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MINI-REVIEW

Experimental methods in chemical engineering: Hazard and operability analysis—HAZOP

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Abstract

Hazards and operability analysis (HAZOP) is one of a dozen-structured Process Hazards Analysis (PHA) methodologies that assess risks associated with operating processes to mitigate their consequences. HAZOP applies to all six stages of process design from discovery to decommissioning. Industry massively adopted PHA methodologies as a consequence of several industrial disasters in the 1970s that increased society's scrutiny of chemical operations. HAZOPs are conducted by multidisciplinary teams that rely on a set of guide words in combination with the system parameters to identify deviations from the design intent. The team discuss the causes and consequences of deviations, and the project owner modifies the process accordingly. It relies on heuristics rather than algorithms, so the formal structure gives practitioners the false sense that the analysis is comprehensive. Academic institutions increasingly apply PHAs to experimental work, but the scope of a HAZOP is often ill-suited for this environment as it requires dedicated personnel with particular expertise. Here, we outline the essential features of a HAZOP analysis for early career researchers engaging in process development for conditions that include, for example, high temperature, high pressure, toxic compounds (Hg, phosgene, CO), and potentially explosive and flammable mixtures like organic peroxides. Web of Science indexed over 100 000 documents that mention safety in 2021 and assigned 1500 to chemical engineering. A bibliometric analysis grouped them into five clusters: (1) lithium ion batteries and nanoparticles, (2) fire, simulation, and combustion, (3) models, risk, systems, and techniques (including HAZOP), (3) models, risk, systems, and techniques (including HAZOP), (4) water treatment, and (5) mechanisms and thermal runaway.

KEYWORDS

deviation, guideword, hazard and operability analysis, hazard assessment, safety

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1 | INTRODUCTION

Safety is a top priority in the chemical industry and has its origins in the early 19th century to manufacture black powder.[1] Milling powder was hazardous due to the risk of explosion, so E. I. du Pont designed a building with solid stone on three sides and with a side made of wood facing the creek.[2] This configuration dissipated the energy from explosions to the other side of the creek that was uninhabited. However, in the 1970s and 1980s, several major disasters shook the confidence of society in industry, so the Canadian government tasked chemical companies with identifying how they could best regulate the industry.[3] Twelve chemical industry leaders initiated Responsible Care® that applied systems to identify practices to ensure safety for workers, communities, and the environment. This management system has expanded beyond Canada to include 73 countries and all society's expectations, including sustainability.[4]

The Organisation for Economic Co-operation and Development (OECD) recorded 30–40 major accidents per year since 1990 (Figure 1). According to the Major Accident Reporting System (MARS) of the European union, the biggest contributors were the chemical manufacturing industry, the petrochemical industry, and the metallurgical industry, with a total of 295, 240, and 70 major accidents, respectively.[5] The chemical industry contributes to roughly 10% of the North American and European gross domestic product (GDP).[6] However, the GDP has doubled since 1980, while the number of accidents has remained essentially constant, which demonstrates that the commitment to safety has improved with time.

Several structured process hazard analysis (PHA) methodologies have been developed along side Responsible Care® (Table 1): HAZOP, 'What-If' (What-If Checklist), failure modes and affects analysis (FMEA), fault-tree analysis (FTA) and event-tree analysis (ETA), cause–consequence analysis, and bow-tie analysis.[7]

HAZOP is one of the most structured techniques to study hazards and operability problems, which explores the effects of any deviations from design and operating conditions. It has its origins in the 1970s, developed by the Imperial Chemical Industries (ICI), but it really became a standard after an explosion in a chemical plant producing nylon intermediate in the United Kingdom that killed 28 people and injured dozens of others (Figure 2). What emerged from this disaster was the need to properly address the management of change (MOC) within a system, including the constant revision and implementation of modifications and improvements. Since then, they have been frequently applied in the chemical and petroleum industries and other sectors like for carbon sequestration processes and hydrogen-related

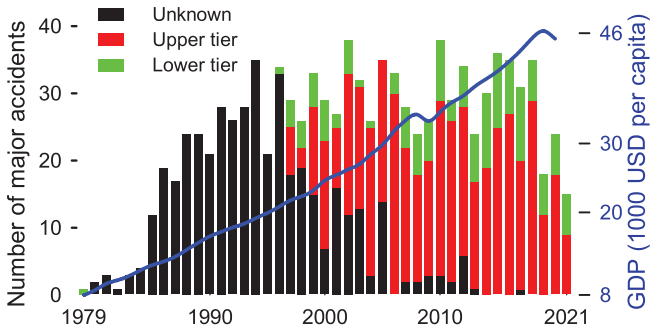

FIGURE 1 Number of major accidents reported by the Organisation for Economic Co-operation and Development (OECD) countries.[5] The blue line represents the growth in gross domestic product (GDP) of OECD countries over the same period. The chemical industry contributes about 10% of the GDP[6]

facilities.[8] HAZOP has become a standard activity in the design of the process systems to obtain safer, more efficient, and more reliable infrastructures.[9] It assumes that any operation problem that may arise in a system or equipment will be the cause of the deviation from the normal operation of a variable or parameter of the related context. The concept of HAZOP study was originally developed by engineers in the United Kingdom, in the mid 1970s, and first appeared intending to detect possible hazards that may occur in systems that manage highly hazardous materials, including harmful, flammable, and unstable compounds.[10] The identification of hazards is fundamental to ensure the safe design and operation of a system at different levels, including pilot plant development, executive design, operation, and decommissioning. The ultimate purpose was to eliminate any cause leading to major accidents, including fire, explosions, and toxic releases. HAZOP is the focus of much of the research to improve the safety of chemical plants that encompass increasingly more complex and sophisticated processes.

From a historical perspective, HAZOP studies were formulated as a disciplined procedure to detect deviations from design operations (equipment focus). Later, the principles were adapted to analyze more complicated processes. The switch from equipment-oriented to process-oriented processes required a rigorous, thorough, systematic, and multidisciplinary methodology. HAZOP studies that analyze the safety implications of the design and operation of systems are essential in any industry where safety is a particular concern.[11] Over four decades, since the first appearance of HAZOP as a PHA strategy,[12] the evolution of HAZOP has been realized according to a plethora of publications, books, and internal corporate guidelines from process industries. Among the most important contributions to this field are those of Kletz,[13] Nolan,[14] Mannan,[15] McDonald and

TABLE 1 Techniques for risk assessment

Method	Approach	Level of detail	Domain of application
Checklist	Inductive	Low	Simple systems
Preliminary hazard analysis	Inductive	Low	Simple systems
What if	Inductive	Medium	Various systems
HAZOP	Inductive	Medium	Various systems, procedures, and control logics
Fault-tree	Deductive	High	Undesired events previously identified (chains)
Event-tree	Inductive	High	Failure events previously identified
Common cause failure analysis	Inductive	Medium	Failure events
Vulnerability analysis	Inductive	Low	Simple systems

Abbreviation: HAZOP, hazards and operability analysis.

FIGURE 2 Nypro UK Flixborough chemical site after a cyclohexanone vapour cloud detonated (1974). PA/Alamy stock photo https://www.alamy.com/stock-photo-disaster-flixborough-explosion-nypro-uk-chemical-plant-north-lincolnshire-107574100.html

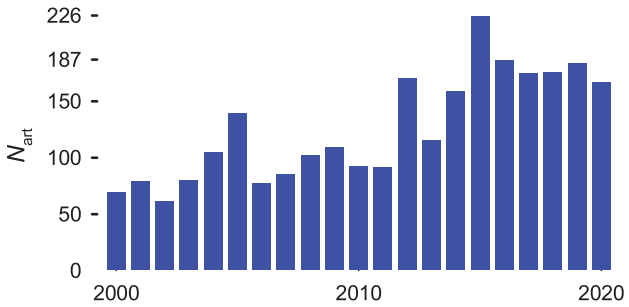

FIGURE 3 Number of articles concerning the hazards and operability analysis (HAZOP) versus time (Elsevier Science Direct)

Mackay,[16] and Lawley.[10] As an example, Nolan[14] compared the HAZOP and 'What-If' technique also concerning time and cost requirements, whereas Kletz[13] has given a detailed specialized background of the HAZOP technique. In 2001, the British Standard published BS IEC 61882:2016 concerning HAZOP and, in the 2016 update, provided guidance on its application, including definition, preparation of examination sessions, documentation, and follow-up. The guidelines proposed in the study by Andow can be taken as reference in the structured application of HAZOP,[17] whereas BS IEC 61882 discusses the standard key requirements for carrying out a HAZOP. Additional resources are available to support hazard evaluation studies, including those developed by the Center of Chemical Process Safety (CCPS).[18,19]

The discipline continues to innovate, as evidenced by the 2600 articles indexed in ScienceDirect® with 150 new articles annually (Figure 3).[20,21]

This mini-review is part of a series of dedicated articles on experimental methods in chemical engineering.[22] A HAZOP study systematically examines planned and existing processes, systems, and operations. Students, engineers, and operators apply it at all stages in the design, construction, and operation phases of a process. Here, we discuss the basic theory of any structured HAZOP approach, typical applications, and limitations and issues related to HAZOP applicability and outcomes.

2 | THEORY

A HAZOP analysis considers a full description of a system and examines every part of it to identify deviations from the design intention and assesses their causes and the consequences.[15] The basic idea is to creatively brainstorm in a controlled fashion to determine all possible ways that a process or operation fails (Figure 4). The focus of HAZOP analyses is to manage very hazardous materials in chemical plants and mitigate their risks. A comprehensive HAZOP now considers situations that can be reasonably expected during the lifetime of the system and extends to systems and sectors beyond the chemical industry. Together with a structured approach, a well-defined set of

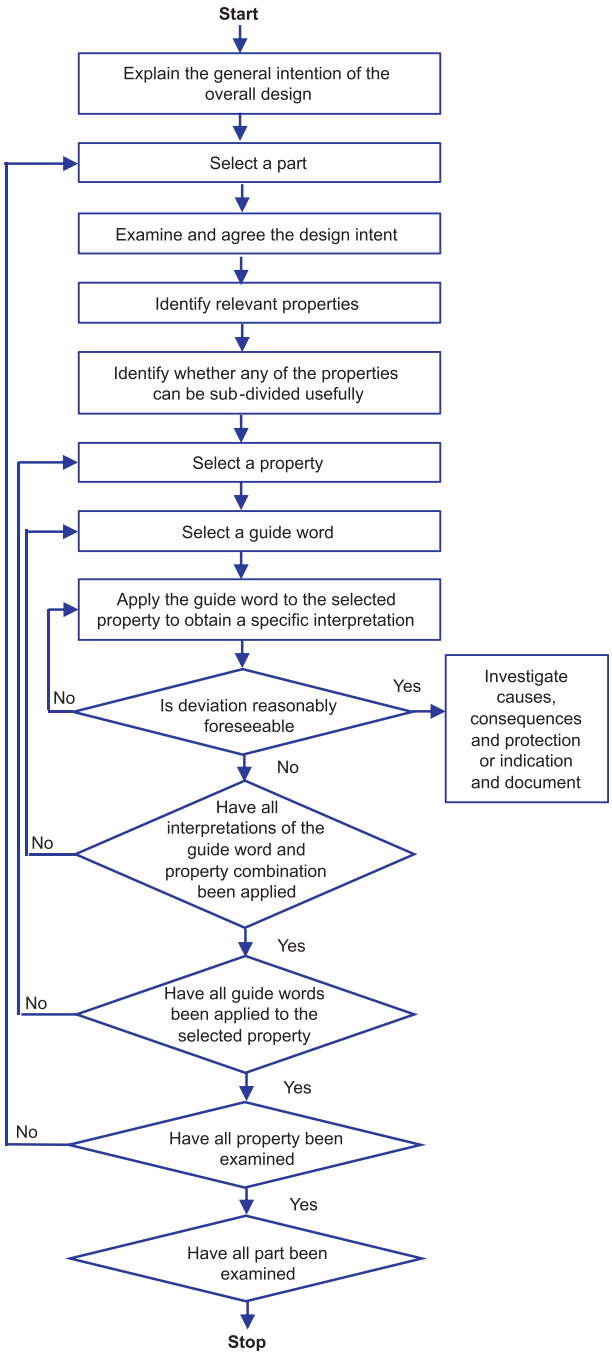

FIGURE 4 Flow chart of the hazards and operability analysis (HAZOP) examination procedure. Adapted from Reference [23]

terms was developed to communicate precisely the elements of the analysis and document the results (Table 2).

2.1 | Study initiation and preparation

The first step of a HAZOP is to collect detailed information on the system: up-to-date process flow diagrams (PFD), process and instrumentation diagrams (P&IDs), equipment specifications, materials of construction, and mass and energy balances. During the design process, a HAZOP will identify areas that engineers must consider to minimize threats (Figure 5). However, the HAZOP technique is not a substitute for a good design.[24]

The HAZOP scope depends on several aspects, including the physical boundaries of the system, the number and level of detail, technical documentation, the scope of any previous studies, and regulatory requirements, standards, and applicable norms. It is carried out by a dedicated multidisciplinary team under the guidance of an experienced study leader. The team comprises a cross-section of

TABLE 2 HAZOP terms and definitions

Availability	The probability that equipment or control system performs the intended task
Characteristic	Qualitative or quantitative property
Consequence	The outcome of an event affecting objectives
Control	Measure that is modifying risk
Design intent	Designer desired or specified range of behaviour for properties that ensure an item fulfils its requirements
Property	Constituent of a part, which serves to identify its essential features
Guide word	Word or phrase that expresses and defines a specific type of deviation from a design intent of a property
Hazard	Source of potential harm
Level of risk	The magnitude of risk or combination of risks expressed in terms of the combination of consequences and their likelihood
Part	Section of the system that is the subject of immediate study
Node	A section into which the system or process is divided for detailed review (a pipe section, vessel, step of a procedure for batch processes, etc.). The intended function and operation of each node can be adequately defined
Risk	Effect of uncertainty on objectives. The risk results from the combination of the frequency and consequence of an event
Risk identification	Process of finding, recognizing, and describing risks
Risk source	The element which alone or in combination has the intrinsic potential to introduce a risk
Risk treatment	The process of modifying a risk

Abbreviation: HAZOP, hazards and operability analysis.

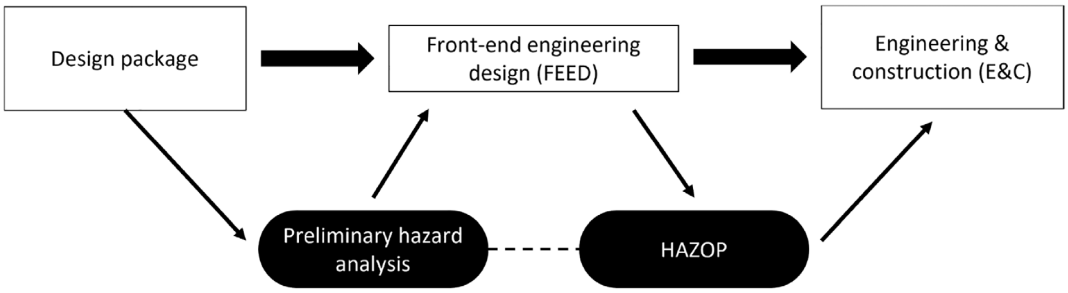

FIGURE 5 System design and safety analysis before the construction of a system. Adapted from McDonald and Mackay.[16] HAZOP, hazards and operability analysis

FIGURE 6 Deviation in hazards and operability analysis (HAZOP): the combination of guideword and system parameter

trained plant, laboratory, technical, and safety specialists and is directed by a HAZOP leader. The definition of roles and responsibilities is a key step at the onset of the study. The viewpoint of the designer and user of the system examined in the HAZOP study is always required.

2.2 | HAZOP study

The HAZOP is a hierarchical procedure, consisting in the following steps (Figure 4):

- selection of a section of the plant/process and explanation of the design intent;
- definition of the purpose of the HAZOP and boundaries of the study;
- formation of the HAZOP multidisciplinary team;
- identification of the important parameters to be studied;
- development of a list of deviations by combining guide-words and parameters;
- for each deviation, identify potential causes, consequences, frequency of deviation, and risk management strategies[25]; and,
- reporting.

The choice of properties and parameters depends on the application and includes the materials involved, the activity being carried out, and the equipment employed. Typical process parameters include flow, level, temperature, pressure, concentration, pH, viscosity, aggregation state, volume, mixing, and reaction. A guide word is applied to the parameter to suggest possible deviations

TABLE 3 Examples of basic guide words and associated deviation types with instances of interpretation for the process industry

Deviation	Guide word	Example of interpretation
Negative	NO	No part of the intention is achieved (e.g., no flow, no concentration)
Quantitative modification	MORE	Quantitative increase (e.g., higher flow rate, higher temperature)
	LESS	A quantitative decrease (e.g., lower flow rate, lower temperature)
Qualitative modification	PART OF	Only some of the design intentions are achieved (e.g., part of fluid transfer)
	AS WELL AS	All design intentions are achieved along with additional activities (presence of impurities, simultaneous execution of another operation)
Substitution	REVERSE	The logical opposite of (reverse flow in pipes, reverse chemical reactions)
	OTHER THAN	A result other than the original intention is achieved (e.g., complete substitution, transfer of wrong material)
Time	EARLY	Early relative to clock time (e.g., process operation, action, step)
	LATE	Late relative to clock time (e.g., process operation, action, step)
Order, sequence	BEFORE	Too early in a sequence (e.g., heating, mixing)
	AFTER	Too late in a sequence (e.g., heating, mixing)

from the design intent (Figure 6). When a possible deviation is identified, we determine the possible causes and consequences that include operational problems or hazards of minor or major concerns.

Typical causes of a deviation belong to the following components of a system:

- hardware (equipment, piping, instrumentation, construction, and materials);
- software (specifications, instructions, and procedures);
- human (management, operations, and maintenance);
- external (services, natural events, and intentional malicious actions).

If there are likely to be numerous causes for a single identified deviation, we brainstorm to diagnose as many causes as possible. All considered causes should be realistic and clearly described because broadly similar causes may lead to different consequences (Table 3).[12] The combinations of property and guide words ask for different interpretations based on the system considered, the phase of the system life cycle, and the available design representation. Some combinations might have no meaning for a given study.

HAZOP analyses consider instrumentation that detects/indicates a deviation along with the expected response. Safeguards encompass hardware and procedures, including relief systems, manual valves, standby pumps, additional sequences, alarms and trips, emergency cooling, detectors, and explosion protection systems. Required actions to treat the risk should be specified, including changes that are expected in other parts of the system because of the recommended modifications. However, when assessing consequences, we exclude considering protective systems or instruments that are already included in the design. However, such systems require proper maintenance and inspection to ensure the desired reliability. Experimental equipment could be highly susceptible to this aspect because of diverse test conditions and users- and even prolonged shutdown periods.

When documenting consequences, we have to keep in mind that a HAZOP estimates the risk, and therefore, an exhaustive description of how hazards develop and their consequences are pertinent. Acceptable risk involves trade-offs between the frequency and the magnitude of an identified scenario. Low-frequency events with minor consequences should not sidetrack the effort in HAZOP, and they may often be declared as acceptable, without wasting time on searching for causes. In this framework, a company may choose to assess the risk with worst-case consequences, with existing safeguards, and with proposed actions. This concept can be expressed in a risk matrix that is a simple mechanism to increase visibility of risks and assist management decision making (Figure 7). Accordingly, we document the worst-case consequences, the mitigation with existing safeguards, and the effects of proposed actions.

The HAZOP team also has the responsibility to investigate what is known about consequences and possible cascade events. Loss of cooling water is the event that cascades to a runaway reaction, vessel over pressure, and release of chemicals is an example.[26] The study produces minutes or uses software to record the deviations, their causes, consequences, and recommended actions.[15,16,20] Depending on regulatory requirements, contractual obligations, company policies, the need for study auditability, and the time and resources available, the entire process is recorded to document all actions taken. This provides evidence that the HAZOP study satisfies regulatory and corporate requirements. Instead of recording the whole proceedings, the documentation may focus on the identified risks and operability issues together with the follow-up actions, excluding deviations that do not lead to risk scenarios.

Software tools are available to guide the team through the process and the outputs include:

- details of identified deviations and risks, including solutions for detection and management;
- recommendations for risk treatment;
- a list of all the parts included in the study, along with a list of the guide words and properties investigated;
- drawings, specifications, datasheets, reports, and recordings.

A worksheet documents the results and comprises a progressive reference number, guide word, property, deviation, cause, consequences, existing controls, and suggested actions (Table 4). The header contains the project name, subject of the study, design intent, part of the system put in analysis, members of the team, drawings examined, date, and page number.

We include a reference column so that each entry can be referred to from other analysis strategies and also allows for traceability to subsequent analysis such as layer of protection analysis (LOPA).[27] Additional information like comments on action items, the responsibility for the action, and the status of the action can also be documented. The final HAZOP study report for the project owner and includes:

- summary;
- conclusions and outputs;

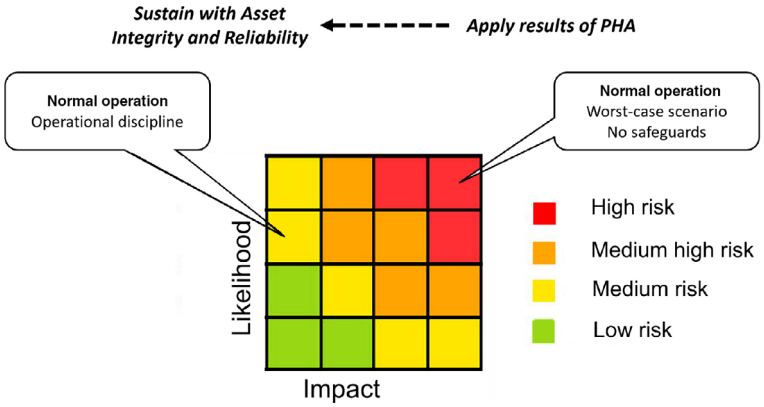

FIGURE 7 Risk matrix considering likelihood of an event (*y*-axis) and its impact (*x*-axis). Risk is the product of likelihood versus impact. PHA, process hazards analysis

TABLE 4 HAZOP worksheet

HAZOP study report	**Project name**			**Reference drawings**	**Revision no.**
Team members				Date	Sheet no. Meeting no.
Part considered, design intent					
Hazard (event or situation)	Causes (sequence of events)	Consequences (immediate, ultimate)	Likelihood, prevention	Emergency measures, mitigation	Action

Abbreviation: HAZOP, hazards and operability analysis.

- scope and objectives;
- worksheets;
- marked-up design representation;
- list of the drawings and documentation referred to;
- historical information used in the HAZOP analysis.

2.3 | After the study

From a methodological perspective, after recommendations are applied, the team revises the context and documentation and might re-valuate the process. The team reviews the design, operation, and maintenance to ensure that no new problems emerge. For instance, when the team identifies a risk whose mitigation is critical to operate the process (by law or internal standards), the team performs an additional HAZOP (full or partial) to ensure the changes are implemented before starting the system or putting it back online.

HAZOP issues are categorized as:

- significant hazard;
- minor hazard;
- standards/operability issues;
- deferred problems; and,
- line diagram errors.

Minor hazards are addressed by the HAZOP team who suggest simple safeguards during the study. Significant hazards may be deferred, and in any case, the PHA team has the only role of identifying hazards, assessing risks, and formulating recommendations.

Safeguards should be decided according to the expected frequency of an event and the severity of the consequences. In this way, risk reduction can be properly addressed with the most appropriate layer of protection. In general, the safeguard should help to reduce the occurrence frequency of the deviation or to mitigate its consequences and, in principle, can be categorized into five categories[28]:

a. Inherent: by minimizing or possibly eliminating the hazard;
b. Spatial: for reducing the hazardous effects (distance and segregation);
c. Passive: process and equipment design features that reduce frequency or consequence without the active functioning of any device or requiring human input (e.g., storage tank dike and fence);
d. Active: safety controls, alarms, and interlocks to detect and respond to deviations;
e. Procedural: management approaches to prevent incidents or minimize the consequences (e.g., policies,

operating procedures, training, administrative checks, etc.).

Typical examples in the process industry include:

- relief systems, pressure relief valves, and rupture disks;
- manual emergency systems, including isolation valves or non-return valves;
- standby pumping system with alarms;
- restrictors against overflow (one-way valves);
- reduction of exposure and mitigation of consequences;
- back-up and independent alarms;
- alarms, interlocks, and safety trips;
- emergency cooling, explosion suppression, and fire deluge systems.

3 | APPLICATIONS

The Web of Science (WoS) has indexed over 1 million articles with safety as a keyword in the search category topic and assigns at least 10 000 articles to 55 of the 250 scientific categories. Pharmacology/pharmacy has the most articles (74 100), followed by electrical/electronic engineering (51 700), and surgery (50 600), while chemical engineering ranks 37th with over 15 000. Since 2017, chemical engineering journals published 5000 articles that mention safety. The subject is attracting more interest as the number of published articles per year has grown from 381 in 2010 to almost 1500 in 2021. The journals that publish the most are (since 2018): *Journal of Loss Prevention in the Process Industries* (536 articles), *Process Safety and Environmental Protection* (531), *Chemical Engineering Journal* (344), *Process Safety Progress* (283), and *Processes* (195).

Battery safety has been the hottest topic and *Energy and Environmental Sciences* has published 4 papers that have more than 350 citations in 4 years: 'New Horizons for Inorganic Solid State Ion Conductors',[29] 'An Extremely Safe and Wearable Solid-State Zinc Ion Battery Based on a Hierarchical Structured Polymer Electrolyte',[30] 'Issues and Opportunities Facing Aqueous Zinc-Ion Batteries',[31] and 'Long-Life and Deeply Rechargeable Aqueous Zn Anodes Enabled by a Multifunctional Brightener-Inspired Interphase'.[32] *The Canadian Journal of Chemical Engineering* has published 1 article since 2018, while 43 journals published 25 or more articles during this time period. The top cited articles in *The Canadian Journal of Chemical Engineering* have focused on plant statistics and reviews/surveys: 'Survey on the Theoretical Research and Engineering Applications of Multivariate Statistics Process Monitoring Algorithms: 2008–2017' (114 citations and the 33rd highest number of citations),[33] 'Chemical Engineering Research Synergies Across Scientific Categories' (22 citations),[34] 'A Novel Data-Driven Methodology for Fault Detection and Dynamic Risk Assessment' (9 citations),[35] and 'Two-Level Multi-Block Operating Performance Optimality Assessment for Plant-Wide Processes' (8 citations).[36]

To evaluate the most prolific research areas related to safety in chemical engineering, we built a bibliometric map of articles using WoS to the category since 2018 (Figure 8). VOSViewer software identified five clusters of research based on co-occurrences of the keywords. The most prolific category is lithium ion batteries (LIB) (red) with 30 of the 110 most mentioned keywords, closely followed by fire (which includes simulation and combustion [green] with 28 keywords). HAZOP is in the blue cluster that is centred on models, risk, and systems (25 keywords). The yellow cluster relates mostly to water treatment (16 keywords), while the magenta cluster (11 keywords) is related to modelling and includes mechanism and thermal runaway.

The objectives of a HAZOP study are to[20]:

- identify all deviations from the normal operation, including causes, and all associated hazards and operability problems;
- decide whether actions are to be taken to control the hazards and/or operability problems;
- identify cases where a decision should be postponed;
- ensure that agreed actions are followed up;
- make operators aware of hazards and operability problems.

In addition, the HAZOP strategy is of valuable support in the identification of reasonable scenarios also in emerging infrastructures, processes, and research.[39,40] Several accidents in universities have reinforced the need to adopt stricter controls and reviews of experiments on flammable and hazardous gases, and operations at high pressure or temperature.

Although the design of a system and plant relies upon the application of codes, standards, and technical regulations and practice, the HAZOP strategy allows the opportunity to supplement these with structured anticipation of the deviations that can occur because of, for example, process operations and conditions, equipment failures, or operator errors. HAZOP studies correct errors and oversights that may emerge during the project schedule before such changes become too expensive. In a university setting, this rigour requires that researchers take the time to evaluate potential risks.

HAZOP is best suited for assessing hazards and risks in facilities, processes, and equipment as it assesses systems from various perspectives. The main applications in

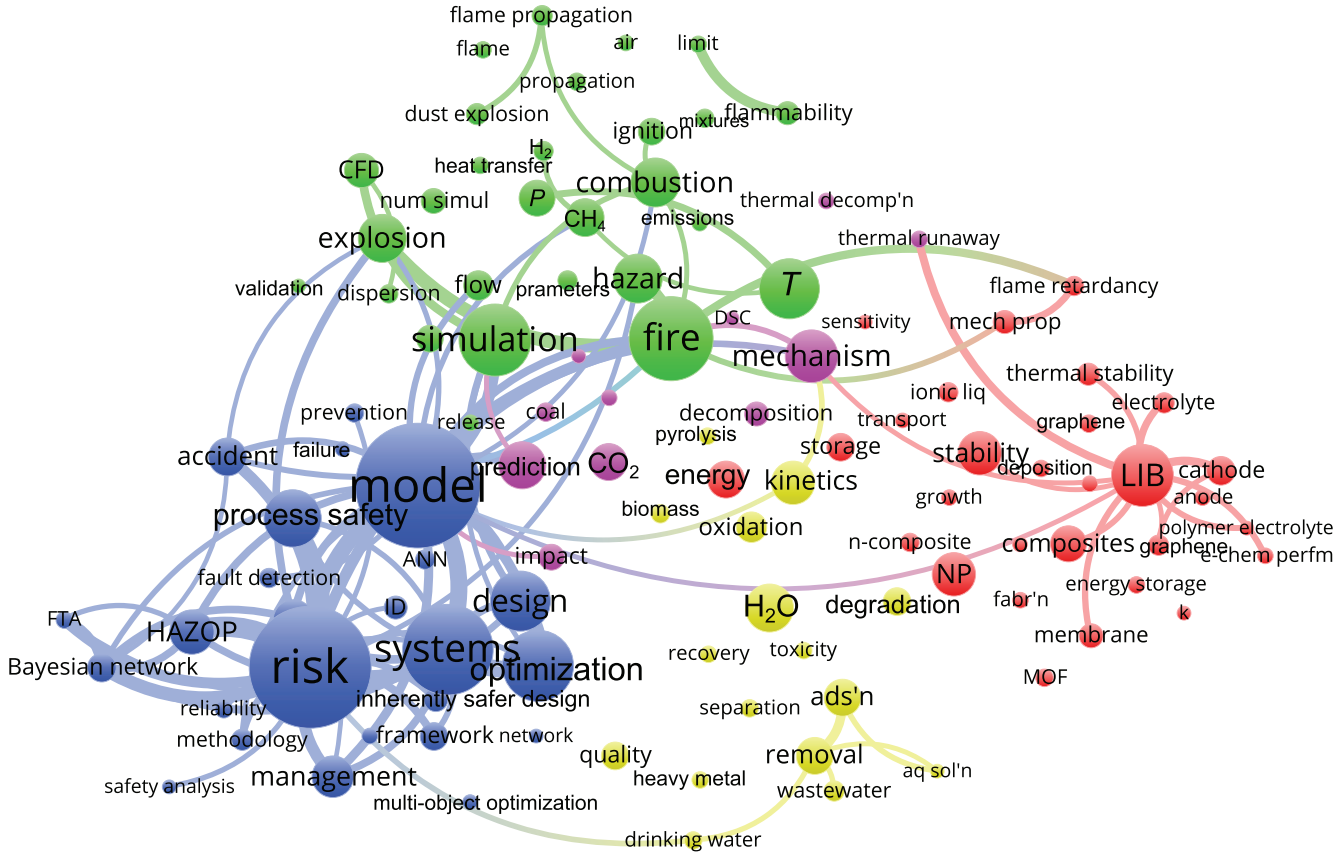

FIGURE 8 Safety keyword map derived from 5400 articles in the chemical engineering category of Web of Science indexed from 2018 to 2021.[37] VOSviewer assigns the same colour to keywords that occur in the same articles and groups them in the same region of the chart. The size of the circle and font size correlate with how many articles cite the keyword.[38] It consists of 110 keywords that occur most: red (30 keywords): LIB (424 articles), green (28): degradation (259 articles), blue (25): model (381 articles and 137 articles with HAZOP), yellow (16): H_2O (148 articles), and magenta (11): mechanism (161 articles). The smallest circles represent 44 articles, and the lines represent citation links. ads'n, adsorption; ANN, artificial neural network; aq sol'n, aqueous solution; C, carbon; CFD, computational fluid dynamics; k, conductivity; DSC, differential scanning calorimetry; e-chem perf, electrochemical performance; fabr'n, fabrication; FTA, fault-tree analysis; HAZOP, hazards and operability analysis; LIB, litium ion battery; mech prop, mechanical properties; MOF, metal organic framework; multi obj optimiz'n, multi objective optimization; n-composite, nanocomposite; NP, nanoparticle; num simul, numerical simulation, *P*, pressure, *T*, temperature; thermal decomp'n, thermal decomposition

the process industry include continuous processes, batch processes, and sequential operations. For example, the HAZOP analysis has been successfully applied at the preliminary stage of innovative processes to select among design options and to improve the conceptual design.[41]

One of the major complaints is the time it takes to prepare and approve and to collect the required information. Furthermore, researchers explore dozens of new chemistries and processes for which they frequently change reagents and operating conditions: at what point do they require to convene a process hazard review (PHR) committee? For these changes, a less onerous methodology is appropriate.

Graduate students and young researchers in academia also have to analyze their process with What-If, HAZOP, or a simple document listing the potential sources of risks. Together with the issues and limitations that HAZOP analyses in academia share with industry (miscommunication, incomplete information, incomplete expertise), other hurdles are faced by professors and students. HAZOPs may require several revisions that prolong the process for months and years. Dedicated staff are solicited heavily and fixing a date to meet with multiple individuals (department heads, technicians, and administration) is cumbersome. Furthermore, schools lack expertise and have guidelines to meet the needs of a broad audience rather than for specialized processes and equipment: the one size fits all kind of safety standard is inapplicable to HAZOPs. Chemical engineering has embraced a plethora of other disciplines within its fold (half of the chemical engineering departments have multiple designations—biochemical, biotechnology, material,

and petroleum).[42] Research in these departments span classic curricula (chemical reactors, transport phenomena, catalysts, and fluidization) to microbiology and vaccines. In the context of the entire university, HAZOP applies to laboratories in chemistry, biology, physics, and other engineering disciplines. Each field has its own specialized equipment and instrumentation with different hazards and risk factors, namely, corrosion, toxicity (chemical), flammability and reactive chemistry hazards (e.g., organic peroxides), bio-hazards, and radioactivity and hazards associated with experimental devices and pilot plants.[43] The cost to staff cross-functional teams at universities is cost prohibitive and thus requires intervention from outside companies with costs that can exceed the infrastructure to run the experiment. Industry build on their expertise while schools are ill-equipped to maintain such a broad mandate. An MSc takes less than 2 years to complete while a doctoral thesis in Europe is only 3 years. So an iterative HAZOP with dozens of revisions and (several hundred hours of team meetings and technician time) is untenable for students. An ideal HAZOP in an academic context includes: (1) thorough operating procedures, including all relevant documents (P&ID, safety datasheets, and equipment specifications); (2) a demonstration of the equipment; (3) HAZOP analysis to identify risks with recommendations to improve the safety; (4) a revision of the operating procedure and equipment to respond to the recommendation; and (5) signatures of the final document from the committee and the department head granting permission to operate.

PHAs are consecutive-failure based techniques, that is, incidents come from consecutive failures.[44] While this applies to large-scale projects, it is more prone to fail in laboratory-scale projects, where the outcome of the experiment is unclear beforehand, or it is only envisaged to those with a thorough understanding of the phenomena. Due to the 'inadequate oversight of safety management',[45] there is the absence of university-tailored protocols, and the insufficient development of research on laboratory safety in academia[46] and accidents in schools do happen and can cause fatalities.[47]

Although the official annual incidence is mostly not reported in a general world-wide registry, it is estimated that the accident rate in universities is far higher than in the chemical industry. Hundreds of accidents occurred in public and private laboratories in the United States from 2001 to 2018,[48] some with severe outcomes ranging from spills and leaks (e.g., National University, Singapore), explosions of flammable and high-energy materials (e.g., Tsinghua University, China, and Texas Tech University, USA), inhalation of toxics (e.g., University of Chicago, USA), and fires (University of California, USA, and University of Health and Sciences of Phnom Pen, Cambodia).[46,48–51] Other examples relate to the failure of pilot plants due to uncontrolled reactions or during exothermic catalytic operations and polymerizations.[51] In 2021, nine people were injured, and two died in the aftermath of an explosion in the chemistry department of Nanjing University of Aeronaturics and Astronautics (NUAA) College of Materials Science and Technology in China.[52] This event followed another explosion at the Institute of Chemistry of the Chinese Academy of Sciences in Beijing in March; one at the Israel Institute of Technology in 2019 that cost the life of the principal investigator of the laboratory; and numerous explosions, poisonings, leaks, exposures, and fires all around the globe in the recent years.[53] China reports an average of 7 accidents and 10 events between injuries or fatalities in its university laboratories per year.[45]

Investigation on accidents and root cause analyses suggest that contributing factors are multiple and include improper procedures and human error, the management of unusual situations (including lack of knowledge and training and insufficient safety awareness), and equipment failure.[46] To prevent accidents, universities must adopt a formal approach to hazard recognition and risk assessment within a documented laboratory safety program. Formal hazard analyses such as HAZOP studies, What-If studies, or FTA are required to characterize the potential hazards and plan for the worst-case scenario. They must review both general and specific safety hazards to reduce associated risks, while accommodating the continuous changes peculiar to laboratories and pilot plants. They refer not only to essential systems integrity and inherently safer design but also to human error, operating procedures in laboratories, and hazards of non-repetitive experiments.

TABLE 5 Typical perspectives approached by a hazards and operability analysis (HAZOP) study

Design of a system	Assessment of the system design capability to meet user specifications and safety standards. Identification of weaknesses in systems.
Physical, operational environment	Assessment of the environment to analyze and ensure the system is appropriately situated, supported, serviced, etc.
Operational and procedural controls	Assessment of engineered controls, sequences of operations, procedural controls, etc. Assessment of different operational modes (start-up, standby, normal run, steady and unsteady states, normal shutdown, emergency shutdown, etc.

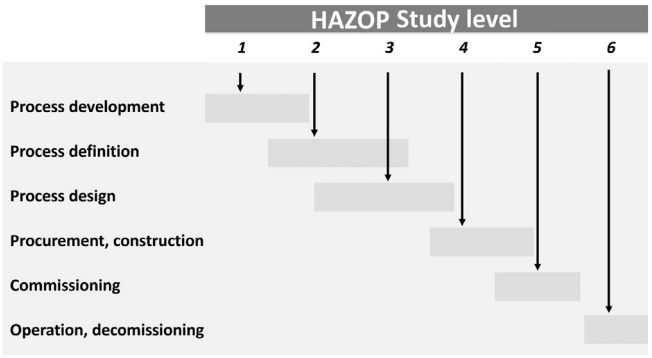

FIGURE 9 Hazards and operability analysis (HAZOP) applied to various project stages

In fact, moving from small-scale laboratory operations to larger-scale pilot plant operations increases the potential risks at each step of the sequence. While the quantities of hazardous materials and the scale of operations are much smaller than industrial process units, there are different factors creating significant challenges in evaluating hazards. These include the proximity of researchers and operators, the lack of established process knowledge, and the use of new equipment, materials, and processes. When dealing with experimental methods and research, the HAZOP methodology may not be as effective because of insufficient information, less experienced personnel in HAZOP, and the inherent uncertainties in research.

HAZOP studies are undertaken during detailed engineering with P&IDs in hand, but the methodology applies from the research stage to the demolition/abandonment stage.[12] Typical perspectives approached by a HAZOP study are given in Table 5. When an action is required, we document the changes and record the date. The HAZOP committee reviews the modification to ensure the changes are incorporated. Considering a process life cycle, a HAZOP comprises six levels, each with a different degrees of detail (Figure 9).

3.1 | HAZOP level 1: Process development

Identifies basic hazards of materials and operations and assembles information on previous hazard experiences. Defines baseline data safety, health, and environmental issues relevant to legislation and constraints. Establishes and identifies the context during a conceptual design stage.

3.2 | HAZOP level 2: Process definition

Assesses process hazard analysis (PHA) as part of the process definition stage. Examines process items on draft flowsheets, identifies problematic designs, assesses strategy versus relevant hazards, and establishes prevention and protection systems and alarms.

3.3 | HAZOP level 3: Process design

Reviews and confirms the detailed flowsheets–P&ID with suggestions to improve process safety and operability (front end engineering design [FEED] stage). Documents include control systems and safety functions that conform to guidelines from level 2. After this stage, additional design changes that alter the plant equipment are evaluated in terms of risk.

3.4 | HAZOP level 4: Procurement and construction

Checks for violations in the design intent after construction (as built). Verifies hardware and implementation of suggested actions. Examines operating and emergency procedures.

3.5 | HAZOP level 5: Commissioning

Appraises operating team's ability to commission the research and development (R&D) laboratory experiments: reviews operating procedures and documentation along with R&D laboratory workers (technicians, students, and principal investigators) training. Reviews prestartup safety, including cleanliness and purging tests, and confirms compliance with company and legislative standards.

3.6 | HAZOP level 6: Operation and decommissioning

Confirms action items identified in previous reviews were addressed post-start up. Verifies that operation matches the considerations made in the previous studies. Documents relevant deviations and alarms frequencies that can be used to improve overall system safety.

In the Appendix A, we summarize a level 2 HAZOP for an early stage process to convert lactose from whey to lactic acid. This brief account demonstrates essential features of the methodology and is meant as a guide for inexperienced researchers and engineers. For novel processes, addressing the main safety issues early on is critical for the success of the project. In fact, already with a low level of detail in the flow diagram, we identified several sources of

possible risk, and the number of equipment, instruments, and safeguards increased considerably. Beginning research projects with lean budgets can screen the uncertainties of their processes through the HAZOP, deciding to channel the investigation efforts only on the basic phenomena with the highest impact on operative or capital cost.

In this light, the CCPS risk analysis screening tool (RAST) assists with hazard identification and screening risks, consistently with best practices, to improve process safety performance.

Besides design, other applications include process modifications (addition or removal of equipment, changing reagents) and test programs (modifying conditions to optimize productivity). A crack in a vessel was the origin of the Flixborough disaster: a bypass line was built that leaked cyclohexanone, leading to the formation a vapour cloud that detonated. A modification of the system occurred without a full assessment of the potential impact and additional risks determined by the modification of the envelope of the system. A successful MOC, that is part of the risk-reducing HAZOP strategy, would almost certainly have prevented the disaster. Variants of the original HAZOP approach include:

- Process HAZOP that assesses R&D laboratories, pilot-plants, and systems;
- Human HAZOP focused on human errors;
- Procedure HAZOP that reviews procedures and/or operational sequences;
- Software HAZOP that identifies software errors;
- Computer hazard and operability (CHAZOP) directed at control systems and computers in terms of process upsets;
- Cyber HAZOP that aims at assessing cyber threats.

In the framework of the process HAZOP, Table 3 lists typical examples of HAZOP deviations and related causes. Common scenarios assessed by a HAZOP study include contamination, relief, instrumentation failure, corrosive processes, service failure, and maintenance-related issues. Contamination comprises leakages, improper system operations, corrosion, and poor management of additives. Instrumentation failure includes improper set points of control and alarm systems, faults in instrumentation components, and human error in manual interventions. Issues related to service failure are typical initiating events of accidental scenarios, including failure of instrument air, steam, cooling water, as well as the failure of hydraulic and electric power. Heating and ventilating systems failure belong to HAZOP deviations.

For each node, a HAZOP considers: normal operation, reduced throughput, routine start-up and shutdown, emergency shutdown, commissioning, and special operating modes. The most common parameters are pressure, temperature, and flow (Tables 6 and 7), which give rise to deviations in level, composition, and pH.

HAZOPS apply to pilot plants and laboratories. These small-scale systems have a greater degree of human interaction, but we recommend HAZOP levels 1–2 (Figure 9), while recognizing that great level of uncertainty. For example, simple and straightforward research activities may benefit from unstructured hazard analysis and risk assessment. However, in specific cases, this can result in a review that does not evaluate exhaustively all areas and steps of a pilot plant or research laboratory. Design intent and limitations of the laboratory and pilot plant must be established together with constraints related to materials (reagents) and experimental conditions. For research

TABLE 6 Parameters examined by the hazards and operability analysis (HAZOP) team

Flow	Composition	Pressure	Temperature
pH	Sequence	Separation	Addition
Signal	Mixing	Time	Stirring
Phase	Operate	Transfer	Speed
Level	Particle size	Viscosity	Conversion

TABLE 7 Typical hazards and operability analysis (HAZOP) deviations of flow, pressure, temperature, and composition, and causes in the framework of process HAZOP

More flow	Increased pumping capacity or suction pressure, increased fluid density, control faults, etc.
NO flow	Blockage, check valve incorrectly operated, leak or rupture, equipment failure, etc.
REVERSE flow	Emergency venting, incorrect operation, defective check valve, etc.
LESS flow	Blockages, restrictions, fouling, etc.
MORE pressure	Gas inadequate venting, defective relief operations/procedures, thermal overpressure, etc.
LESS pressure	Vacuum conditions, condensation, restricted suction line of pump/compressor, leakage, drainage, etc.
MORE temperature	External conditions, fouling in heat exchangers, fire, control failure, runaway reactive systems, etc.
LESS temperature	External conditions, pressure reduction, loss of heating, etc.
AS WELL AS composition	Leakage of isolation, phase change, incorrect/substituted feedstock, inadequate quality control/check, undesired reaction, etc.

laboratories, support systems—ventilation (hoods and elephant trunks), building air and water, electricity, safety devices (gas detectors), and equipment are part of the HAZOP as well as preparatory and sampling stages that come with the research activity. The HAZOP team necessarily includes idea developer, technicians, laboratory analysts, equipment specialists, and the maintenance manager.

Many organizations often fail to account for human error in the HAZOP process, including the time and performance pressures most researchers operate under. This may push to try to complete the hazard analysis process as quickly as possible, omitting specific areas of concern of research laboratories.

HAZOP can be extended to machines and automated plants in very much the same way as for processes, but also to electrical systems, and electronic control systems. Control systems and programmable logic controllers (PLCs) are considered in the CHAZOP that, differently from the Process HAZOP, can show the effects related to failures of subsystems, controller units, and power failures within the control system.[16] We recommend CHAZOP when considering control systems for multistage processes, alarm management systems, PLC networks, fire and gas detection systems, and emergency shutdown systems (ESDs). Many accidents are related to computer control systems,[54] which require a greater resourcing of electrical engineers and programmers.

Procedure HAZOPs examines existing and planned activities to check for hazards and causes that may compromise operations, quality issues, delays, and unacceptable safety risks. It considers both human errors and failures of technical systems and is best suited for detailed assessments. Different from the conventional process HAZOP and the application of specific guide-words to intention, procedure HAZOP breaks down operations into steps/individual actions. For each step, the intention is defined and boundary conditions are established. Finally, we apply the guide-words to each step of the procedure. Another major difference from HAZOP applied to processes is that causes and deviations are generally ascribed to human factors.[55] Besides omissions, other causes include poorly written procedures or layout, poor lighting, and information overload like excessive nuisance alarms. Human-system interactions introduce accidents (50%–90% are due to human error) that better training or instructions, operational strategy, and design mitigate.[21]

4 | LIMITATIONS OF HAZOP

The HAZOP is the most commonly used PHA method in the world today. However, it is not without its weaknesses. Although HAZOP is based on a simple set of principles, the procedure is meticulous and time consuming and is unwarranted for systems where the risk is slight. It relies on heuristics rather than algorithms, and the formal structure gives the practitioners the sense that a thorough analysis is being performed. However, there are no guarantees that all-important deviations, initiating events, and scenarios have been identified. For this reason, HAZOP studies are susceptible to being incomplete, and the potential for incompleteness increases owing to the increase in the number of items considered and the complexity of the system.

Weaknesses also exist in the identification of the design intent, deviations, guide words, and initiating events. In fact, novices may confuse the differences between guide-word, parameter, and deviation, leading to erroneous conclusions and reduced quality of HAZOP studies. Conceptually, focusing on the design intent of a system may be challenging during a HAZOP. Crucial aspects relevant to safety are scattered across different designs and documents that must be consulted and analyzed. In this regard, to successfully complete a HAZOP study requires a team with detailed knowledge of the systems, while the study only considers the components, sections, or activities that appear on the design representation.[24] Moreover, the HAZOP analysis often focuses on the design intent for study nodes. The team may not realize that even small deviations in one part of the system may significantly affect other parts. The HAZOP poorly represents how deviations propagate, particularly when this step is based on checklists that contain only the most common process parameters.

Multiple deviations complicate the analysis—the combination of some guide words with a process parameter that may generate more than one deviation, or compound deviations involving multiple potential failures. Missed deviations lead to missed scenarios or when some deviations are not recognized as valid by the study team. Despite the emphasis on deviations in the HAZOP study, the team should not be distracted by the more critical issue of identifying causes of deviations, that is, initiating events.[56] Unfortunately, the HAZOP study does not provide any guidance on this. The team typically brainstorms credible causes using engineering judgements, but automating the generation of common initiating events may support the PHA team. For example, the CCPS RAST software contains a library of potential initiating events that could lead to a significant loss of containment. These scenarios may determine significant risks and will need evaluation by the team.

A HAZOP analysis identifies both hazards and operability, but the R&D HAZOP teams are less likely to

identify hazards associated with operations. In addition, they may ignore minor hazards such as less-obvious chemical reactivity hazards arising from loss of control of intended chemical reactions, self-reacting materials, and chemical incompatibility.

4.1 | Sources of error

Errors arise during the planning, execution, and follow-up stages of HAZOP studies. A PHA based on a HAZOP takes more time than other methods and produces more documentation. Time management is the most frequent miscalculation. An insufficient amount of time limits discussion that jeopardizes the thoroughness of the study. Identifying the minimum essential expertise for the team helps ensure a focussed effort. Too many individuals encumber discussions while too few risks overlook essential elements. For example, the Flixborough caprolactam plant installed a pipe to carry cyclohexanone (a flammable compound) without mechanical engineering expertise to certify the design for high-pressure operation. Incomplete, inaccurate, and unavailable information on system safety impair the identification of scenario elements. This undermines the quality and reliability of the entire HAZOP. The process owner has the responsibility to check the integrity of the information.

Executing a HAZOP requires a dedicated team that is isolated from exterior distractions. The facilitator's instructs the participants and maintains the group focus. This person allocates resources and time for sessions to minimize errors, such as the omission of keywords and the exclusion of non-obvious deviations, and ensures a comprehensive review while applying pre-built templates. The combination of pairs of keywords and parameters encourages strategic discussion on hazard and operability problems, moving beyond a mere form-filling exercise of the HAZOP table. These aspects directly impact the quality and completeness of a HAZOP study.

Some HAZOPS issue recommendations for any scenario with negative impacts, while others exclude non-specific, excessive, or irrelevant recommendations. However, the intent of a HAZOP is to identify issues and recommend actions, including design modifications or areas to investigate further. Nevertheless, all recommendations should involve stated actions and require proper wording. The final document must avoid feeble verbs like 'recommend' and 'consider' in favour of vigorous verbs such as 'investigate', 'install', or 'add'.

Another common source of error is attempting to address risks or to re-design the system during the HAZOP study itself. The HAZOP lists actions and recommends changes. Some have not clear-cut solutions and require further research and investigation in other forums. Deficiency in the follow-up stage includes management's failure to act promptly. The process owner must evaluate each recommendation, take proper actions, and track them to final resolution and closure.

HAZOPs must be updated and re-validated as the current knowledge of hazards, consequences, and recommendations for risk reduction changes being proposed. If the HAZOP on process changes is not proposed, the R&D personnel may not identify new causes of process deviations or operability issues, and any changes in safeguards may not be understood or documented.

The sources of error represent the main inconvenience of the HAZOP technique, making it relatively high-cost in terms of time and people to be involved in the analysis sessions. The HAZOP needs to be carried out optimally, avoiding these errors to ensure the success of the process. An optimal and successful HAZOP analysis avoids these common sources of errors. To do this, research organizations must use structured hazard analysis and risk assessment that evaluate all areas and steps of the process, including the impact of human error in R&D activities. Even the simplest tasks are affected by a probability of error. The activities performed by technicians, researchers, and students need to be recognized, evaluated, and perhaps mitigated. In dealing with pilot plants and experimental activities, vague hazards must be avoided for realistically detailed scenarios that can be re-evaluated later if new information arises. Research involves new materials, products, and processes, and it is essential to gather complete information to not underestimate hazards and risks. This also holds valid for operations in research. If a common operation is not clearly identified or described, it may not be evaluated at all. In addition, it is essential to ask how undefined activities will be performed and be alerted for normalization of deviations, leading to no longer truly safe operations.

5 | CONCLUSIONS

HAZOP is a disciplined and structured methodology that companies worldwide apply to identify hazards and analyze their risks. A version of the HAZOP method can be used during every step of process design. It explores the consequences of deviations from design conditions and recommends areas that the process owner must address before operations proceed. In the last 20 years, over 2500 articles mention HAZOP analyses,[57] which makes it the most popular PHA methodology and the foundation of process safety and management programs. At the same time, various accidents and problems were documented

in academic laboratories and during pilot plant operations. This has fostered a special focus on hazard and risk assessment in research. In fact, the research laboratory is a unique, ever-changing environment and research experiments change frequently, involving a wide variety of hazards. Hazard identification, hazard evaluation, and hazard mitigation in laboratory operations are critical skills that must be part of any laboratory worker's education, driving a holistic approach to the inherently safer design and operation of laboratory activities and pilot plants for a safe working environment. In this framework, the HAZOP method is a robust hazard review approach based on a simple set of principles supported by guide word instructions for deviations from the design intent. This approach provides it with the versatility required to address safety in chemical plants, for design, operations, maintenance, and research environments. The flexibility of HAZOP has proven to be a strength when addressing these applications. The HAZOP can help researchers to fully appreciate the nature and extent of the potential hazards of research activities and experiments for an ultimate reduction of risk to an acceptable level. The benefits of HAZOP go beyond a risk mitigation as it changes individual and organizational attitudes and promotes a safety culture. The success of a HAZOP in identifying hazards depends on the knowledge and experience of the HAZOP team members, and this is a crucial topic considering that some accidents were related to inexperienced teams that missed some hazards.[58] Weaknesses in existing or proposed systems can be identified with the HAZOP, but it is best addressed early in the design stages. This allows for major changes to be practically accommodated in the design and development of R&D activities and experimental systems. In this light, HAZOP is an integral part of the overall design of processes, and the most efficient technique to identify risks within a risk management process.[59]

At the same time, the HAZOP can be used for conducting routine reviews of laboratory activities, but it is a valuable support for identifying and reviewing hazards, whether they are due to not only routine procedures but also modifications to current research or entirely new endeavours. It is applied in conjunction with other hazard and risk identification strategies, including FMEA, FTA, and LOPA, to quantify the likelihood of a failure event or ascertain the amount of risk reduction achieved.

Hazard analysis and risk assessment would support the lowering of accident rates in academic laboratories experience while understanding the hazards and implementing hazard minimization controls and conditions before starting and during research activities. In this way, participants in the research team will be familiar with some of the problems likely to occur and be prepared to identify and address them effectively.

AUTHOR CONTRIBUTIONS

Paolo Mocellin: Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; project administration; resources; software; supervision; validation; visualization; writing – original draft; writing – review and editing. **Jacopo De Tommaso:** Conceptualization; data curation; formal analysis; investigation; methodology; validation; visualization; writing – original draft; writing – review and editing. **Chiara Vianello:** Conceptualization; formal analysis; validation; writing – original draft; writing – review and editing. **Giuseppe Maschio:** Conceptualization; formal analysis; funding acquisition; methodology; resources; supervision; validation; writing – original draft; writing – review and editing. **Thomas Saulnier-Bellemare:** Conceptualization; formal analysis; methodology; software; validation; visualization; writing – original draft; writing – review and editing. **Luis D. Virla:** Conceptualization; formal analysis; validation; writing – original draft. **Gregory S. Patience:** Conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology; resources; supervision; validation; visualization; writing – original draft; writing – review and editing.

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APPENDIX A: CASE STUDY

We demonstrate the HAZOP methodology with a process that converts lactose from whey permeate to lactic acid.[60] Whey permeate is a liquid waste from the dairy industry that is composed of 95% water, 4%–5% lactose, and some minerals. The process treats 400 kt · year^{-1} of whey. In Section 100 (reaction), a continuous stirred tank reactor (CSTR) hydrolyzes the lactose at a pH of 2.3, and a catalytic packed bed reactor (PBR) converts the lactose hydrolysates to lactic acid (Figure A1).[61] The 4.14 m^3 CSTR operates at 5 MPa and 150°C, while the PBR operates at 5.5 MPa and 180°C. Adding HCl and NaOH controls the pH. Heat exchangers cool the lactic acid stream exiting the PBR (HX-01 and HX-02). The reactors are the backbone of the process, so deviations in their operation have a large impact on the process stability. For this demonstration, we only consider deviations in their operations and assess the major risks during the HAZOP analysis (Level 2).

Reverse osmosis membranes and nanofiltration separate the products in Section 200 (filtration),[62] which is vulnerable to fouling and clogging and other unknown deviations. A cascade of low-pressure evaporators separates the crude liquor from water to produce 99% pure lactic acid in Section 300 (purification). The generated vapour from each step, first condenses and then feeds the upstream evaporator.[63] Aspen simulations on this section demonstrated that this purification unit is sensitive to deviations in operating conditions because any failure in this section directly affects the quality or quantity of the final product.

The preliminary design of the process, through the main equipment sizing,[60] and the definition of an early flowsheet, is detailed enough to perform a level 2 HAZOP. The analysis identifies major risks and preventive and mitigation strategies to implement and further design steps that are required to ensure process safety, following the procedure defined in Figure 4 and the guide words listed in Table 3. The HAZOP also improved the definition of the flow sheet and the understanding of the operation of the equipment by adding control loops, safety measures, and installed spares (Figure A1).

Completing the HAZOP at such an early stage maximized the impact on the future process development,[64,65] which is of particular importance for novel processes. A bottom-up approach not only ensures safe process operations but also guides the process design from the first flow sheets forward. For the sake of clarity, we report here all the main findings of the HAZOP panel, but we show only the details of Section 100.

A.1. | Expected hazards

In general, Section-100 is sensitive to:

- Temperature, pH, and flowrate from an economic point of view. A deviation of these variables directly affects the product quality, and throughput (Table A1). Temperature and pH are the reaction main parameters. Overheating caramelizes the lactose and water evaporates, which could increase the vessel pressure. Whey permeate has some suspended solids in the liquor, which is why this equipment is prone to clogging, fouling, and pump malfunction.
- Pressure in terms of process safety. The reactors operate above 5 MPa, which is high pressure for the food industry. Overheating or pump malfunctioning can cause a pressure buildup in this section, with severe consequences on the process, equipment, and ultimately personnel (Table A1).

Reverse osmosis and nanofiltration are pressure-driven filtration methods. Therefore, pressure or flow deviations in Section 200 will cause an incomplete separation, compromising the final product quality.

The cascade of Section 300 adjusts the water content of the lactic acid through three stages of heat-integrated evaporators. The only energy input of the section comes

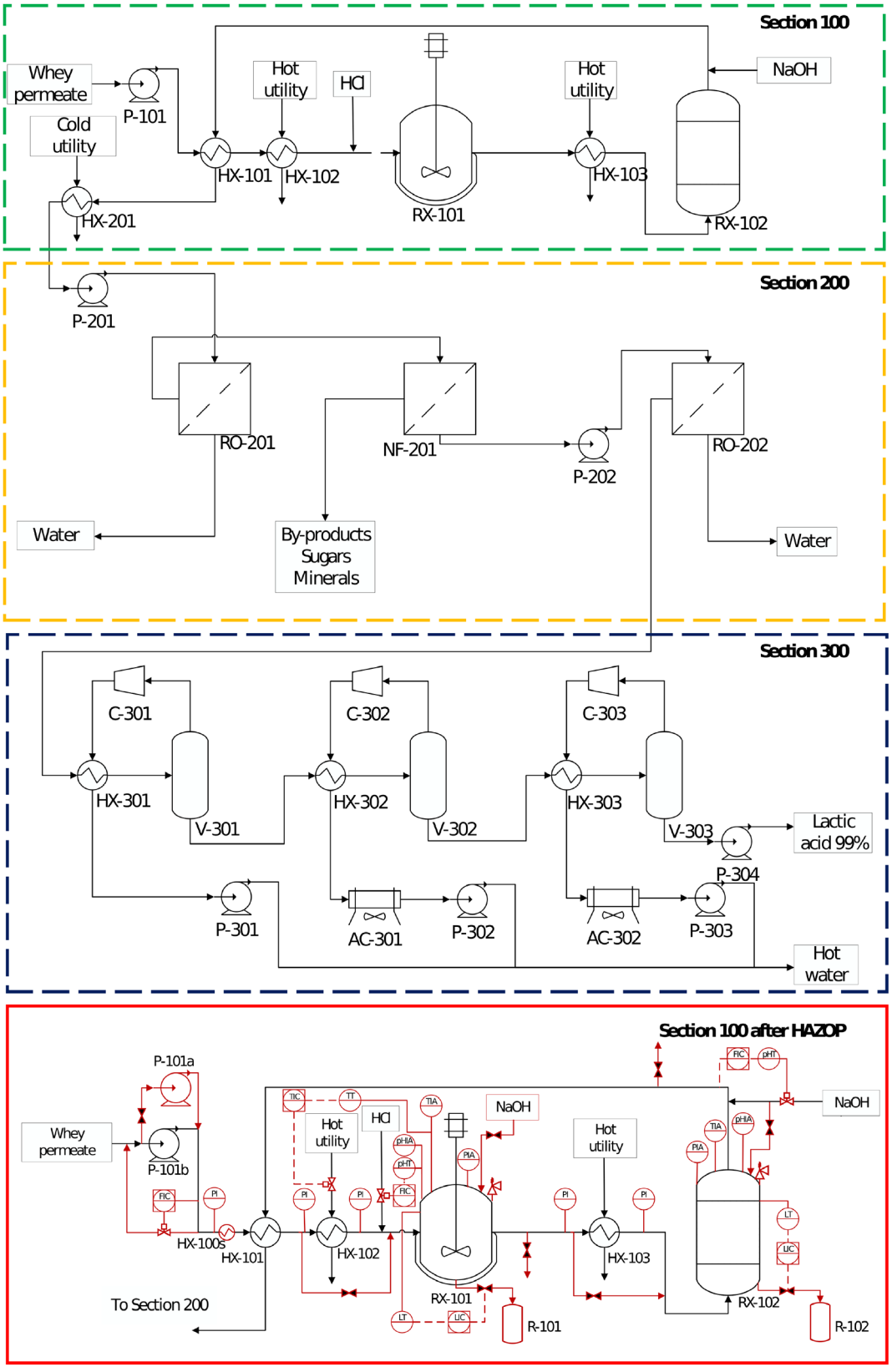

FIGURE A1 Process flow diagram of the lactic acid production plant from whey permeate for Sections 100, 200, 300, and 100 updated after HAZOP analysis modifications (red mark-up). HAZOP, hazards and operability analysis

TABLE A1 Hazards and operability analysis (HAZOP) analysis of hydrolysis reactor RX-101

HAZOP study report	**Lactose to lactic acid: Whey valorization**			**PFD no.1**	**Revision no. 1**
Team members				November 2021	Sheet no. 1 Meeting no. 1
Hydrolysis reactor RX-101					
Hazard	**Causes**	**Consequences**	**Likelihood and prevention**	**Emergency and mitigation**	**Action**
No flow	P-101 failure, Total blockage of HX-101 or HX-102	Process stop	Very unlikely Periodic pump maintenance. Measure HX ΔP	Add a spare pump. Add a by-pass stream on HX-102	Dynamic analysis of the process start-up sequence
Less flow	Malfunctioning of pump P-101	Lower residence time. Lower conversion. Lower LA production	Likely Periodic pump maintenance	HX clean-up procedure. Add HX-102 by-pass	Model HX fouling, design a pressure reducing orifice on pump P-101
More flow	Malfunctioning of pump P-101	Higher residency times, sugar degradation, possible overflow	Unlikely Periodic pump maintenance, improve vessel design to reduce overflow likelihood	Emergency overflow tanks implementation (level control)	Design a pressure-reducing orifice on pump P-101
Less pressure	Malfunctioning of pump P-101	Partial evaporation, reaction rate gets reduced	Unlikely Periodic pump maintenance	HX clean-up procedure	Design a pressure reducing orifice on pump P-101
More pressure	Malfunctioning of pump P-101, partial blockage of HX-101 or HX-102	Damage to reactor and instrumentation (for very high pressure)	Likely Periodic pump maintenance, periodic inspection of vessel and instrumentation	Pressure alarm on RX-101, instrumentation replacement procedure, pressure relief valve installation	Design a pressure reducing orifice on pump P-101
Less temperature	Too low hot utility flow in HX-102, Dirty HX	Less lactose thermal degradation, reaction rate gets reduced	Likely Control loop on hot utility flow, valve maintenance	Valve manual adjustment and reparation procedure, add a start-up heater before HX-102	Model HX fouling, dynamic modelling of temperature control, dynamic analysis of the process start-up sequence
More temperature	Too high hot utility flow in HX-102	Possible caramelization of sugars, partial evaporation of water	Likely Control loop on hot utility flow	Undesired products purge stream, temperature alarm on RX-101	Dynamic modelling of temperature control, analysis of sugar caramelization parameters
Less pH	Too high HCl flow	Possible degradation of equipment, reactor leak	Unlikely Control loop on HCl flow	Low pH alarm, emergency NaOH input stream in the reactor	Dynamic modelling of pH control
More pH	Too low HCl flow	Less lactose degradation, reaction rate gets reduced	Unlikely Control loop on HCl flow	No mitigative measure	Dynamic modelling of pH control

(Continues)

TABLE A1 (Continued)

HAZOP study report	Lactose to lactic acid: Whey valorization			PFD no.1	Revision no. 1
No Mixing	Broken mixer	Bad mixing, reaction rate gets reduced	Very unlikely Periodic maintenance of mixer, periodic product sampling	Mixer replacement procedure	Study of acidity effect on mixer blades
Less mixing	Badly adjusted mixer	Bad mixing, reaction rate gets reduced	Unlikely Periodic mixer maintenance, periodic product sampling	Mixer adjustment and reparation	Mixing modelling and optimization
More mixing	Badly adjusted mixer	Bad mixing, vortex formation, reaction rate gets reduced	Unlikely Periodic mixer maintenance, periodic product sampling	Mixer adjustment and reparation procedure	Mixing modelling and optimization

Abbreviation: PFD, process flow diagrams.

from the three inter-stage compressors C-301/2/3. Because the rest of the heat is provided by the integration of the produced steam with the liquid coming upstream, any temperature (or pressure) deviation has a snowball effect on the performance of this section.

A.2. | HAZOP outcome

The HAZOP analysis confirmed the main hazards. In Section 100, we mitigated (Figure A1) the consequences of pressure, temperature, pH, and flowrate deviation. After the HAZOP, the process has a spare whey permeate feed pump (P-101 b), that is on standby and operates in case P-101 a fails, which guarantee a constant feed rate (and therefore pressure) to RX-101. Similarly, high pressure safety valves, and pressure indicators and alarms, to monitor the situation on-line from the control room were included in the design. HX-102 and HX-103 now have a by-pass line as an additional manual control feature in case of overheating. The HAZOP required a study to determine the fluid dynamics in RX-101, the corrosion resistance of the reactor internals due to the low pH, and the overheating over time. Because the temperature is a critical parameter, we added a start-up electrical heater (HX-101) to bring the process up to a steady state. A level control on the reactors is now the last resort on the reactor overflow. At this stage, because any transitory evolution of the process parameters (T, P, pH, etc.) requires further study, we endorsed electrically operated valves rather than pneumatic ones.