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CONFERENCE ABSTRACTS

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Industrial pharmacy

Green pharmaceutical practices in industry: A review

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Introduction: The increased use of pharmaceutical products and greater awareness of the environment have resulted in increased subtherapeutic concentrations of active pharmaceutical ingredients being detected in the environment. Each stage of a pharmaceutical product's lifecycle contributes to the issue of pharmaceutical pollution, with the manufacturing industry being the focus of this study. The application of green pharmaceutical practices during pharmaceutical processes strives to minimise the environmental impact of the pharmaceutical industry.

Purpose: To identify green pharmaceutical practices applied in the manufacturing industry which reduce environmental impact.

Method: A literature review was conducted to identify and evaluate the green practices implemented in the manufacturing industry. This was carried out by searching for related terms such as “green pharmaceutical practices”, “green chemistry” and “green pharmacy” using the databases Google Scholar, PubMed and Hydi which is a collection of databases available at the University of Malta. Articles were analysed according to relevancy to the topic in question.

Results: The green pharmaceutical practices utilised within the manufacturing industry identified through the literature review mainly related to 4 broad categories: solvents and their use, wastewater treatment systems, renewable energy and green chemistry.

Solvent recovery and solventless synthesis were measures identified for reducing solvent use in manufacturing processes. The use of green solvents and solvent selection guides were identified as safer and more efficient alternatives in developing sustainable choices, especially in the research and development phase. Wastewater treatment systems are a necessity to reduce organic and slow biodegrading contaminants. These can be subdivided into conventional treatment processes, such as conventional activated sludge processes, which are the more commonly applied due to low cost and effectiveness, and advanced treatment processes. Advanced treatment processes are more efficacious processes in removing pollutants from water used in secondary wastewater treatment with techniques identified, including advanced oxidation and membrane filtration processes. In terms of renewable energy, solar energy, as an alternative for heat and energy generation, and fuel cells, as an alternative to combustion engines and boilers, were identified as providing cleaner energy and reduced emissions. The use of green metrics such as atom economy, process mass intensity, process yield and E-factor aid in optimisation by quantifying efficiency and environmental impact. Continuous manufacturing was identified as an alternative to batch manufacturing, which was noted to reduce material and energy use, while a one-pot synthesis approach reduced solvent and waste production by removing isolation and purification steps.

Conclusion: Different measures along the pharmaceutical lifecycle are necessary to decrease the environmental impact of the pharmaceutical industry. As the environmental consequences are being made more evident through continuous studies, reports and field testing, enforcement of new legislations is key in ensuring a more sustainable future.

Harnessing the power of ICHQ14 in analytical method development

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Background: The incorporation of ICHQ14 stands as a revolutionary force for method development, reshaping the very foundation of their robustness. This paradigm shift unlocks a new era, where methods will be developed under a scientific-based approach, using risk and knowledge management as key enablers. Known as Analytical QbD (AQbD), this approach will increase the robustness of the method while reducing the risk of failure through its lifecycle. guideline.

Purpose: This work seeks to demonstrate the benefits of implementing AQbD principles in the development of an RP-LC method for analysing the assay and related substances of a commercial API, aligned with the requirements outlined in the recent ICH Q14.

Method: The AQbD approach starts with the end in mind, where method goals pre-definition and its quality requirements complete the Analytical Target Profile (ATP) criteria. For that purpose, an appropriate technology is selected, and the best operating conditions (Normal Operable Range (NOR) and Method Operable Design Region (MODR)) are defined based on a risk assessment exercise, where potential sources of variability are identified through experimental studies (Design of Experiments (DoE)) and prior knowledge. This AQbD methodology ends up with ATP verification and a risk mitigation phase, where all sources of variability are reduced and controlled through an effective Analytical Control Strategy (ACS). A fit for the intended purpose method is the expected output of this methodology, where Risk Management (RM) and Knowledge Management (KM) are the key enablers.

Results: AQbD was followed, highlighting the results of the following steps: Prior knowledge: physical-chemical properties of the analytes, namely the distribution of micro species and the Log D vs pH, were predicted due to their impact on RP-LC. This information supported the selection of the optimal working pH and the most suitable column chemistry. DoEs (Design of Experiments) were used to test several parameters, with only a few experiments, using a central composite face-centred cube (CCF) experimental design. This study allowed the identification of critical parameters for the separation of the analytes, as well as the impact of each parameter and possible interactions between them.

Conclusions: A method for the determination of related substances of a commercial molecule was successfully developed using AQbD. A selective, accurate, and precise method was obtained. The gain of knowledge about the method's performance, increased robustness, cost reduction, and confidence in failure risk reduction are some of the benefits of this approach, aligned with the requirements presented in the more recent guideline ICH Q14.

Crisis management in pharmaceutical industry and wholesale during the COVID-19 pandemic

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Background: Pharmaceutical supply chains around the globe have experienced increased demands, manufacturing capacity issues and distribution problems due to the Coronavirus disease 2019 (COVID-19) pandemic. The pharmaceutical industry and wholesale have implemented several actions to secure the manufacture and supply of medicines and to develop innovative vaccines against the virus. Despite the central role in managing the pandemic, there is a lack of crisis management theory-based empirical research in this sector.

Purpose: The purpose of this study was to investigate the crisis management in pharmaceutical industry and wholesale during the COVID-19 pandemic using crisis management theory as a theoretical framework.

Methods: A national cross-sectional survey was developed based on crisis management theory and sent to managing directors in the pharmaceutical industry and wholesale in Finland (n=69) during the second wave of the pandemic in November 2020. Descriptive statistics were calculated, and qualitative data from open-ended responses were grouped by question based on similarities.

Results: The response rate was 29% (n=20), including 11 managing directors and nine other directors or managers from production, quality, public relations, or business management functions. Fifteen (75%) organisations had a pre-existing preparedness plan. During the pandemic, 19 organisations (95%) tailored a new plan for the pandemic situation. The first responses to the pandemic included activating crisis management plans and teams, securing API (Active Pharmaceutical Ingredient) delivery from China, ensuring supply chain management function, and initiating

guidelines for infection prevention. A pandemic crisis team was established in seventeen (85%) organisations. The focus was on ensuring the production and supply of critical medicines and securing the safety of employees. Collaboration and communication with other actors in the pharmaceutical supply chain increased or improved in 14 (70%) organisations, whereas in six (30%), it decreased or was unchanged. Learned lessons included setting clear priorities for crisis management, effective and fast actions at the onset of the pandemic, the importance of increased internal and external communication, and the importance of improving crisis preparedness with plans and rehearsal during normal times.

Conclusions: Despite challenges posed by the pandemic, the pharmaceutical industry and wholesale were able to maintain pharmaceutical supply and operations in Finland. Key actions in crisis response were swift activation of crisis management, increased communication and collaboration and changes in operations, such as focusing on the manufacturing of high-demand medications. Learned lessons could be used to improve preparedness for future crises. Crisis management process theory provided a structured and holistic framework for analysing the results. In the future, the results will be complemented by data triangulation through an interview study.

Medicines shortages monitoring system: The French Chamber's tool becoming official and mandatory for stakeholders

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Background: In February 2024, French authorities issued the national roadmap of measures to counter medicines shortages. The "DP-Ruptures", a tool developed by the French Chamber of Pharmacists, has a central place in this strategy. A bill is currently being discussed to make it mandatory for all actors in the pharmaceutical chain.

Purpose: The purpose of this tool is to improve communication between supply chain actors to mitigate the impact of medicines shortages.

Method: The shortages monitoring system allows the 20,000+ community pharmacies to report shortages to the operating pharmaceutical company either automatically via their dispensing software (in community pharmacies) or manually through the Internet (in hospital pharmacies). In return, the chief pharmaceutical officer of the operating pharma company provides them with information such as the planned return date, alternative medicines, etc. Wholesale pharmacists access this information as well. Dispensing pharmacists also notify when shortages end on their side (i.e. when they have been able to obtain at least partial supplies).

The system allows quantifying shortages (impacted therapeutic classes, shortage rate, shortage duration) thanks to an extensive coverage, and fosters communication with pharmacists at every step of the chain.

Results: On average, 1 million shortage declarations are sent each month via the system. 98% of French community pharmacies, 85 subscribing pharmaceutical companies (representing 84% of medicines dispensed in the community setting), and 11 subscribing wholesalers (representing 98% of the market) are connected. The French Medicines Agency has had access to the platform since February 2023 and can check and monitor the data available.

A bill on shortages is currently being examined by the Parliament, which would make the use of the Chamber's system mandatory for community and hospital pharmacies.

The government chose to rely on this tool to facilitate the exchange of information between all the actors of the pharmaceutical chain and to reinforce its use by all as outlined in its 2024 roadmap to fight shortages of medicines.

Conclusion: This measure is in line with the future European pharmaceutical legislation (currently under negotiation), which contains a set of actions to counter medicines shortages at the European level, including provisions to ensure efficient information and notifications of shortages at the national level.

Connecting the dots between pharmaceutical manufacturing activities in meeting health challenges and climate change across the globe

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Introduction: Climate change as a global concern has been established to be a threat to public health. Climate change, manifesting in changes in wind, conditions of precipitation and elevated temperature, enhances the transmission of infectious diseases and causes respiratory disorders and cardiovascular diseases. Considering vector-borne diseases, the life cycle of their vectors, reproduction and feeding are influenced by the nature of the climate. In Africa, Predictions suggest that climate change will result in a proportionate increase in the spread and prevalence of malaria, dengue, and Zika. The role of pharmaceutical manufacturing is to provide medications to solve the world's growing health challenges.

However, pharmaceutical manufacturing processes can be detrimental by driving climate change, with indirect detrimental public health implications.

Method: A literature search was conducted, combining keywords such as "pharmaceutical manufacturing", "climate change", and "public health" using boolean operators. Specified inclusion criteria were used to identify relevant titles and articles. Original articles written/available in English, published in reputable journals accessible through indexing platforms and other grey academic literature were included. The articles which met the inclusion criteria were then analysed to explore themes in the nexus of pharmaceutical manufacturing and climate change.

Results: Pharmaceutical manufacturing contributes largely to the world's greenhouse emissions. Pharmaceutical manufacturing activities lead to the release of active pharmaceutical principles and greenhouse gases into the ecosystem. The presence of greenhouse gases is detrimental to climate and human health. While pharmaceutical manufacturing activities are targeted at solving the world's health needs, its detrimental effect on climate leads to cardiovascular diseases, respiratory diseases and heat-related illnesses and deaths. Additionally, Increased demand for medications will require increased pharmaceutical manufacturing activities, increasing its effect on climate. The pharmaceutical industry is also vulnerable to the effects of climate change, most especially on the supply chain. Extreme weather events can cause a delay in the supply of raw materials for production and compromise cold chain storage. Manufacturing activities can also be impeded when manufacturing sites are located in areas affected by weather events, which is evident in the cessation of production by Pfizer, Merck and Norvatis at their southeast US operations due to Hurricane Florence in 2018.

Conclusion: Pharmaceutical manufacturing is important for meeting the world's healthcare needs. However, the cycle of solving health problems while creating more health problems needs to be addressed through sustainable pharmaceutical manufacturing. In trying to meet the world's healthcare needs, pharmaceutical manufacturing potentially impacts the ecosystem negatively. This further compromises human health, leading to increased pressure on the health system and increased demand for pharmaceutical manufacturing to meet increasing health needs. The increased demand will influence the need for pharmaceutical manufacturing companies to scale up to meet the increasing demand, which further increases the influence on climate change and worsens public health outcomes. There is a need to champion sustainable manufacturing practices in global pharmaceutical manufacturing industries.

Formulation of paediatric dosage form for the selected antiretroviral drugs

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Introduction: In 2020, it was estimated that 1.7 million young children were living with HIV and AIDS, and only 53% were on antiretroviral therapy (ART). Most ARVs available in powdered and liquid forms on the market have a bitter taste that can affect patient adherence. The accurate dosing of liquids is a problem that may result in overdosing or underdosing, leading either to toxicity or a lack of therapeutic effects of a drug. In addition, liquid formulations generally have poor stability profiles.

Purpose: The study aimed to formulate a single-dose lamivudine and a fixed-dose combination of abacavir sulfate, zidovudine, and tenofovir orodispersible tablets (ODTs) for use in paediatric patients. The ODTs require no water to administer, have fast dispersion rates, ensure accurate dosing, and avoid first-pass metabolism.

Method: The differential scanning calorimetry (DSC) technique was employed as a preliminary study for the evaluation of the compatibility between the selected excipients (i.e., avicel PH 200, sodium starch glycolate, sodium lauryl sulfate, and stearic acid) and active pharmaceutical ingredients (APIs) (i.e., lamivudine, abacavir sulfate, zidovudine, and tenofovir). The characterisation of the powder properties, such as particle size distribution, morphology, and flowability (i.e., angle of repose, bulk and tapped densities) of the excipients and APIs were investigated. The solubility of all APIs was conducted according to South African Health Products Regulatory Authority (SAHPRA) guidelines using the flask-shake technique. The feeder performance tests were carried out for different blenders (i.e., abacavir sulfate + tenofovir + zidovudine + avicel PH 200, sodium starch glycolate + avicel PH 200, lamivudine + avicel PH 200, sodium starch glycolate + stearic acid + avicel PH 200, and sodium starch glycolate + sodium lauryl sulfate + avicel PH 200) using spiral and concave pairs of screws. The variability of the powder flow was monitored on Lab-View software, and the results were further analysed on an Excel spreadsheet.

Results: The DSC profiles revealed that lamivudine is compatible with avicel PH 200, stearic acid, and sodium starch glycolate, while abacavir and zidovudine showed an endothermic peak match with sodium lauryl sulfate, avicel PH 200, and sodium starch glycolate. A solubility test validated that phosphate buffer at pH 6.8 was a suitable dissolution medium for APIs. These were evidenced by a dose-solubility

volume of less than 250 mL. The feeders configured with concave screws showed consistent variability in blender mass flow compared to feeders with spiral screws. These were confirmed by the percentage relative standard deviation of the mass flow rate, which was found to be less than 3% with concave screws. Based on the above, an experiment design (DoE) will be employed to optimise the process parameters and formulation in continuous manufacturing. Stability studies will also be executed on a final product, as well as critical quality attributes.