slight amount of α -MCH and β,γ -DCH was detected (0.6 and 2.4% in moles, respectively). The chlorohydrins mixture was separated by distillation. In the first step, dichlorohydrins (α,γ -DCH and β,γ -DCH) were removed due to their lower boiling point (respectively 174 and 184°C) compared to that of monochlorohydrins (213 for α -MCH and 268°C for β -MCH). Monochlorohydrins mixture was conveniently converted (yield of 99%) with high selectivity (100%) to glycidol at room temperature in an alcoholic solution of KOH in only 30 minutes. A significant increase in yield was observed compared to the results reported by Rider and co-workers³⁴ for the conversion of α -MCH to glycidol while, to the best of our knowledge, we performed the first preparation of glycidol from β -MCH. In order to better underline this aspect, that was certainly much more attractive if related to the

ECH production, we also prepared glycidol using pure β -MCH, obtained through monochlorohydrins mixture distillation. β -MCH was successfully converted into glycidol, in the same reaction conditions previously adopted for the mixture, with high yield and selectivity. Reaction schemes are shown in Figure 5.

In both cases, only KCl and water were formed as by-products after the reaction and ethanol could be removed by rotary evaporator and then reused. Glycidol production was promoted by the basic action of KOH that favor the chlorine elimination through oxiranic function formation. A schematic representation of the reaction mechanism is depicted in Figure 6.

In order to verify the feasibility of the innovative route, which seems to valorize more of the ECH chain, the simplified AES analysis was applied to compare the alternative pathway in which the β -MCH is recovered as a feedstock with the traditional process where this fraction is treated as a waste. Results from the preliminary assessment are collected, per each index, in Table 1.

As shown above and clearly depicted by the Figure 7, the adoption of the green chemistry principles at an early design stage leads to potential benefits: higher the green bars, greater the improvements reached per AES indicator. Numbers in bold represent the percentage reduction as a consequence of the innovative route application in comparison to the traditional one (red bars). Green metrics indicators seem to show great benefits except value

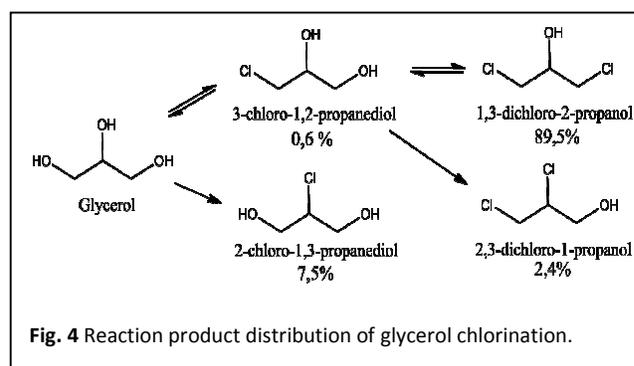


Fig. 4 Reaction product distribution of glycerol chlorination.

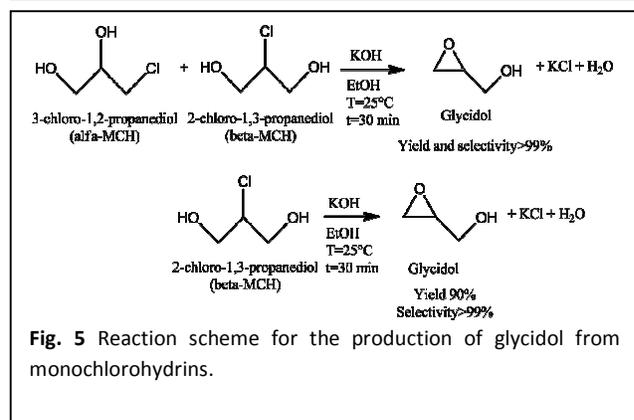


Fig. 5 Reaction scheme for the production of glycidol from monochlorohydrins.

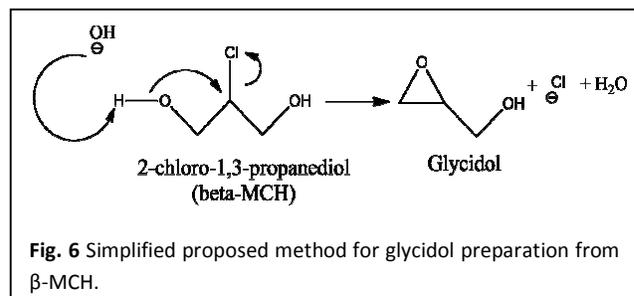


Fig. 6 Simplified proposed method for glycidol preparation from β -MCH.

reached for the PMI. cEF and AE achieve considerable decreases around 37% and 35% respectively. Almost 13.5g of β -MCH per 150g of glycerol are recovered by the alternative route and used as a substrate to synthesize glycidol (8.1g). This pathway drastically reduces the amount of substances to be treated and increases the quantity of the valuable products in the output mixture. The cEF decrease -which is directly proportional to the waste flows- underlines the importance behind the application of the first green chemistry principle, extending its meaning: the by-products mix has to be considered a high value mine of organic feedstock. This perspective results perfectly in line with the basic principles of the bio-refineries and more in general of the industrial ecology,⁶⁸ where undesired streams are avoided because byproducts are employed in replacement of fresh raw materials for other purposes and activities. In addition to the cEF, AE results to be positively affected by the increase of valuable substrates in the output flow. Both AE values are quite closer to the unit, however the avoided discharge of the β -MCH lead to a +3% in the final AE score which means a reduction of 35% if the difference to reach 100% is considered. This is a further confirmation of the reduction percentage shown previously: higher the amount of waste incorporated within the products, thus avoiding the discharge (lower cEF), closer the AE to the desired target. Differently from the former cases, the reduction of the PMI value is limited to 2%. Although the trend underlines some potential benefits as a consequence of the application of the green chemistry principles, the decrease is much lower than to the others. This is mainly driven by the fact that the innovative route does not use different amounts of raw materials, but it works on the output flows reducing the environmental load thanks to their recovery as a valuable substrate. Mass of the input raw materials (numerator) differs just in the amount of the auxiliaries (KOH and ETOH) used in the neutralization and distillation procedures (see **Table S1**). However, these quantities are necessary to recover more than 201g of valuable products which is sensibly higher than the 193g of the traditional route.

Although benefits presented above seem higher if compared with the scores reached by the other indicators, in order to avoid hasty conclusions, the nature of the green metrics indexes should be taken into consideration during discussion. As reported earlier in

Performance index	Traditional	Innovative
cEF	0.1	4.0E-2
PMI	1.4	1.4
AE	93%	96%
CF (kg CO ₂ eq.)	3.8	2.3
WF (m ³)	2.4E-02	1.9E-02
CED (MJ _{eq.})	81.3	70.0
SS (Pt)	0.6	0.5

Tab. 1 AES assessment results of the alternative routes to chlorohydrins.

the manuscript they represent a quick and useful way to express the process performance in a *gate-to-gate* perspective, e.i. without considering the embodied and avoided impacts among the entire chain. Therefore, the adoption of a life cycle approach becomes essential to evaluate these indirect effects. According to the **Figure S1** and the **Figure S2**, the LCA analysis considers the avoided production of glycidol starting from allyl alcohol, which constitutes the main route nowadays. Therefore, this approach (well known as attributional LCA)⁶⁹ should be considered as a snapshot of the

actual worldwide situation. The avoided traditional route leads to a considerable improvement, depicted by bold values. CF^Y, always considered a fundamental indicator for the bio-based industry, shows a reduction around 33% of the cumulative impacts: 3.8 vs 2.3kg CO₂ eq. per kg of valuable products. The network tool was adopted in order to verify the contribution to the category. **Figure S3** clarifies the significant aid of the avoided traditional chain to glycidol, visualized by the use of green arrows: thicker are the flows higher is the avoided burden to the global score. On the contrary, thicker are the red arrows and higher is the contribution to the global score. In this case, an avoided production of 8.1g of glycidol from fossils helps to reduce the CF of 1.1kg CO₂ eq. per kg of valuable products. The network is useful to display which stage has the higher impacts within the entire chain. The avoided usage of ethyl acetate (solvent) contributes positively to CF with -0.4kg CO₂ eq. per FU. Moreover, even if not displayed by the network, the avoided use of allyl alcohol (replaced by glycerol) has its positive effect to the reduction: personal CF is around 2.8kg CO₂ eq. per kg of allyl alcohol produced.

Smaller reduction was evaluated in the case of WF (-20%). Great water requirements are due to the HCl and glycerol manufactures. (**Figure S4**) Rapeseed nowadays constitutes the major worldwide triglycerides source in the biodiesel and glycerol production, therefore non-dedicated crops seem necessary to mitigate the WF effects. On the other hand, contribution to WF of the HCl chain (almost 0.01m³ per functional unit) seems mainly driven by the energy requirements: electric grid is one of the major responsible of the embodied water withdrawals, in particular when thermoelectric systems are considered in the national mix. Given the higher energy consumption within the chemical industry (4.2 × 10¹⁰ GJ in 2010)⁷⁰ the evaluation of the WF as a rough estimation of the *water-energy* nexus seems mandatory to complete the discussion. Nevertheless, thanks to the benefits due to the avoided fossil-based pathway for glycidol the global WF score reaches potential reduction of 1/5 compared to the traditional route. CED, together with CF and WF, is a single-issue indicator which expresses the resources depletion considering their energy content (MJ_{eq.}). Process implementations, as a consequence of the green chemistry principles adoption, lead

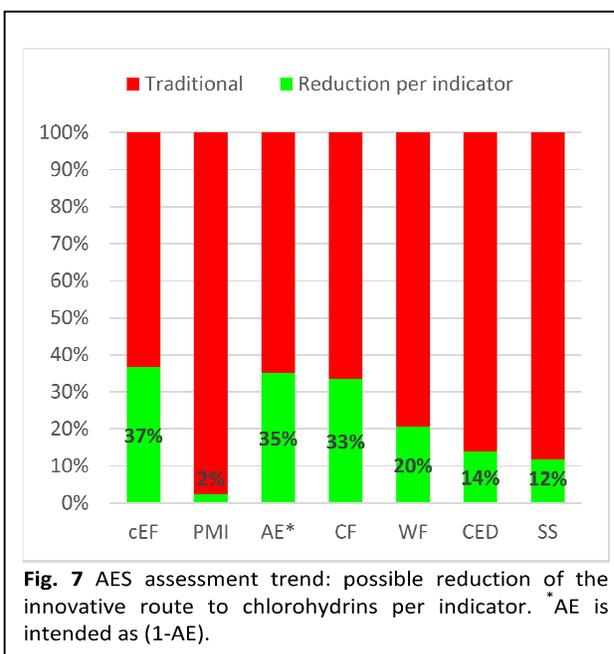
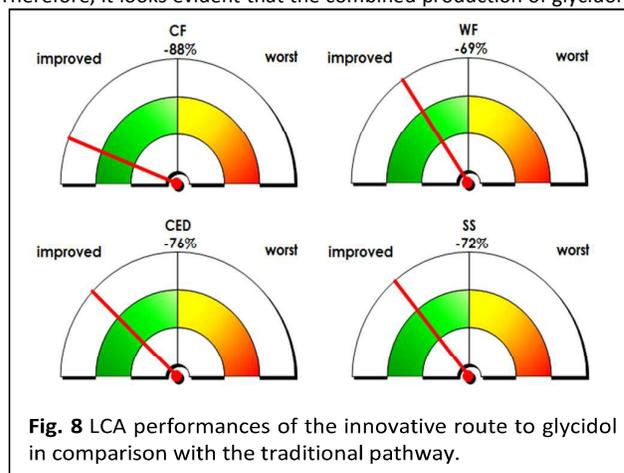


Fig. 7 AES assessment trend: possible reduction of the innovative route to chlorohydrins per indicator. *AE is intended as (1-AE).

to a sensible reduction of the environmental loads of 14% on laboratory scale. **Figure S5** collects the contribution of each resource typology to the cumulative score. As expected, the glycerol supply seems to be the principal parameter responsible for the final score with a renewable resources consumption around 42MJ eq. in both cases. However, the major benefits are reached in terms of fossils consumption: the avoided dispersion of the β -MCH and its exploitation as drop-in chemical to synthesize glycidol results in -40% of the fossil resources utilization (33 vs 20MJ_{eq.}). Using ReCiPe method (midpoint level), the same results were translated in terms of avoided fossil fuels extraction: almost -0.3kg of equivalent oil per kg of valuable products. This score is a further confirmation of the process mass efficiency intensification, which leads to the mitigation of the non-renewable resources depletion and of the overall socio-economic issues related with it. Moreover, as already suggested by literature,⁷¹ the CED method and its lower data requirement are relevant characteristics when products or processes on early design stage are under investigation, as a consequence of their limited information availability.

Finally, **Figure 7** shows a reduction around 12% of the ReCiPe single score (SS, evaluated using the endpoint level), a value that is quite similar to the previous one reached for the CED indicator. This comparable trend is not casual, since both CED and SS are considered valuable screening indicators of the overall impact of products, thanks to their ability to express a wide range of environmental burdens.^{6,72,73} In fact, the ReCiPe SS was adopted to cover eighteen impact categories which affect negatively the three main receptors: human health, ecosystems quality and resources depletion. **Figure S6** depicts considerable reduction in each case. Major benefits are obtained in the preservation of the resources availability: -34% mainly due to the avoided non-renewables glycidol manufacture and in particular to the embodied consumptions of the ethyl acetate chain, with an avoided contribution of -23.9mPt (**Figure S7**). On the other hand, reduction on the human health indicator is lower than the former (-19%). The main reason is the higher contribution of the climate change midpoint category (**Figure S8**). In fact, ReCiPe method is able to express CF value (kg CO₂ eq.) in terms of impact on climate change and then translate it into a double potential damage as a function of the average worldwide temperature increase: 1) on human health (increase of the health risks) and 2) on ecosystems quality (extinction of species). Other non-negligible contributions to human health come from the particulate matter formation and the human toxicity categories, both affected by the emissions during the energy supply chain. However, lowest reduction is reached in the case of the ecosystems quality (-4%, **Figure S6**) and the principal cause is the great contribution of the glycerol supply chain (**Figure S8** yellow bar) to that receptor, in particular to the agricultural land occupation and terrestrial eco-toxicity due to the use of fertilizers. The extended exploitation of fertilizers and the releases of P- and N-based compounds also affect the eutrophication of water, intended as fresh- and marine. In particular, the rapeseed cultivation (downstream process to glycerol) seems have greater negative effects on both eutrophication categories (5.8E-04kg of P eq. and 1.3 E-02kg of N eq. respectively) if compared with petrochemical-based glycerine (3.7E-04kg of P eq. and 1.2 E-04kg of N eq.).⁶¹ Therefore, in order to reduce all these negative contributions, the adoption of organic waste or non-dedicated crops as a triglycerides

source is required. So far our efforts were focused on the AES evaluation of the benefits (and drawbacks) as a consequence of the laboratory improvements in the chlorohydrins synthesis. However, the main goal achieved is the development of a high efficiency new route to glycidol from a process byproduct. Therefore, it seems appropriate to assess the potentialities of this innovative pathway in comparison to the basic route from fossil. Thus, a simplified cradle-to-gate approach was applied to the production of 1kg of glycidol (FU), comparing the use of allyl alcohol (**Figure S2** and **Table S2**) with glycerol. System boundaries for the innovative route are depicted in **Figure S9**. They are different from the previous reported above (**Figure S1**) as a consequence of the functional unit change (1kg of valuable products vs 1kg of glycidol). Therefore, **Figure S9** excludes the production of the α,γ -DCH and β,γ -DCH mixture from α -MCH. Nevertheless, differently from the fossil-based route, the innovative pathway is a multi-output process which also produces further valuable products (α,γ -DCH and β,γ -DCH): in this case, as already explained by literature,⁵⁷ an allocation procedure is mandatory to avoid the further system boundaries expansion and prevent mistakes in the assignment of the environmental impacts. A mass allocation was adopted on the basis of the mass yield for glycidol (**Table S3**). Results of the cradle-to-gate analysis are collected in the supporting information (see **Table S3**). In addition, the percentage reductions reached by the innovative route per each LCA indicator are depicted in **Figure 8** using the *greenness performance chart*: the more the pointer is directed to the green part, the greater will be the reduction achieved. Although the glycidol obtained from glycerol represents only the 7% of the inlet moles, since the process is more oriented to the α,γ -DCH/ β,γ -DCH mixture production (92%), the higher overall yield (99% vs 43% allyl alcohol to glycidol) and the greater selectivity (99% vs 93%) drive the innovative process to fewer amounts of discarded material per feedstock used and therefore to lower impacts per each LCA indicator. Greater reductions are reached in terms of CF (-88%) and CED (-76%), as a further confirmation of the maximization of the material efficiency due to the valorization of the β -MCH fraction. Therefore, it looks evident that the combined production of glycidol



within the ECH chain could be helpful to integrate or replace (depending on the market request) the traditional and less efficient fossil pathway.

In addition to the LCA analysis, GREEN MOTION[®] tool developed by MANE¹⁸ was adopted to verify the process performances of both routes to glycidol. GREEN MOTION[®] is a free and peer-reviewed methodology able to evaluate the process greenness and critical issues grouping the twelve green chemistry principles in seven fundamental concepts: raw material, solvent, hazard and toxicity of the reagents, reaction, process, hazard and toxicity of the final product and finally waste. More details can be found in literature.¹⁸

Figure 9 shows the results of the analysis: the greater the total score, the greener the route. Moreover, different colors are indexes of the process sustainability: red represents critical issues, light green indicates possibility to improve the pathway and dark green is an indicator of good choices. Given that the maximum value is 100, the traditional route to glycidol reaches the global score of 53 and seems still to have some critical aspects in particular in the raw material category (allyl alcohol is a fossil-based substrate) and in the solvent choice (ethyl acetate). In addition, unacceptable conditions are reached also in the case of the process requirements

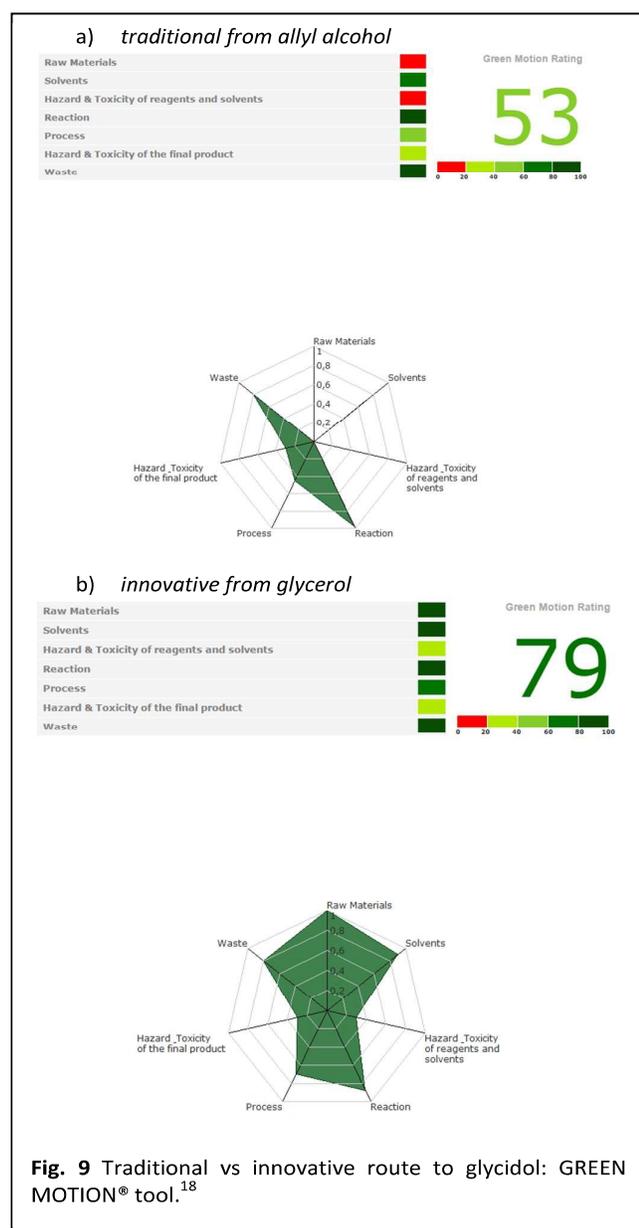
(e.g. reaction time of 4 hours and mass yield of 56%) and in terms of product hazardousness and toxicity, since glycidol is a toxic, explosive and flammable chemical. Given that the product hazardousness and toxicity are common to both routes and they do not depend from the pathway chosen, this indicator can be considered just as a further warning information for users. On the other hand, the lower reaction time (30 min.), the higher mass yield (60%), the usage of a more eco-friendly solvent (EtOH) and renewable feedstock (glycerol) lead the final score of the alternative route to 79 and confirm its higher sustainability.

Results presented so far refer in large part to direct experimental measurements carried out during the development of the innovative synthetic pathway. Therefore, according with the *pedigree matrix* on life cycle inventories by Weidema and Wesnaes,⁷⁴ they represent a valuable and reliable source of data to complete LCA models, and a good approximation of trend on industrial scale. Chemical yield, selectivity and conversion are expected to remain the same during the scaling up. On the contrary, some differences could be revealed in the energy consumptions, in particular during the distillation procedures (average literature data).⁷⁵ Therefore, a detailed feasibility study prior to commercialization is recommended. Together with the environmental and economic evaluations, a sensibility analysis (e.g. Monte Carlo) is strongly suggested to assess results variability as a consequence of different ranges of uncertainty (higher for estimations).

Conclusions

The adoption of the green chemistry principles at the early design stage is a fundamental way to add value (economic and environmental) to the new synthetic routes. However, sustainability behind the application of these principles has to be verified by a preliminary assessment. In this manuscript, we proposed a simplified AES analysis of a new route aimed to enhance the process efficiency in the synthesis of the chlorohydrins. The AES assessment was thought in a simplified way to encourage its adoption as a support and screening tool of the laboratory experiments: inorganic and organic chemists should check the environmental benefits of their research activity in order to direct the efforts on the main critical issues. Even if simplified, the AES approach proposed includes the investigation of several indicators. Among these, green chemistry process metrics are easy to apply and able to predict wide range of process performances in terms of waste production, atom efficiency and raw materials utilized. Nevertheless, as outlined above, the gate-to-gate and non standardized approach represents the main limitation. Therefore, a widely-recognized approach like the cradle-to-gate life cycle analysis seems necessary to support the discussion. Moreover, according with an already published methodology,⁵⁷ several indicators are recommended when bio-based processes are under investigation: *i*) CF to verify carbon neutrality or not, *ii*) WF to assess water withdrawal within the chain, *iii*) CED to simulate resources requirements and *iv*) SS as a cumulative indicator of the environmental impacts.

In this study, the recovery of the β -MCH fraction from the products mixture of the glycerol chlorination and its utilization as a starting feedstock in the glycidol synthesis seem to increase the environmental sustainability of the entire ECH chain. Moreover, the replacement of the fossil-based glycidol with the alternative bio-



based leads to potential reduction in the environmental loads as a consequence of the maximization of the overall process efficiency thanks to the recovery of a waste stream. Therefore, results from the AES assessment show overall potential benefits in the environmental sphere; for that reason the development on industrial scale could be suggested as an affordable solution, subject to prior detailed economic analysis.

The approach presented in the manuscript, finalized to the waste valorization through the production of valuable products, is in line with the basic principles proposed by the *industrial symbiosis*:⁷⁶ utilization of a waste stream as a starting raw material in a different production. However, this way of thinking was always part of our society since the beginning. Well-known is the quote of August Wilhelm von Hoffman, German chemist who declared in 1848 "*in an ideal chemical factory there is, strictly speaking, no waste but only products. The better a real factory makes use of its waste, the closer it gets to its ideal, the bigger is the profit*".

Therefore, it looks clear how it represents the key approach to close the cycles, mitigate the emissions and prevent the resources depletion in order to pursue the targets suggested by the sustainable development.

Abbreviations

α -MCH	3-chloro-1,2-propanediol
β -MCH	2-chloro-1,3-propanediol
α,β -DCH	2,3-dichloro-1-propanol
α,γ -DCH	1,3-dichloro-2-propanol
AE	Atom Economy
CED	Cumulative Energy Demand
CF	Carbon Footprint
EATOS	Environmental Assessment Tool for Organic Syntheses
ECH	Epichlorohydrin
EPA	US Environmental Protection Agency
EtOH	Ethanol
FID	Flame Ionization Detector
FU	Functional Unit
GC	Gas Chromatographic
GHG	Greenhouse gases
GREENSCOPE	Gauging Reaction Effectiveness for ENvironmental Sustainability of Chemistries with a multi-Objective Process Evaluator
GWP	Global Warming Potential
IPCC	Intergovernmental Panel on Climate Change
LCA	Life Cycle Assessment
PMI	Process Mass Intensity

RME	Reaction Mass Efficiency
SS	Single Score
TS-1	Titanium Silicate
WF	Water Footprint

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Notes and references

[†] Accepted CF definition according with literature⁷⁷ is "the measure of the total amount of carbon dioxide (CO₂) and methane (CH₄) emissions of a defined population, system or activity, considering all relevant sources, sinks and storage within the spatial and temporal boundary of the population, system or activity of interest and calculated as carbon dioxide equivalent (CO₂ eq.)".

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