CHEMICAL ENGINEERING TRANSACTIONS

VOL. 95, 2022

A publication of AIDIC
The Italian Association of Chemical Engineering
Online at www.cetjournal.it

Guest Editors: Selena Sironi, Laura Capelli

ISBN 978-88-95608-94-5; **ISSN** 2283-9216

DOI: 10.3303/CET2295039

Environmental Evaluation of a Vaccine production Plant in North-East Colombia

Ángel Darío González-Delgado[a*], Janet B. García-Martínez[b], Andrés F. Barajas-Solano[b].

[a]Nanomaterials and Computer-Aided Process Engineering Research Group (NIPAC), Chemical Engineering Department, Faculty of Engineering, University of Cartagena, Cartagena 130015, Colombia
[b]Department of Environmental Sciences, Universidad Francisco de Paula Santander, Av. Gran Colombia No. 12E-96, Cucuta 540003, Colombia.
agonzalezd1@unicartagena.edu.co

Influenza is a respiratory illness that may cause serious consequences for the vital organs of the body. In 2019, between 99,000 – 200,000 annual deaths were attributable to Influenza infection. As a result, it is critical to prevent the disease from spreading by developing vaccinations. In Colombia, there is no company specialized in the manufacture of this type of vaccine. On the other hand, the manufacturing vaccinations process might impact negatively the environment. Therefore, the environmental potential impacts (PEI) of vaccine production using Madin Darby Canine Kidney (MDCK) cells were analyzed in this study. The mass balance and energy necessary for the process were calculated, and the generated and output impacts were found under eight categories for each case study. Cases 1 and 3 had negative generated impacts, indicating that the process is environmental impact-consuming. The impacts generated in cases 2 and 4 were positive but not significant, indicating that the process presents a good environmental performance. In comparison to other chemical processes, the output PEIs were minimal. The toxicological categories human toxicity potential by ingestion (HTPI) and terrestrial toxicity potential (TTP) obtained the highest values of PEIs, and for the atmospheric impacts, the highest PEI was achieved by acidification potential. Finally, the impact of the energy source on the PEI was studied, with the energy from gas proving to be the less environmental affectation.

1. Introduction

Influenza is a contagious viral disease, caused mainly by influenza viruses A or B, which can affect both people and animals (Uribe-Soto et al., 2020). The nose, bronchi, and lungs are among the respiratory organs that might be affected by this condition. It can be transmitted from person to person through respiratory droplets (Moghadami, 2017). In early 2019, the annual number of death worldwide due to the influenza virus was estimated at 99,000 to 200,000 (Paget et al., 2019). Because of its high death rate, this is a disease of major concern for the public health of a country. Influenza outbreaks are most common in the winter, but they are less predictable in tropical climates. Besides, studies reported that Influenza was one of the viruses discovered in children suffering respiratory infections in the Colombian regions of Comunera and Garcia Rovira in Santander (García et al., 2016).
Furthermore, respiratory infections are one of the most common reasons immigrants visit the doctor; outbreaks of respiratory diseases are quite likely to arise owing to the lifestyle and overcrowding in the type of shelters (Holguin et al., 2017). Colombia has received a large number of immigrants from Venezuela in recent years, specifically in the departments of Santander and Arauca (Mercado, 2021). On the other hand, according to studies, significant amounts of carbon dioxide are emitted by large-scale vaccine production which contributes to global warming (Hasija et al., 2022). Manufacturing, packing, and transporting vaccines require a lot of energy that impact negatively to the environment (Kurzweil et al., 2021). Since there is no industry specialized in producing influenza vaccines in Colombia (Contreras-ropero et al., 2022), it is critical to focus on vaccine production to control influenza. Besides, it is important to perform an environmental assessment of a chemical

Paper Received: 22 February 2022; Revised: 10 July 2022; Accepted: 15 July 2022
Please cite this article as: Gonzalez-Delgado A.D., Garcia-Martinez J.B., Barajas-Solano A.F., 2022, Environmental Evaluation of a Vaccine Production Plant in North-east Colombia, Chemical Engineering Transactions, 95, 229-234 DOI:10.3303/CET2295039

process to identify areas for improvement and quantify the environmental benefits of transforming raw material into a product. In this work, an environmental assessment of the production of influenza vaccines from MDCK cells was performed using the waste reduction algorithm (WAR) methodology.

2. Materials and methods

The assessment was performed in the WARGUI software, which was developed by Environmental Protection Agency (EPA). This open-source software allows diagnosing processes from an environmental viewpoint by calculating both the output potential impacts and generated potential impacts of the processes (Gonzalez-Delgado et al , 2021). The mass balance and the amount of energy required by the process were entered into the software and the total PEI was obtained in each category. Four case studies were established to provide a better analysis of the process. In this way, it is possible to analyze where the highest contribution of potential environmental impacts comes from, that is, if they are caused by the flow of product, the amount of energy required, or the nature of the process. In case 1, neither the potential environmental impact of the product stream nor the potential environmental impact of energy was considered in the analysis. The potential environmental impact of the product stream was taken into account, but not the potential environmental impact caused by energy required in case 2. Case 3 considered PEIs caused by the energy required but not by the product. Finally, case 4 considered both PEIs caused by the product and PEIs caused by the energy required.

2.1 Process description

The initial stage of the process is cell propagation, where MDCK cells grow in a DMEM culture medium, which has a large number of essential amino acids, vitamins, pyruvic acid, and glucose (Yan et al., 2021). DMEM (Dulbecco's Modified Eagle Medium) culture medium, which is used to favor cell growing, is sterilized by dry steam. It then enters a series of reactors (R-1, R-2, R-3, and R-4) where scaling up to 500L takes place. The time of residence in each reactor is 4 days. The cells are transplanted into the fermenters after reaching the desired cell concentration, in each of them carbon dioxide, antibiotics, and bovine fetal serum are injected. In this stage, 70% of the cells are infected. The resulting stream passes to the bead mill (BM-101) where the virus is released due to cell lysis. The DNA solubility is decreased with the use of isopropanol, in this way the genetic material is separated and passes to the centrifugation stage. The virion particles are chemically inactivated so that they can be recognized by the immune system without affecting it and generate antibodies that destroy the envelope. Subsequently, it is purified by using salts in the washing stage (WSH-102), then these are eliminated in the microfiltration stage (MF-101) as well as suspended solids, bacteria, and proteins that may be in the dormant virus. Finally, in the formulation stage (V-103 and V-104), adjuvants, penicillin, and salts are mixed, and the vials are packed with a volume of 1 mL. 285,176,100 t/y of the product are obtained with an energy requirement of 161.44 MJ/h, whose source in the base case is coal. These results were obtained from previous research work based on experimental data performed by the authors.

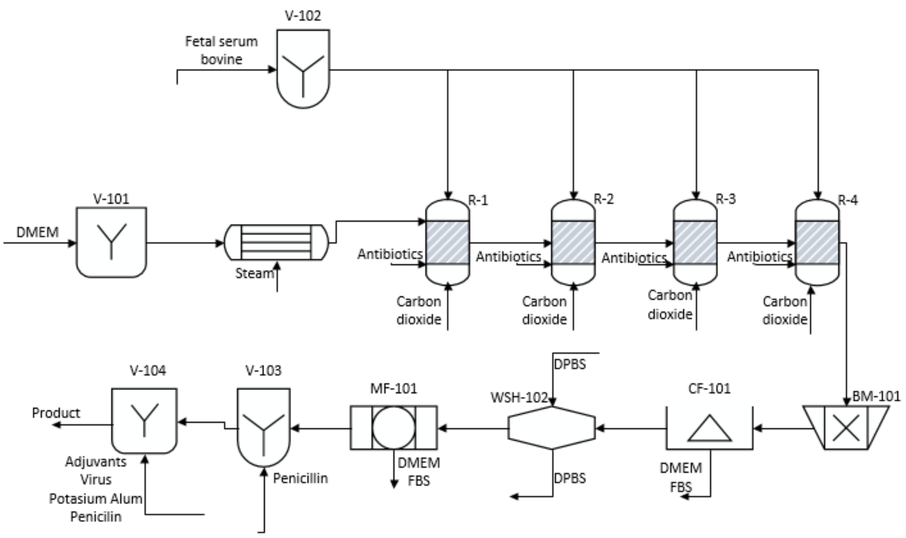

Figure 1. Process diagram of the vaccine production process using Madin Darby Canine Kidney (MDCK) cells.

2.2 Environmental assessment

An environmental assessment quantifies the potential environmental impacts of a chemical process. The WAR algorithm is a proposed methodology to perform this evaluation, it introduces the concept of potential environmental impact (PEI), which is defined as the impact that could be caused by a certain amount of mass or energy released into the environment. This algorithm has two classes of indices, which are the potential environmental impact generated and the output. PEI generated and outputs per mass of product and unit of time are calculated using equations 1 to 4. The WAR algorithm allows to evaluate 8 categories of impacts, which are divided into two large areas, toxicological and atmospheric impacts. The four toxicological impacts are the human toxicity potential by ingestion (HTPI), the human toxicity potential by inhalation or dermal exposure (HTPE), the aquatic toxicity potential (ATP), and the terrestrial toxicity potential (TTP). The four atmospheric impacts are Global Warming Potential (GWP), Ozone Depletion Potential (ODP), Acidification or Acid Rain Potential (AP), and Photochemical Oxidation Potential or Smog Formation Potential (PCOP) (Herrera-Aristizábal et al., 2017).

$$\hat{i}_{out}^{(t)} = i_{out}^{(cp)} + i_{out}^{(ep)} + i_{we}^{(cp)} + i_{we}^{(ep)} \quad (1)$$

$$\hat{i}_{out}^{(t)} = \frac{i_{out}^{(cp)} + i_{out}^{(ep)} + i_{we}^{(cp)} + i_{we}^{(ep)}}{\sum_p P_p} \quad (2)$$

$$\hat{i}_{gen}^{(t)} = i_{out}^{(cp)} - i_{in}^{(cp)} + i_{out}^{(ep)} - i_{in}^{(ep)} + i_{we}^{(cp)} + i_{we}^{(ep)} \quad (3)$$

$$\hat{i}_{gen}^{(t)} = \frac{i_{out}^{(cp)} - i_{in}^{(cp)} + i_{out}^{(ep)} - i_{in}^{(ep)} + i_{we}^{(cp)} + i_{we}^{(ep)}}{\sum_p P_p} \quad (4)$$

Where $i_{in}^{(ep)}$ and $i_{out}^{(ep)}$ correspond to PEI input and output rates for the power generation process, $i_{in}^{(cp)}$ and $i_{out}^{(cp)}$ represent the PEI input and output rates for the chemical process, $i_{we}^{(cp)}$ and $i_{we}^{(ep)}$ are the PEIs associated with residual energy (Cassiani-Cassiani et al., 2018).

3. Results and discussion

Figure 2 shows the total PEIs generated and output of an anti-influenza biological production from MDCK cells. PEIs output and generated were low values compared to other chemical processes which environmental performance was evaluated using this methodology since vaccine manufacturing has not been assessed under this method. Pájaro et al. reported higher PEIs for a refinery unit for sulfide absorption (Pájaro et al., 2018). PEI generated are negative in cases 1 and 3, where product stream was not considered. Cases 1 and 3 generate lower potential impacts than cases 2 and 4, which means the product stream affects generated potential impacts to a greater degree than energy usage. Besides, cases 1 and 3 have negative values of generated impacts, which means the process is environmental consumer. The PEIs at the input are lower than at the output due to the transformation of the substances potentially toxic to the environment into substances less harmful. Despite positive values of PEI generated in cases 2 and 4 (1.84×10^{-1} PEI/h and 1.25 PEI/h, respectively), the process has a good environmental performance by having not significantly high values. The impacts both outputs and generated were slightly larger in case 4 than in case 2 due to energy usage being considered in case 4.

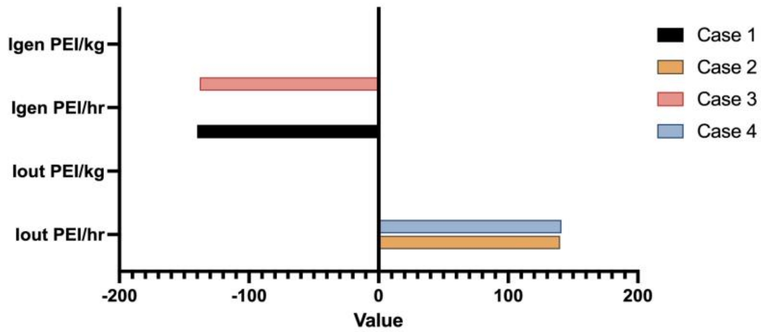

Figure 2. Total potential environmental impacts of a vaccine production process using Madin Darby Canine Kidney (MDCK) cells per unit of time and unit of mass for each case.

From figure 3, an anti-influenza biological production from MDCK cells presents lower toxicological impacts outputs than bio-hydrogen production from residual biomass of palm cultivation (Gonzalez-Delgado et al., 2017). The highest values were in the categories HTPI and TTP in cases 2 and 4, which contribute 67.4 % of the total toxicological impacts output in each case. This might be related to the presence of cholesterol and potassium alum in the product stream. The highest values in HTPI and TTP categories were obtained by these substances. A high level of cholesterol in the blood may increase the risk of death. The output potential environmental impacts by dermal exposure or inhalation were estimated at 17.1 PEI/h in case 4, which indicated the substances emitted by this process are safer for human exposition than the output stream in the agar production from macroalgae *Gracilaria sp*. (103 PEI/h) (Cassiani-Cassiani et al., 2018). The third highest bar represents the ATP category in cases 2 and 4, which value was affected by the presence of penicillin in the product stream. Studies report that pharmaceuticals emitted into the aquatic environment might cause genetic alterations to fish tissues (Yang et al., 2020). It is important to note that this methodology must be expanded since it does not take into account the potential environmental impacts that can be caused by viruses.

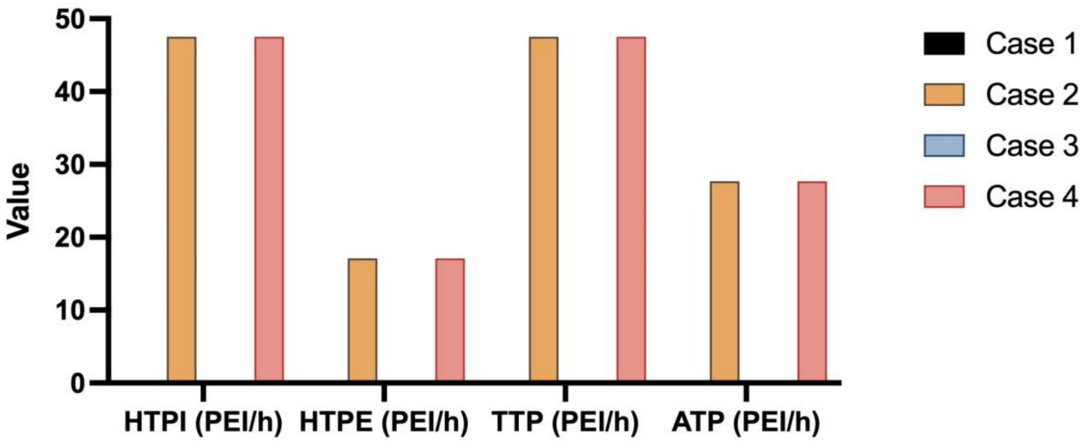

Figure 3. Potential toxicological impacts of a vaccine production process using Madin Darby Canine Kidney (MDCK) cells per unit of time for each case.

Figure 4 shows the atmospheric impacts of anti-influenza biological production from MDCK cells. Cases 1 and 2 do not have an impact in any category, except for GWP due to the presence of carbon dioxide in the product stream as this substance causes global warming (Williams et al., 2017).

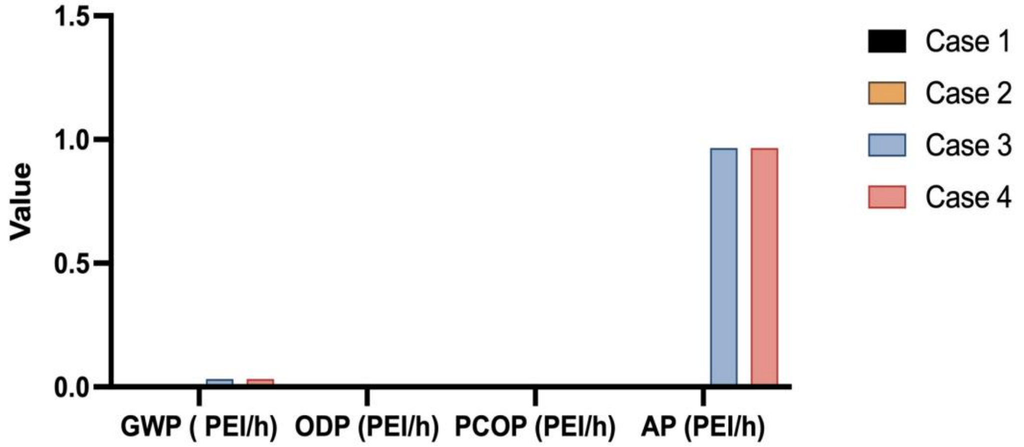

Figure 4. Potential atmospheric impacts of a vaccine production process using Madin Darby Canine Kidney (MDCK) cells per unit of time for each case.

Cases 3 and 4 present low values in the PCOP category, which means this process does not favor potential smog formation. Regarding the ODP category, low values were obtained, indicating that the product stream contains a little amount of chloride and bromine. The highest values were obtained in the potential acidification

(AP) category in each 3 and 4, where energy usage was taken into account in the result since, during carbon combustion, H+ can be resealed to the atmosphere, favoring the acid rain occurrence (Balat, 2007).

3.1 Effect of the energy sources

The effect of each energy source (fuel, coal, and gas) was evaluated. The potential environmental impacts were obtained in all categories (HTPI, HTPE, ATP, GWP, ODP, PCOP, AP) including the energy consumption and excluding product stream to analyze the effect of energy sources. From figure 5, the highest values in most toxicological categories (HTPI, HPTE, and TTP) were obtained when oil was used as the energy source. Potential health impacts have been reported because of human exposure to oil such as neurological symptoms, liver damage, and cancer (Butz et al, 2017). The second highest values in these categories were obtained using energy from coal. The inhalation of coal particles and their constituents might cause human diseases (Gasparotto et al., 2021). The maximum ATP value was reached using coal as an energy source. Studies have reported that coal microparticles in aquatic ecosystems might trigger physical and toxic damage to organisms (Tretyakova et al., 2021). In atmospheric categories (GWP, ODP, PCOP, and AP), the highest values were obtained utilizing energy from coal. Coal-fired power plants emit a large amount of carbon dioxide into the atmosphere which contributes to global warming. Besides, other substances are emitted such as sulfur dioxide, which is associated with acid rain (Shindell & Faluvegi, 2010).

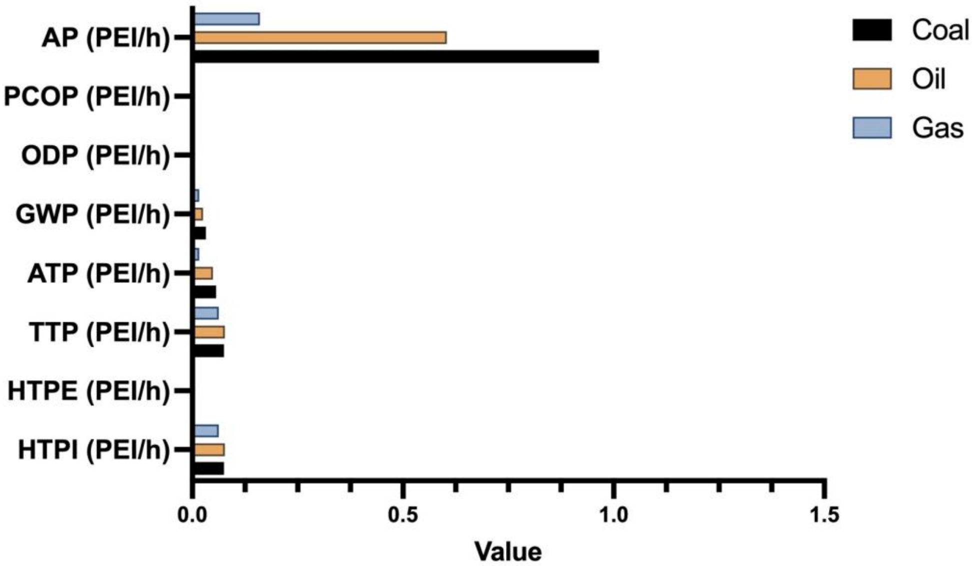

Figure 5. Source of energy effect on potential toxicological and atmospheric impacts of a vaccine production process using Madin Darby Canine Kidney (MDCK) cells per unit of time.

4. Conclusions

In this work, an environmental evaluation of the vaccine production process using MDCK cells was carried out, which has a production rate of 285,176,100 t/y. Four case studies were established. PEIs are significantly low compared to other chemical processes assessed using this methodology. The toxicological categories with the highest PEI were HTPI and TTP due to the presence of substances such as cholesterol and potassium alum in the product stream. The acidification potential presented the highest values in cases 3 and 4 due to the use of energy since during the combustion of coal substances are released that can favor acid rain. Finally, energy from gas showed to be the best source of energy in environmental terms.

Acknowledgments

The authors thank Francisco de Paula Santander University (Colombia) and the University of Cartagena for providing the equipment required to perform this study. The authors also thank the Ministry of Science and Technology for supporting the Francisco José de Caldas scholarship program for doctorates.

References

Balat M, 2007, Influence of coal as an energy source on environmental pollution, *Energy Sources, Part A: Recovery, Utilization and Environmental Effects*, *29*(7), 581–589.

Butz A. M., Christopher S. & Von Bartheld J. B., 2017). Impact of upstream oil extraction and environmental public health: a review of the evidence. *Physiology & Behavior*, *176*(12), 139–148.

Cassiani-Cassiani D., Meza-González D. A. & González-Delgado Á. D., 2018, Environmental evaluation of agar production from macroalgae Gracilaria sp, *Chemical Engineering Transactions*, *70*, 2005–2010.

Contreras-ropero J. E., Ruiz-roa S. L., García-martínez J. B., Urbina-suarez N. A., López-barrera G. L., Barajas-solano A. F., Zuorro A, 2022, A simulation analysis of an influenza vaccine production plant in areas of high humanitarian flow. A preliminary study for the region of norte de santander (colombia), *Applied Sciences (Switzerland)*, *12*(1).

García Corzo J., Niederbacher Velasquez J., González Rugéles C., Rodríguez Villamizar L., Machuca Pérez M. & Torres Prieto A., 2016, Aguda En Niños Menores De 5 Años, *Revista de La Universidad Industrial de Santander*, *48*(2), 240–245.

Gasparotto J., Da Boit Martinello K., 2021, Coal as an energy source and its impacts on human health. *Energy Geoscience*, *2*(2), 113–120.

Gonzalez-Delgado A. D., Cuenca M., Martinez E. & Rincón B, 2021, Evaluación ambiental asistida por computador del proceso de producción de hidromiel a escala piloto en el Departamento de Boyacá y Bolívar (Colombia), *Ingeniería Y Competitividad*, *24*(1), 1–10.

Gonzalez-Delgado, A.D, Parejo V. & Herrera T, 2017, Computer-Aided Environmental Evaluation of Bio-Hydrogen Production from Residual Biomass of Palm Cultivation, *Contemporary Engineering Sciences*, 10, 773-783.

Hasija V., Patial S., Raizada P., Thakur S., Singh P., Hussain C. M, 2022, The environmental impact of mass coronavirus vaccinations: A point of view on huge COVID-19 vaccine waste across the globe during ongoing vaccine campaigns, *Science of the Total Environment*, *813*, 151881.

Herrera-Aristizábal R., Salgado-Dueñas J. S., Peralta-Ruiz Y. Y. & González-Delgado Á. D, 2017, Environmental evaluation of a palm-based biorefinery under North-Colombian conditions, *Chemical Engineering Transactions*, *57*, 193–198.

Holguin F., Moughrabieh M. A., Ojeda V., Patel S. R., Peyrani P., Pinedo M. & Roman J., 2017, Respiratory health in migrant populations: A crisis overlooked, *Annals of the American Thoracic Society*, *14*(2), 153–159.

Kurzweil P., Müller A. & Wahler S., 2021, The ecological footprint of covid-19 mrna vaccines: Estimating greenhouse gas emissions in germany, *International Journal of Environmental Research and Public Health*, *18*(14).

Mercado R., 2021, Representaciones sobre la inmigración Venezolana en Norte de Santander (colombia), 1920-1930, Thesis, University of Cartagena, Cartagena, COL.

Moghadami M., 2017, A narrative review of influenza: A seasonal and pandemic disease, *Iranian Journal of Medical Sciences*, *42*(1), 2–13.

Paget J., Spreeuwenberg P., Charu V., Taylor R. J., Iuliano A. D., Bresee J. Viboud C, 2019, Global mortality associated with seasonal influenza epidemics: New burden estimates and predictors from the GLaMOR Project, *Journal of Global Health*, *9*(2), 1–12.

Pájaro M., Ramos K. & Gonzalez-Delgado A., 2018, Computer Aided Environmental Evaluation of a Refinery Unit for Sulfide Absorption and Mercaptans Oxidation, *Chemical Engineering Transactions*, 70, 1999–2004.

Shindell D., Faluvegi G., 2010 , The net climate impact of coal-fired power plant emissions, *Atmospheric Chemistry and Physics*, *10*(7), 3247–3260.

Tretyakova M. O., Vardavas A. I., Vardavas C. I., Iatrou E. I., Stivaktakis P. D., Burykina T. I. & Golokhvast K. S., 2021, Effects of coal microparticles on marine organisms: A review. *Toxicology Reports*, *8*, 1207–1219.

Uribe-Soto M. Gomez A. P., Ramirez-Nieto G., 2020, Influenza needs an approach as a "one health" problem in Colombia, *Acta Biologica Colombiana*, *25*(3), 421–430.

Williams R. G., Roussenov V., Goodwin P., Resplandy L. & Bopp L., 2017, Sensitivity of global warming to carbon emissions: Effects of heat and carbon uptake in a suite of earth system models, *Journal of Climate*, *30*(23), 9343–9363.

Yan W., Wang T., Zhao L. & Sun C., 2021, Modified DMEM xenic culture medium for propagation, isolation and maintenance of Balantioides coli. *Acta Tropica*, *214*(September 2020), 105762.

Yang C., Song G., Lim W., 2020, A review of the toxicity in fish exposed to antibiotics, *Comparative Biochemistry and Physiology Part - C: Toxicology and Pharmacology*, *237*, 108840.