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RESEARCH ARTICLE

Risk Assessment and Communication in Pharmaceuticals: Recognizing the Differences in Occupational Health and Medication Safety

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Abstract

Pharmaceuticals are the most common medical intervention. Ensuring workers and members of the public get the most benefits from advances in modern medicine is a critical component of improving the health care system. Pharmaceuticals bring healing to patients but increased risk of illness have been reported among workers manufacturing, handling and administering pharmaceutical products with inadequate attention to personal safety. Their potential for both helping and harming human health can be predicted based on health-based risk assessment. This assessment process for occupation and medication (product/patient) safety is similar yet provides different sets of information. Understanding the hazards and risks of pharmaceuticals and conveying appropriate safety messages to workers is essential. Workplace training in differentiating the use of safety data sheets (SDS) from drug product information (DPI) sheets, effectively communicating the difference between safe work practices (SWP) and good manufacturing, laboratory and clinical practice (GMP, GLP and GCP) quality guidelines will direct workers' attention to the essential chemical hazard and risk information. The increase in knowledge on the proper use of SDS and SWP will encourage appropriate self-protective behavior in reducing chemical exposure amongst workers and improve safety at work.

Keywords

Pharmaceuticals, Occupational health, Risk assessment, Safety data sheets (SDS), Drug product information (DPI), Safe work practices (SWP)

Introduction

The use of evidence derived from research and that which is observed in practice to influence policy is the latest approach to effectively promote and improve public and occupational health. Exposures to hazardous chemicals in pharmaceuticals have been long recognized to have both positive and negative effects on human health [1,2]. While the potential therapeutic benefits of drugs outweigh the risks of side effects for patients, exposing pharmaceutical industry and health care workers to the same side effects is an unacceptable outcome. It is important for users to understand the complexities and uncertainties of occupational health and medication safety, thus a safer use of medicines.

Regulatory Considerations

Regulatory guidelines for protecting workers from exposure to hazardous chemicals while at work are in place to some extent around the world, however in large part they are not effectively enforced. This differs from the vigorous legal and tight regulatory requirements for pharmaceuticals and its industry which have long been in place to ensure drugs are safe and effective for use by patients.

Extensive effort has been made to reduce business burden through harmonization of regulatory requirements. The International Conference on Harmonization

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of Technical Requirements for Pharmaceuticals for Human Use (ICH) has been in operation for over 20 years. The ICH not only facilitates simultaneous submission, approval, and launch of new drugs, it also requires further stringent compliance of good manufacturing, laboratory and clinical practices (GMP, GLP and GCP) quality guidelines and regulations.

In work, health and safety (WHS), there is the recent introduction of Globally Harmonized System for classification and labelling of chemicals (GHS). This is a single internationally agreed system of chemical classification and hazard communication through labelling and Safety Data Sheets (SDS) that impact and improve safety for workers. It encourages consistent and simplified communications on chemical hazards and practices for safe handling and use of chemicals. However, unlike drug product information (DPI) sheets provided for pharmaceuticals SDS for hazardous chemicals do not require authorization by a government agency. SDS must be prepared with a scheduled format and are otherwise, self-regulated, in compliance.

Health Based Risk Assessment and Exposure Standard Considerations

During manufacturing and preparation of pharmaceuticals, workers can be exposed to various chemicals, including the potent active pharmaceutical ingredients (API), chemical intermediates, as well as other chemicals such as solvents, catalysts, acids and bases [2]. To comply with both the drug and WHS regulations, manufacturers must determine chemicals they produce are hazardous. The API are the key components of a drug and in most cases, have serious toxicity profiles [3]. Health-based risk assessment tools are especially needed for these potent chemicals and standard animal tests have been developed to predict their hazard properties.

Pharmaceutical companies have long recognized that animals and clinical studies undertaken on pharmaceuticals to establish patient safety must be supplemented with additional toxicology studies to identify other occupational hazards. This is because pharmaceuticals can potentially have different hazard profiles to workers and to patients. Their hazard profile to workers can be distinct from the primary pharmacological effects such as eye and skin irritation and sensitization. For example, antibiotics like penicillin and cephalosporins that are designed for antimicrobial activity, are known to induce allergic contact dermatitis and asthma in occupationally-exposed individuals [4].

In addition, airborne exposure to pharmaceuticals tends to be more relevant to workers than patients. This is because, for the most part, drugs are powders and any handling of powders may result in airborne dispersion [5]. Pharmacodynamic evidence shows that occupational exposure to airborne therapeutic substances can be associated with a much higher risk of an adverse health effect, especially on the lungs or skin than by their therapeutic administration [6]. Similarly, pharmacokinetics studies indicate that for certain therapeutic substances occupational exposure by inhalation results in a more rapid and complete systemic absorption than a similar dose administered (usually orally) for therapeutic purposes [6]. Inhalation studies are therefore relatively more important for occupational health risk assessment unless the route of administration of the medicine is through inhalation.

Health-based risk assessment is required, both qualitatively and quantitatively. The risk assessment process for occupation and medication (product/patient) safety is similar yet it provides different sets of information. When performed from an occupational standpoint, qualitative health-based risk assessment, based on toxicity and potency of API, can contribute significantly to risk management. These include determining adequacy of controls of potential exposure, safe work procedures (SWP) and practices for worker protection which may involve use of personal protective equipment (PPE) or specially designed/separate facilities [5,7]. Whereas from a patient safety standpoint, the understanding of the drug's mechanism of action, safety and efficacy profile could inform prescribers in how to optimize a treatment based on benefit-risk analysis [8].

Quantitative risk assessment involves understanding uncertainties in the data, selecting events of interests and weighing multiple events as criteria for assessment. This requires evaluation and interpretation of toxicological, pharmacological, and clinical data, selection of the appropriate critical studies/endpoints, determining point of departure (PoD) to estimate No Observed Adverse Effect Level (NOAEL) or Lowest Observed Adverse Effect Level (LOAEL), and extrapolation to acceptable levels from these studies using appropriate factors [7]. In occupational health, this involves measuring airborne levels of the contaminant and assessing whether the levels exceed workplace exposure standards (WES). The WES defines the maximum concentration of a hazardous chemical that can be tolerated in the air of the production room without imparting any negative effect on the health of the workers. In patients' safety, the determination of maximum recommended therapeutic dose (MRTD). MRTD estimates the upper limit beyond which a drug's efficacy is not increased and side effects begin to outweigh beneficial effects. The determination of MRTD and WES procedure is almost similar because they are both based on the same dose-response and hazard information collected from animal and clinical data, although additional information (in most cases, inhalation studies) is usually needed for setting WES [5,7]. The key difference between calculating these two exposure/risk values is that MRTD is for patient safety and may sometimes need to consider sensitive subgroups (e.g. the elderly and children), whereas

the WES is for worker safety and is applied, generally to a healthy working population. Other factors to be considered include route of exposure and difference in bioavailability [9,10]. Appropriate safety or uncertainty factors are therefore needed to be applied to each PoD to arrive at supportable health-based values to reflect the differences. In most cases, lower/less safety factors are applied when setting WES than MRTD [6]. It is worth noting that in some cases WES is a 'pragmatic' level based on consensus rather than purely health-based. They are set at a level that is 'reasonably practicable' to achieve, considering several factors like the health costs, compliance costs and technical feasibility [11].

Research Evidence on Workplace Practice

Many of the workplace incidents that occur in health care workers are deemed to be preventable. A recent study by Hon and Abusitta [12] suggested poor communication, inadequate controls, and lack of training to be the key contributing causes of antineoplastic drugs incidents. Other studies demonstrated that good safe work practice and engineering controls can minimize spillages and contamination during administration of antineoplastic drugs [13-15].

As stated above, SWP is part of risk management to ensure workers are aware of, and understand how to, minimize risks in their work tasks. They also tell workers how to protect themselves and avoid injury or illness while performing those tasks. SWP should not be confused with GMP, GLP and GCP. Those good practices are international quality standards and are therefore enforced and audited for product safety, ethnicity of trial subjects as well as quality of laboratories and clinical studies in drug development.

Safe Work NSW, as the NSW WHS regulator, conducted several programs to verify regulatory compliance on the safe use of cytotoxic drugs in compounding pharmacies and in the health care sector [16-19].

Results showed active drug contaminants at work areas where well trained healthcare professionals performed their duties. These workplaces which included GMP and GCP accredited organizations, demonstrated satisfactory compliance with WHS regulations related to chemical management. However, they did not reflect its intended purpose in preventing workers exposure to active drug contaminants. This suggests that formulating and/or administering a safer medicine for patients is not equal to a safer workplace for workers.

Observation in Practice on the Difference in SDS and DPI

At SafeWork NSW, we observed a potential misunderstanding on the use of DPI sheets instead of SDS for pharmaceuticals with the same API. Although both documents provide safety information to their audiences, their content can be different because, as mentioned earlier, pharmaceuticals can potentially have a different hazard profile to workers and patients.

SDS provide useful information on chemicals, describing the hazards (adverse health effects) the chemicals present, its WES, routes of exposure at work, and provide workers and emergency service personnel with essential information on handling, storage and emergency measures in an accident. Whereas, DPI sheets including Summary of Product Characteristics (SmPC), Package Insert (PI) and Patient Information Leaflet (PIL), Consumer Medicine Information (CMI), provides information about the medicine, including the MRTD, dosage regimen, pharmacology profile, mechanism of action, adverse reactions, potential drug interaction, etc. The DPI sheets are intended to assist healthcare professionals on using the medicine safely and for patients and member of the public to be better informed about the medicines [20,21]. They do not address workers' safe use and handling of such products.

SDS and DPI sheets are documents prepared for difference purposes and target audiences. Most importantly, the safety information provided in SDS is hazard based. It describes the intrinsic properties of a chemical and its potential to do harm to workers regardless of any hygiene control measures to prevent exposure, whereas DPI sheets are risk based. It represents the potential for a chemical to cause adverse health effects to a patient when used under the recommended route of administration and dosage regimen (i.e. the likelihood that any hazard will actually cause somebody harm under specific conditions). In other words, taking a certain medicine can cause harm to a patient, however, the risk is acceptable under medical supervision.

Conclusions

In pharmaceuticals, achieving marketing authorization of a medicine is the goal of every company in the industry. It is a statutory requirement before placing a medicine on the market to be used by patients. Once a new medicine is marketed, it generates profit to the company and incentives to the workers. Compliance to GMP, GLP and GCP is part of the requirement in this legalized authorization process. It ensures quality of products/studies, appropriate ethics for non-clinical and clinical trial subjects. Occupational safety is another focus in the pharmaceutical and health care industry. This is for the protection of workers who handle hazardous chemicals, particularly the API. SWP are required and generally developed in-house to comply with WHS regulations.

In the ideal world, workers practice all good pharmaceutical practices (GMP, GLP and GCP) as well as safe work practices. However, from a social psychological standpoint, it was shown that people's attention is

directed to the rewards and tend to lose focus on the tasks when immediate interest is not present [22,23]. Our previous studies on regulatory verification on safe use of cytotoxic drugs have showed residue API contaminants in compounding pharmacies and health care centres where SWP were in place. This paper has highlighted that by raising hazard awareness through information and training, it will influence immediate interest in the worker to protect their own health. This, in turn, will help engage workers in preventive safe work practices [16-19].

This paper has also emphasized the similarity and differences in conducting health based risk assessment for worker and patient safety. We also demonstrated through our observation in practice that there is potential misuse of SDS and DPI in the workplace. A key element in sustaining WHS compliance involves training. By training workers to recognize the differences among product quality, patient and worker safety, it allows workers to understand the purposes of various procedures and why SWP, in addition to GMP, GLP and GCP, are developed separately in protecting their health. It is also important to provide readily available health information and encouraging information seeking behaviour [24] to allow workers to obtain further details at any time. The importance of differentiating the use of SDS and DPI cannot be understated. Both documents are for communicating safety information but are written for different audiences. By recognizing the difference in content of each document, each audience (worker, patient and health care professional) will be able to use the documents appropriately and be properly informed to exercise appropriate decisions and actions in relation to hazard and risk. The SDS, in addition to providing advice on safety precautions to worker, gives an employer the ability to develop an active program of worker protection measures and training that are specific to the workplace. By protecting workers from occupational hazards, a safer workplace with positive morale can be resulted.

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