INCORPORATING ENERGY GENERATION PROCESS IN ENVIRONMENTAL ASSESSMENT OF A BIOPHARMACEUTICAL PROCESS

AUNI HAMIMI BINTI IDRIS

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LIST OF SYMBOLS

$\langle(Score)\rangle$	average impact factor
$(Score)$	impact factor
F	mass of fuel
H	mass flowrate of utility steam in stream *h*
Stream-h	streams containing utility steam
Streams-gas	streams containing gas
Streams-solid	streams containing solid
EF	emission factor
I	rate of PEI
M	ratio of mass of pollution to mass of product
i	normalized specific PEI
x	mass fraction of a component
y	input stream for fuel
(ep)	energy process
mp	unit mass of product
t	unit of time
s	normalized specific PEI
c	impact category
E	energy
EF	emission factor for gas pollutants *g*
F	mass of fuel

g	gas pollutant
h	stream of utility steam
j	stream
k	chemical component
m	energy stream
M_j	output stream flow rate
in	input
out	output
gen	generated
WFI	Water for Injection
p	product
$\sum_p M_p$	mass flow rate of product produced
α	relative weighting factor
δ_{gas}	total energy in the streams containing gas
δ_{solid}	total energy in the streams containing solid

LIST OF ABBREVIATIONS

ACGIH	American Conference of Industrial Hygienists
AP	Acidification Potential
ATP	Aquatic Toxicity Potential
ATPE	Aqueous two-phase extraction
CFC-11	Trichlorofluoromethane
CFU	colony forming unit
CIP	Cleaning in Place
CO	Carbon oxides
CO_2	Carbon dioxide
EDTA	Ethylenediaminetetraacetic acid
EP	European Pharmacopoeia
EPA	United States Environmental Protection Agency
GMP	Good Manufacturing Practices
GWP	Global Warming Potential
HIC	Hydrophobic Interaction Chromatography
HTPE	Human Toxicity Potential by either Inhalation or Dermal Exposure
HTPI	Human Toxicity Potential by Ingestion
IEX	Ion Exchange Chromatography
JP	Japanese Pharmacopoeia
KCl	Potassium chloride
KH_2PO_4	Potassium dihydrogen phosphate
LC_{50}	Lethal concentration of a chemical which causes death in 50% of test specimen

LCA	Life Cycle Assessment
LD_{50}	Lethal dose on rats by oral ingestion that causes 50% death of the rats
MAb	Monoclonal antibody
MED	Multiple Effect Distillation
Na_2HPO_4	Disodium hydrogen phosphate
NaH_2PO_4	Sodium dihydrogen phosphate
NIOSH	National Institute for Occupational Safety and Health
NO_2	Nitrogen dioxide
NOx	Nitrogen oxides
ODP	Ozone Depletion Potential
ODS	Ozone depleting substance
OH	hydroxyl radical
OSHA	Occupational Safety and Health Administration
PCOP	Photochemical Oxidation Potential
PMI	Process Mass Intensity
PEI	Potential Environmental Impact
ppb	parts per billion
PS	Pure steam
PSG	Pure steam generator
PW	Purified Water
RO	Reverse Osmosis
SIP	Sterilization in Place
SO_2	Sulphur dioxides
SOx	Sulphur oxides
sPEI	Specific Potential Environmental Impact

TLV	Threshold limit values
TOC	Total Organic Carbon
TTP	Terrestrial Toxicity Potential
TWA	Time-weighted averages
USP	United States Pharmacopoeia
USP-NF	United States Pharmacopoeia – National Formulary
VCD	Vapour Compression Distillation
WAR	Waste Reduction
WFI	Water for Injection

ABSTRACT

Biopharmaceutical industries consistently applied Water for Injection (WFI) as a solvent during their production stage. Generally, water is considered as non-hazardous material, but in the pharmaceutical industries the involved treatments to produce WFI typically consumes a large amount of energy. This energy usually comes from the use of utility steam as well as electricity to heat the water as part of the purification process. Consequently, generation of utility steam and electricity needed to produce WFI releases gas pollutants and directly affecting the environment. However, such potential environmental impact (PEI), which is associated to the demand of WFI in a biopharmaceutical process, is typically not included in the environmental assessment of the process as water is considered benign. Therefore, this work aims to estimate the PEI value from WFI and pure steam generation using a simple algorithm which is modified from Waste Reduction (WAR) Algorithm. The PEI is estimated based on the gas pollutants emitted from the energy generation process, which is in this case, the electricity and utility steam. In order to determine the energy needed in WFI and pure steam generation, their generation system was modelled and simulated in SuperPro Designer®. WFI is typically produced in Multiple Effect Distillation (MED) system or Vapour Compression Distillation (VCD) system and meanwhile pure steam is produced in pure steam generator (PSG). A hypothetical large-scale of monoclonal antibody (MAb) production is used as a case study to demonstrate the environmental impact assessment using WAR Algorithm inclusive of PEI from WFI and pure steam demand during manufacturing process. From the case study, it can be concluded that the WFI generation, regardless of using MED or VCD, occupied the largest percentage of energy consumption. The PEI shows a major contribution to the total PEI value, particularly in global warming potential. The hotspot based on the highest WFI consumption is Protein A chromatography. This equipment is used in the downstream processing step to purify the target product. As biopharmaceutical process needs a large amount of WFI in the manufacturing process, therefore it is important to include PEI from WFI as part of the environmental assessment. This result is essentially useful as a tool for decision-making in order to create a more sustainable process.

ABSTRAK

Industri biofarmaseutikal sentiasa memerlukan air untuk suntikan (WFI) dalam pemprosesan mereka untuk digunakan sebagai medium pelarut. Secara umumnya air adalah bahan yang tidak berbahaya, tetapi proses penulenan yang digunakan di dalam industri farmaseutikal untuk menghasilkan WFI kebiasaannya menggunakan sejumlah besar tenaga. Sumber tenaga ini adalah elektrik dan wap air panas yang digunakan untuk memanaskan air sebagai sebahagian proses penulenan air. Akan tetapi, proses penghasilan tenaga ini membebaskan bahan tercemar dan boleh menjejaskan alam sekitar. Walaubagaimanapun, potensi pencemaran alam sekitar (PEI) ini yang boleh dikaitkan dengan permintaan jumlah WFI biasanya tidak dimasukkan ke dalam keseluruhan penilaian alam sekitar sesebuah proses biofarmaseutikal disebabkan anggapan bahawa air adalah satu bahan semulajadi dan tidak memberi kesan kepada alam sekitar. Oleh itu, tesis ini bertujuan untuk menganggarkan nilai PEI dari penghasilan WFI dan wap air tulen menggunakan algoritma mudah yang telah diubahsuai dari Algoritma Pengurangan Bahan Buangan (WAR Algoritma). PEI ini dianggarkan berdasarkan bahan pencemaran yang dibebaskan semasa proses penjanaan tenaga, di mana dalam kes ini ialah elektrik dan wap air panas. Sebuah model sistem penjanaan WFI dan wap air tulen tersebut telah dibangunkan menggunakan SuperPro Designer® dan simulasi proses penghasilan utiliti tersebut telah dijalankan untuk menentukan jumlah tenaga yang diperlukan. WFI biasanya dihasilkan menggunakan sistem Penyulingan dari Kesan Berbilang (MED) atau sistem Penyulingan dengan Wap Mampatan (VCD) dan wap air tulen pula dihasilkan dalam penjana wap air tulen (PSG). Sebuah proses monoclonal antibody (MAb) yang berskala besar telah digunakan sebagai kajian kes untuk menunjukkan cara menggabungkan PEI dari WFI dan wap air tulen tersebut ke dalam keseluruhan penilaian alam sekitar. Dari kajian kes, boleh dilihat bahawa WFI menyumbang kepada peratusan terbesar dari jumlah keseluruhan penggunaan tenaga. PEI dari WFI juga mempengaruhi jumlah keseluruhan PEI, terutamanya dalam potensi pemanasan global. Protein A kromatografi telah dikenalpasti sebagai titik panas di mana jumlah WFI yang diperlukan untuk proses ini adalah yang terbanyak berbanding unit pemprosesan yang lain. Alat ini digunakan semasa proses penulenan produk untuk mengasingkan bahan-bahan yang tidak diperlukan dari produk sasaran. Ini menunjukkan bahawa adalah penting untuk mempertimbangkan PEI dari WFI dalam penilaian alam sekitar sesebuah proses biofarmaseutikal kerana lazimnya proses ini memerlukan jumlah WFI yang besar. Kesimpulan dari tesis ini dapat membantu membuat keputusan bagi memilih proses yang lebih mapan.

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