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Integrated hazard identification within the risk management of industrial biological processes

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A B S T R A C T

In recent years bioprocesses are becoming a cornerstone of the production industry and have been implemented for large scale production. Despite its importance, the safety of such processes has not been yet systematically analyzed and studied. The hazards of biotechnological processes entail both conventional chemical process hazards and biohazards related to the presence of microorganisms. In the present study a specific methodology for hazard identification in biotechnological processes has been developed, aimed at the integrated assessment of conventional hazards and biohazards at industrial scale. The potentialities and outcome of the methodology were tested by its application to the anaerobic digestion of animal manure for biogas production, which represents a widespread bioprocess for energy production from renewable sources.

1. Introduction

A biotechnological process (bioprocess in the following) is a process that uses microbial organisms, animal or plant cells, or components of cells such as enzymes, to obtain products or to complete a chemical transformation (Doran, 2013). Bioprocess engineering, meant as the integration between chemical engineering and biotechnology (Shuler and Kargi, 2005), is becoming a crucial industrial sector, and bioprocesses are spreading from pharmaceuticals to food and energy production, from polymers to paper and biological materials preparation, to waste water treatment (CCPS – Center for Chemical Process Safety, 2010). The industrial implementation of these innovative processes and of the associated technologies as well as their scale-up to industrial production (Marques et al., 2010; Neubauer et al., 2013; Olson et al., 2012; Shuler and Kargi, 2005; Takors, 2012) caused an increase in the number and potentiality of facilities where bioprocesses are carried out (CCPS – Center for Chemical Process Safety, 2010).

Although bioprocesses are generally perceived as safer technologies, having a lower impact than conventional chemical processes, in recent years several accidents affected this industrial sector (Casson Moreno et al., 2016b; Casson Moreno and Cozzani, 2015; CCPS – Center for Chemical Process Safety, 2010). Moreover, in some events (Casson Moreno et al., 2016b) the accident scenarios that took place where not detected during the hazard identification step, thus may be considered atypical scenarios according to Paltrinieri et al. (2013). Such accidents may be considered as early warnings of an emerging risk issue, defined by IRGC as *a risk that is new, or a familiar risk in a new or unfamiliar context or under new context conditions* (International Risk Governance Council (IRGC), 2009), related to atypical scenarios (Paltrinieri et al., 2013). Furthermore, these events may suggest that some limitations may be present in the hazard identification techniques presently applied (CCPS – Center for Chemical Process Safety, 2010), mostly developed to address hazards in conventional chemical processes.

Actually, in industrial scale biotechnological processes both conventional chemical hazards and specific biological hazards (*biohazards*) may be present (Jan et al., 2012). A recent review of risk assessment methods pointed out that holistic techniques for hazard identification (HazId) specific to industrial scale bioprocesses are not available (Casson Moreno et al., 2016a; Giacomini, 2015). Only few studies attempted to investigate the problems in the application of conventional methods for risk assessment (e.g. FMEA, HAZOP, bow-tie analysis) to bioprocesses (Angel et al., 2015; Harms et al., 2008; Mollah, 2005; Pietrangeli et al., 2013; Pinkenba and Statement, 2006; Scarponi et al., 2016, 2015; Casson Moreno et al., 2018). Caskey et al. (2010) remark that there is not a specific and standardized methodology to approach biological risk assessment in industrial processes. Furthermore, existing methods and regulations addressing biohazards are mostly focused on the protection of workers from exposure to biological agents (Pietrangeli et al., 2013), as required e.g. by European Directive 2000/54/CE (European Parliament, 2000) and by several European Union Member States regulations (Bassett et al., 2012; De Giudici et al., 2011; Health and Safety Executive (HSE), 2013; U.S. Environmental Protection Agency (EPA), 2007).

In this panorama, the main aim of the present study is to make a

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Table 1
Summary of the state of the art on risk assessment methods in bioprocesses.

Institution and year	Title	Summary
Health and Safety Executive (2007)	A review of the regulatory framework for handling animal pathogens (Callaghan, 2007)	– Focused on laboratories – The aim is to make recommendations based on the existing regulations: • The Control of Substances Hazardous to Health Regulations 2002 – general and biological agents provisions: COSHH, an implementation of the EC Directive 2000/54/EC • The Genetically Modified Organisms (Contained Use) Regulations 2000 • Specified Animal Pathogens Order 1998 – Define the required containment based on the hazard classification of the microorganism: it is qualitative!
U.S. Environmental Protection Agency (EPA) (2007)	A compendium of prior and current microbial risk assessment methods (U.S. Environmental Protection Agency (EPA), 2007)	The compendium includes 135 of the most relevant studies (published between 1994 and 2004) catalogued as follows: • Exposure assessment studies, collecting works focused on the evaluation of exposure on human beings • Dose response (hazard characterization) studies, in which the quantitative evaluation of the adverse health effects associated with microorganisms is evaluated • Risk characterization studies, aimed at the estimation of the probability of occurrence and severity of know or potential adverse health effects in a given population based on hazard identification, hazard characterization and exposure assessment
United States Department of Energy – Sandia National Laboratories (2010)	Biosafety risk assessment methodology (Caskey et al., 2010)	– Focused on laboratories – The Sandia team worked with internationally recognized experts to define what biosafety risk is – Limitations pointed out: • Biological risk assessment has historically been "a subjective and qualitative process that relies heavily on expert opinion and unique personal experiences" • There is not a clearly structured and unified approach to perform biological risk assessment • There is also the consciousness that an hazard identification based on assigning classes could be no longer sufficient; and that's the reason why it is possible to find in literature different development made by national and international institutions
Agence de l'Environnement et de la Maîtrise de l'Energie (2011)	Microbiologie et Déchets: Évaluation Des Risques Sanitaires (De Giudici et al., 2011)	– The result of a collaboration among industry, public agencies and researchers interested in the determination of the risk for health associated to water and food – The aim is to describe specific methods used in microbial risk assessment and to analyze similarities and differences with the risk assessment methodologies commonly used in chemical industry – The main outcome was that the steps of the analysis were those typical of risk assessment (Casson Moreno and Cozzani, 2017) in process technology: 1 – Hazards identification2 – Characterization of the hazards3 – Estimate of the exposure4 – Characterization of the risk – Limitations pointed: • Microorganisms have the capacity of multiply also in a host organism • There is the possibility of a secondary transmission among individuals therefore methods have to be specifically developed
The International Life Sciences Institute (2012)	Tools for microbiological risk assessment (Bassett et al., 2012)	– The focus is on food safety – The risk assessment methods are divided in 2 main categories: • Qualitative, in which a non-numerical description of the likelihood is performed • Quantitative, sub-divided into deterministic and stochastic methods
Health and Safety Executive, United Kingdom (2013)	An update on HSE's work to consolidate legislation on human pathogens, animal pathogens and genetically modified organisms following the Callaghan and Löfstedt Reviews (Health and Safety Executive (HSE), 2013)	An update of the previous version (first entry of the present table) with the aim of simplifying, and including changes according to the European legislation (European Parliament, 2000)

step forward toward the definition of a specific methodology for hazard identification of major accidents addressing both biohazards and conventional chemical hazards in the framework of process safety. A specific layered approach to hazard identification in industrial bioprocesses was developed. The methodology addresses two levels: a checklist and a HazOp analysis, modified to consider both engineering and biotechnological aspects, and their interactions (BioHazOp). A scoring chart aimed at prioritization of the counter measures against process deviations is also proposed. The goal of this new tool is to foster the integration of biotechnological aspects and related hazards to conventional chemical engineering process hazards, and the identification of their cause-consequence relations.

In the following, the specific approach developed to bioprocess HazId is described and applied to a widespread bioprocess, i.e. the production of energy from renewable sources. A standard facility for biogas production via anaerobic digestion of animal manure was analyzed.