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NIOSH list of hazardous drugs in healthcare settings, 2024 The NIOSH List of Hazardous Drugs in Healthcare Settings is a tool designed to help healthcare workers and employers identify which drugs are considered hazardous. The list was updated in 2024 to include new drugs and make changes to the existing ones. The FDA's Center for Drug Evaluation and Research (CDER) has issued a new list of hazardous drugs that pose risks to healthcare workers handling, preparing, dispensing, administering, or disposing of these substances. The public was invited to comment on this draft list, with 132 submissions received from a diverse range of institutions, including hospitals, pharmacies, pharmaceutical companies, and individual healthcare professionals. NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings Update: A Reevaluation of Toxicity Information ========== The National Institute for Occupational Safety and Health (NIOSH) has revisited its categorization decision regarding antineoplastic and other hazardous drugs in healthcare settings. The agency seeks to address concerns raised by public commenters on the draft policy and procedures for developing the NIOSH List of Hazardous Drugs. This update aims to improve the accuracy and relevance of the list. In 2018, NIOSH issued a notice outlining its approach to categorizing hazardous drugs in healthcare settings. The agency received 55 public comments, which led to revisions in the draft policy and procedures. The updated document, titled "Procedures for Developing the NIOSH List of Hazardous Drugs in Healthcare Settings," was finalized in April 2023. A critical aspect of this update is the consideration of toxicity information. NIOSH has revisited its methodology for reviewing toxicity data to ensure that it remains effective and relevant. The agency has also published two reevaluation reports, one on liraglutide and another on pertuzumab, which were added to the NIOSH List in 2014 and 2016, respectively. NIOSH encourages public commenters to review these updates and provide feedback. The agency is committed to maintaining a rigorous review process that balances the need for frequent updates with the requirement for thorough scientific evaluation. Employers are advised to regularly review potential hazard information on newly approved drugs, even if they have not yet been evaluated by NIOSH. This approach will help mitigate risks associated with hazardous drugs in healthcare settings. References: * Procedures for Developing the NIOSH List of Hazardous Drugs in Healthcare Settings (NIOSH 2023a) * Managing Hazardous Drugs Exposures: Information for Healthcare Settings (NIOSH 2023b)

forward to seein everyone at the meeting tomorow and discussin our strategies for drugs that don't meet the NIOSH criteria. ========== NIOSH not identifyin the drugs that have been reviewed and failed to meet the NIOSH criteria 'cause doin' so might be misinterpreted as meanin' those drugs are free of potential hazards. Even if a drug ain't on the List, it still might have some hazards associated with exposure. In addition, NIOSH keeps reviewin' drugs as new information and warnings get added to their package inserts, which would make publishin' the names of reviewed drugs confusing, 'specially since info changes over time. Some drugs don't meet the criteria due to lack of data, so they ain't on the List. The 2024 List hasn't been changed in response to comments about this, though. Niosh List Classification And Hazard Information ========== NIOSH provided the list of drugs in the 2024 List with some information on how the listed drugs are classified and used. Six drugs were added to the list as part of a new rule, which will provide users with more information about potential hazards posed by these drugs. Some commenter requested that NIOSH include more specific information about the relevant hazards posed to healthcare workers in the List to provide healthcare workers access to more information and improve safety. NIOSH response: The List identifies drugs that meet the criteria specified in the Procedures, but it is not intended to be a comprehensive review of every hazard potentially posed by a drug. Drugs are repeatedly reviewed as new information and warnings are added to their package inserts, some drugs do not meet the criteria due to current lack of data. NIOSH suggests that workplaces review the potentially hazardous drugs handled in their facilities to identify specific details on the hazard of those drugs. Table 1 was reorganized from the 2020 draft with a new criterion to include only “drugs with MSHI [manufacturer's special handling information] in the package insert and/or those that meet the NIOSH definition of a hazardous drug and one or more of the following criteria: are classified by NTP as known to be a human carcinogen or are classified by IARC as Group 1 carcinogenic to humans or Group 2A probably carcinogenic to humans.” Eight commenter suggested that the reorganization was appropriate, but some commenters were concerned that the change would confuse some users and that some drugs with shared mechanism of action ended up on different tables. NIOSH reorganized Table 2 in the 2024 List to include “drugs that meet the NIOSH definition of a hazardous drug and do not have MSHI, are not classified by NTP as known to be a human carcinogen, and are not classified by IARC as Group 1, carcinogenic to humans, or Group 2A, probably carcinogenic to humans. (Some may also have adverse developmental and/or reproductive effects.)“The identification of hazardous drugs with potential developmental and reproductive hazards has garnered significant interest, prompting NIOSH to revise Table 2 in the 2024 List by adding a new column for easier drug discovery. Blinatumomab blinatumomab blinatumomab blinatumomab and carfilzomib have been left off the list at this time. One issue is whether molecular weight stops it from being considered dangerous. NIOSH wants to use that idea for future updates to the drug. If you dont consider how the molecules weigh, you will not know if they are a risk or not. They want to make sure that people can see which drugs are at risk and what steps can be taken to prevent them. NIOSH is not trying to say that all these drugs are bad, but it just wants to make sure that people know the risks.NIOSH's decision to maintain certain drugs on their list of potential reproductive and developmental hazards is based on evidence suggesting they may pose a risk to workers' health. Experimental animals exposed to eslicarbazepine at low concentrations showed signs of developmental effects, which raises concerns about the potential for occupational hazards in humans. NIOSH emphasizes that their 2024 List aims to identify potential hazards to aid employers in assessing risks to workers. Several drugs have been identified as posing reproductive and developmental risks: cabergoline, clonazepam, fluconazole, plerixafor, riociguat, and ziprasidone. Reviewing public comments, it appears that many experts agree with NIOSH's stance on these drugs. While some commenters suggested removing certain drugs due to limited evidence or conflicting results, NIOSH found sufficient reason to maintain them on the list. In particular, fluconazole was noted for its potential teratogenic effects at high doses, and ziprasidone showed embryofetal toxicity even at low doses. Animal studies also highlighted concerns about cabergoline, clonazepam, plerixafor, and riociguat. NIOSH acknowledges the scarcity of occupational exposure data but emphasizes the need to prioritize worker safety. The review of public comments on icatibant has not been completed yet, as the text provided appears to be truncated.Repeated exposure to hazardous drugs or contaminated surfaces in an occupational setting is not unexpected, resulting in potential adverse effects in humans. NIOSH notes that data indicate fetal death, preimplantation loss, and delayed parturition in rats at doses lower than human doses, as well as increased abortion rate, fetal death, preimplantation loss, and preterm births in rabbits at doses lower than the maximum recommended human dose (MRHD). Reproductive effects were also observed in dog studies affecting both males and females, though these effects were reversible 4 weeks after exposure ceased. Given that occupational exposures may lead to chronic or repeated exposures, NIOSH intends to consider reevaluating certain drugs during a future update to the List. Regarding leuprolide, one commenter noted that it requires continuous systemic exposure for 2-3 weeks to cause a decrease in sex hormones leading to fetal toxicity or reproductive harm. Another suggested removing it from the List due to the availability of extended-release formulations decreasing occupational exposure risk. NIOSH response acknowledges these points but notes that working with hazardous materials may lead to chronic exposures, and the List does not differentiate based on dosage form. As for olaparib and teriflunomide, one commenter suggested removing them from the List due to low risk of direct occupational exposure when handling intact capsules. NIOSH response reaffirms that the List is a hazard identification tool, and many factors affect the risk associated with handling hazardous drugs, including formulation, proper handling technique, and personal protective equipment (PPE) utilization. Regarding oxytocin and other oxytocic drugs, commenters asked to remove them from the List as there are no documented cases of routine handling resulting in occupational hazard. NIOSH response notes that these drugs were initially added to the List as a class in 2004 and have been maintained since then, with some acknowledging differences in their mechanism of action. ========== Several substances appear to have a similar mechanism of action, but their safety profiles vary widely. Oxytocin and methylergonovine pose a risk to fetuses in the third trimester of pregnancy, resulting in their retention on the 2024 List. On the other hand, ergonovine has never been approved for use in humans by the FDA and is therefore not included on the list. Paroxetine is currently listed due to studies indicating potential harm to fertility in males and increased congenital malformations in developing fetuses. Although some commenters suggested removing paroxetine from the list due to inconclusive studies and lack of data on occupational exposures, NIOSH has determined that the totality of evidence supports maintaining it on the list. Spironolactone is also listed due to studies showing significant increases in hepatocellular adenomas and testicular interstitial cell tumors in rats. Although some commenters suggested removing spironolactone from the list due to limited long-term exposure data, NIOSH has determined that the available evidence supports its inclusion on the list. Topiramate poses a potential hazard to fetal development due to studies demonstrating limb malformations and reduced fetal body weights in rats exposed to doses half the recommended human dose. Human data also suggest an increased risk of cleft palate and being small at gestational age for infants exposed in utero. Ulipristal is currently listed, but one commenter suggested removing it from the list. However, more information is needed to make an informed decision about its inclusion on the list. No changes were made to the 2024 List based on public comments.Ulipristal and Vigabatrin: NIOSH Weighs Teratogenic Risks ========== NIOSH keeps ulipristal on pregnancy prevention list due to teratogenic concerns. Ulipristal poses a potential hazard to unborn offspring, according to NIOSH. Vigabatrin may also affect development in the womb when taken during pregnancy. NIOSH maintains vigabatrin on pregnancy prevention list despite lack of reported fertility issues in rats. Carfilzomib and dasatinib imatinib placement sparks debate among commenters. ==========NIOSH List of Hazardous Drugs, 2024: Response to Public Comments ========== Some drugs on the list are potential carcinogens, and their inclusion is based on various criteria. The tables comprising the list are not intended to stratify risk, and facilities should evaluate the hazards of each drug in their formulary to make appropriate exposure control management strategies. For example, estrogen/progesterone combination drugs are classified as Group 1 carcinogenic to humans by IARC due to sufficient evidence that they cause cancer of the breast and endometrium. The importance of identifying specific hazards related to drugs in a workplace's formulary cannot be overstated, and it is crucial that workplaces develop effective exposure management strategies to mitigate these risks. # Changes to the 2024 List Despite public comments, no changes were made to the 2024 List. One commenter suggested that vandetanib should be placed in Table 2 similar to other EGFR tyrosine kinase inhibitors. However, NIOSH notes that the tables are not hierarchical and that drugs with similar information can be listed on different tables. # Specific Drug Classification/Identification Triptorelin is identified on the List in Table 2 as having both AHFS classifications "68:18:08 Gonadotropin Agonist/Antagonist" and "10:00 Antineoplastic." NIOSH suggests that facilities evaluate all the hazards present in their formulary, as a designation of antineoplastic by AHFS does not identify special hazards. # Revision of Generic Drug Names NIOSH revised the 2024 List to include the FDA assigned prefixes (i.e., ziv-, ado-, and fam-) in generic drug names to correct issues caused by removing prefixes that were part of several generic drug names. # Editorial Improvements NIOSH accepted editorial, spelling, and correction comments in the 2024 List, as appropriate. ========== ========== To what extent does pertuzumab pose a health risk? Should oligohydramnios be used as the primary metric for evaluating its effects on human health? Moreover, is needlestick injuries a reasonable route of exposure for healthcare workers, and are their assumptions about pertuzumab exposure in healthcare settings realistic? Pertuzumab's potential hazard to healthcare workers has been a subject of debate. NIOSH received comments from various stakeholders, including trade associations, pharmaceutical manufacturers, and private individuals. These commenters provided feedback on the reevaluation process for monoclonal antibodies like pertuzumab. A critical point raised by public commenter 1 is that the evaluation methods used by NIOSH may not be sufficient to identify hazards, rather than assessing risk. They argue that physical properties of a drug molecule should be considered when determining its hazard level. However, NIOSH clarifies that they evaluate hazards based on maximum human recommended dose via all relevant routes of exposure and consider molecular properties in relation to specific adverse effects. The recent reevaluation of pertuzumab has led to some changes in NIOSH's recommendations. The agency acknowledges that their initial assessments may not have been entirely accurate, prompting them to revisit and refine their evaluations. This process ensures that healthcare workers are aware of potential hazards associated with pertuzumab exposure. Considering the complexities surrounding pertuzumab's evaluation, it is essential to examine alternative approaches for characterizing its hazard potential. By doing so, NIOSH can provide more accurate guidance for healthcare settings, ultimately prioritizing worker safety and well-being.Looking forward to discussing everyone at the meeting tomorrow and figuring out our strategies for dealing with the healthcare workers who are exposed to hazardous drugs in the workplace. ========== NIOSH considers the molecular properties of these drugs when evaluating their potential risks to healthcare workers. The commenter thinks that NIOSH should be careful not to make assumptions about occupational exposure based on commercial packaging, as some dosage forms may not offer the same level of protection in the future. In fact, pharmacy employees who handle bulk active pharmaceutical ingredients can be exposed to higher levels and more frequently than typical healthcare workers. When assessing exposure risk, NIOSH agrees that evaluating duration and intensity are important factors. However, NIOSH also believes that molecular properties should be taken into account, even if a route of exposure is unlikely given currently available formulations. For example, a large peptide molecule may not lead to the same level of exposure via inhalation as it would through other routes. The commenter thinks that repeated exposure and absorption to peptide-based drugs like liraglutide are unlikely in many clinical settings, but they still want to emphasize the importance of considering physical properties for hazard identification. Since carcinogenic effects and fetal abnormalities cannot be ruled out in humans, liraglutide meets the existing criteria for hazard identification. NIOSH is taking a similar approach, considering intrinsic molecular properties when characterizing potential hazards to healthcare workers. The NIOSH hazardous drugs definition takes into account these molecular properties because they may not necessarily reflect the actual occupational hazards posed by a drug. Overall, it seems that NIOSH and the commenter are on the same page when it comes to prioritizing the safety of healthcare workers who handle potentially hazardous drugs in the workplace. By considering both exposure routes and molecular properties, we can better understand the risks involved and develop strategies for mitigating them.The Exclusion of Pertuzumab from the NIOSH List: A Discussion of Occupational Exposure and Hazard Evaluation ========== Due to intrinsic molecular properties of the drug, pertuzumab may be excluded from the list, focusing on drugs with potential toxicity due to occupational exposure. This exclusion aims to characterize the hazard posed by pharmaceutical ingredients more specifically. However, the commenter questions whether assumptions made about healthcare workers and environments are valid when defining a hazard. The NIOSH response acknowledges that whether a hazard is reversible alone is not enough to determine if a drug is hazardous to healthcare workers. In the case of pertuzumab, data from related drugs show that continuous exposures can cause delayed-genitourinary development-related oligohydramnios, leading to further fetal complications. Healthcare workers are unlikely to experience prolonged and consistent exposure to pertuzumab in the workplace, as limited availability of systemic exposure and rarity of incidental needlestick injuries with significant volumes reduce the risk of sustained high systemic exposures. The commenter agrees that considering physicochemical properties of pertuzumab is an appropriate method for evaluating potential exposure. They also support evaluating minimal volume delivery to healthcare workers when assessing needlestick scenarios. It is unclear whether oligohydramnios is the best health effect to evaluate, as other effects should be considered if it is not deemed sufficient.perutzumab could be inhaled to result in significant exposure ========== The potential health effects of Perjeta® are primarily related to embryo-fetal toxicity and left ventricular dysfunction, both of which are associated with therapies that target HER-2. The protective effect of HER2 activation in cardiomyocytes may also play a role. However, it is unlikely that healthcare workers would be exposed to significant doses of pertuzumab through inhalation, dermal, or oral routes, as the bioavailability of monoclonal antibodies like pertuzumab via these routes is minimal. In a healthcare setting, needlestick injuries are the most likely route of exposure for healthcare providers. However, it is unclear whether assuming that this is the only reasonable route of exposure is sufficient. The amount of exposure to pertuzumab in such settings may be difficult to quantify, and additional precautions should be taken to minimize risk. The low bioavailability of pertuzumab through inhalation makes it unlikely to result in significant pharmacologically active doses. Similarly, dermal or oral exposure would likely have a minimal impact. While healthcare workers may still be exposed to pertuzumab through less stringent measures such as tubing and gloving, this is not considered a relevant route of exposure for the purposes of evaluating potential risks. In summary, while needlestick injuries are a concern, it is unclear whether assuming this is the only reasonable route of exposure is sufficient. Further evaluation may be necessary to determine the most effective precautions for healthcare workers handling pertuzumab.In order to determine systemic exposure associated with adverse effects, healthcare settings can produce dusts or aerosols that meet this criterion. ========== NIOSH takes into account not just commercially available formulations, but also powders or aerosol exposures when evaluating the potential hazard to healthcare workers. The agency's assessment is based on assumptions of unlikely exposure in commercially available formulations and the intrinsic properties of active pharmaceutical ingredients, rather than a specific formulation or treatment product. ========== Pharmacy professionals are concerned that moving medications like Pertuzumab to the non-hazardous list would reduce safety features, such as needle sticks protection. They argue that these medications can be compounded for extended periods, potentially exposing technicians to hazardous levels and causing harm if they don't know they're pregnant or have other underlying health issues. ========== NIOSH evaluated the molecular properties of Pertuzumab and its bioavailability after exposure via different routes, including needlesticks, dermal exposure, ingestion, and inhalation. The agency uses a recommended human dose as a benchmark to indicate high levels of concern, typically only considering toxic effects below this level. ========== Healthcare workers are unlikely to be exposed to therapeutic agents at levels greater than those patients receive, which reduces the risk of pharmacological effects. However, in situations where exposure may occur, NIOSH considers the potential hazard to workers. Some changes were made to the NIOSH Final Reevaluation Determination of Pertuzumab on the NIOSH List of Hazardous Drugs in Healthcare Settings to clarify this aspect. ========== The use of a relevant human dose is highly protective against percutaneous exposure, but NIOSH evaluated worst-case scenarios. Incidental exposure through needlesticks is unlikely to result in high levels of Perjeta; however, the agency considered alternative formulations and treatment products that may pose a greater risk. ========== The oral bioavailability of monoclonal antibodies like Pertuzumab is negligible, reducing the potential for oral exposure. Sterile preparation and administration procedures further minimize this risk. ========== To characterize the potential hazard to workers, alternatives such as modifying formulations or using different compounds could be considered. However, more research is needed to determine the efficacy of these approaches.monoclonal antibody-based products are now widely used in cancer treatment, their properties are well characterized and occupational risk profiles are distinct from traditional chemotherapies. However, the process of evaluating these products for potential inclusion on the List is initially based on hazard assessment, with exposure-related factors being secondary considerations. An alternative approach would be a risk-based paradigm that considers exposure potential, which could simplify the nomination and review process by excluding products with little potential to cause health effects in workers. Potential exceptions to this approach may include immunoglobulin-based products with high potency or those conjugated to low-molecular weight components. However, such examples are relatively rare and can be readily identified based on the description in the prescribing information. NIOSH considers each drug individually, taking into account its intrinsic hazard, including molecular properties such as molecular weight. The process of excluding a whole class of drugs may miss some hazards for certain healthcare workplaces. The use of risk-based paradigms in identifying hazards that many drugs may pose in various healthcare settings is also uncertain. Public comments have raised questions about the consideration of adapter devices to prevent needle exposure during compounding, as well as clarification on the lack of oral, inhalation, or dermal exposure studies for therapeutic monoclonal antibodies. ==========Pertuzumab characterization as potent developmental hazard may cause confusion among healthcare workers. ========== The doses associated with adverse developmental outcomes in therapeutic contexts for pertuzumab are relatively high compared to other pharmaceuticals or chemicals. This characterization of pertuzumab as a potent developmental hazard might be misleading due to its relatively high doses. In contrast, the available data from nonclinical studies and human experience demonstrate a dose-responsive effect that is unlikely to occur at far sub-therapeutic exposures for pertuzumab.The occupational exposure to liraglutide can occur through various routes, such as inhalation or dermal exposure, but neither of these routes produces significant systemic bioavailability. On the other hand, needlestick injuries may also lead to a small amount of drug being injected into the body, which is usually insignificant in most cases. ========== In response to this comment, NIOSH did not make any changes to its final determination, as it was satisfied with its evaluation of liraglutide's hazards in healthcare settings. ========== Reviewer 2 pointed out that substances with molecular weights greater than 1000 Daltons show little to no absorption through the skin, making dermal exposure in a healthcare workplace highly unlikely. This is due to the skin being a barrier for such large molecules. The peptide in question has a molecular weight of approximately 3750, further supporting this claim. ========== However, Reviewer 2 also stated that needlestick exposures may still occur in healthcare settings, but the mechanism of action for chronic carcinogenic effects would not be triggered by these incidents due to the toxicokinetics of peptides. As a result, peak concentrations of liraglutide would likely not be sustained long enough to produce chronic effects. ========== In response to this comment, NIOSH acknowledged that inhalation routes of exposure had been evaluated, but it did so without limiting its evaluation to current formulations. Despite this, the agency still concluded that liraglutide would not pose a hazard to workers even via inhalation. ========== Reviewer 1 supported the determination that the amount of exposure to liraglutide in healthcare settings does not constitute a hazard for healthcare workers. Given the mechanisms of action of liraglutide, sustained exposure is required for significant effects, which would be unlikely in an occupational setting where medication is handled and administered as indicated. ========== Reviewer 2 also agreed with this assessment, citing evidence from literature that suggests the hazards associated with liraglutide are low. They pointed out that some cases of thyroid tumors may have been related to existing thyroid disease, which should have been excluded from studies. Furthermore, the mitogenic mode of action suggested by these effects would require continuous exposures, which are unlikely. ==========NIOSH's reevaluation of liraglutide's potential hazard to workers in healthcare settings involved considering various factors, including surveillance of OSHA reportable injuries or illnesses related to occupational exposure to liraglutide. Additionally, the Medullary Thyroid Carcinoma (MTC) registry could provide valuable data that might impact future evaluations of liraglutide's hazards. It was also proposed that a literature search on studies regarding adverse effects in occupational exposures to insulin, a common peptide hormone with 100 years of clinical experience, could be conducted as a worst-case scenario analogue for estimating the incidence of liraglutide exposures and potential risk. However, NIOSH agreed that using insulin as a surrogate would involve several caveats, including absorption, effect intensity/duration, and different specific mechanisms of action. These uncertainties would make the resulting evaluation less useful for hazard identification purposes. In terms of additional information to consider in the reevaluation of liraglutide, one reviewer suggested that decisions should be based on the best available data at the time, with further reevaluations conducted as new data becomes available about potential health effects or emerging issues.Reviewer 1 pointed out the need for more quantitative information on pertuzumab's effects, including potential downstream and upstream impacts on fetal health. They questioned the reliance on trastuzumab as a model for pertuzumab's behavior due to differences in molecular signaling. NIOSH responded that evaluating workplace exposure scenarios was beyond their scope, citing the variety of possible scenarios and different hazardous drug properties. They considered maximum occupational systematic exposure via all routes to be less than a full therapeutic dose, relying on molecular properties and worst-case exposures. Reviewer 1 also highlighted the limited evidence supporting assumptions about pertuzumab's oral bioavailability, requesting quantitative data and clarification on this point. NIOSH acknowledged the lack of quantitative data but suggested that low oral bioavailability was due to degradation in the GI tract and poor absorption through the epithelium. The reviewer expressed concerns about oligohydramnios being reversible, noting that downstream and upstream effects should be considered. NIOSH discussed a single case study on human exposure during pregnancy, co-exposure with trastuzumab, and the lack of long-term follow-up on exposed children. Finally, Reviewer 1 suggested removing pertuzumab from the List based on strong evidence in humans showing no risk of renal effects in fetuses following low exposure doses. NIOSH acknowledged only one case study identifying human pregnancy exposure to pertuzumabTrastuzumab and Pertuzumab: Reversible Effects on Fetus Development The safety profile of trastuzumab, a monoclonal antibody targeting HER2, has been extensively evaluated in cynomolgus monkey studies. Similarly, pertuzumab's effects on fetal development have been investigated. Data suggest that the effects of both drugs are reversible and dependent on exposure duration. In human pregnancies, in utero exposure to trastuzumab has been associated with reversible effects. A study by Lambertini et al. [2019] found 12 cases of potential exposure, with all but one child born healthy after cesarean delivery at 34 weeks due to growth retardation. The mother had received radiation therapy for brain metastasis and died 17 days post-delivery. The mechanism of action of pertuzumab appears to be similar to that of trastuzumab, with both drugs targeting the HER2 pathway. However, pertuzumab is not expected to induce activation of the PI3K cell survival pathway as efficiently as trastuzumab. According to NIOSH, the available data suggest that there are no significant fetal effects associated with pertuzumab exposure in humans during pregnancy. The use of a similar monoclonal antibody, trastuzumab, was chosen as a model for human exposure because the primary target pathway is shared. However, some reviewers have expressed concerns about the safety of pertuzumab based on its molecular properties. Reviewer 1 noted that the lack of a NOAEL (no-observed-adverse-effect level) suggests that a strong case is needed to exempt pertuzumab from regulations based on its "molecular properties."the estimated exposure limits for pertuzumab may be an overestimate of potential exposure in a healthcare setting. The data from Pfister et al. [2014] suggests that the 5% value represents a maximum bioavailability for proteins >40 kDa, with a median of 1.7%. However, this method of administration is not likely to occur in a healthcare setting. According to the package insert, pertuzumab has an approximate molecular weight of 148 kDa, which falls above the threshold for proteins >40 kDa used in the exposure assessment. The use of intratracheal instillation in these studies provides valuable data on bioavailability through respiratory tract tissues, although this route is not typical for drug exposure in healthcare settings. The NIOSH response acknowledges that while intratracheal instillation may pose a risk, it is unlikely to occur in practice. Reviewer 2 suggests that assessing respiratory sensitization in workers could be useful, but only if there are identified hazards in clinical trials or post-marketing settings. Further, Reviewer 3 comments on the potential health effects of Perteza treatment, including heart problems associated with cardiac failure and congestive heart failure. However, these concerns do not seem to have been raised by previous studies, and it is unclear whether occupational exposure concentrations would be high enough to cause such issues. The NIOSH response clarifies that while systemic exposures in healthcare workplaces may reach levels near treatment doses, the cardiac effects are unlikely to be relevant in occupational settings due to their association with treatment-level exposures. Even in worst-case scenarios, needlestick accidents or inhalation risks are deemed negligible. Lastly, this update to the NIOSH List of Hazardous Drugs in Healthcare Settings includes 25 new additions and removes seven drugs, including pertuzumab. The revised list reflects changes made since the publication of the 2016 list and is now available on the NIOSH website.to humans (Group 1) or likely carcinogenic to humans (Group 2A). In the 2016 List, Table 1 focused on antineoplastic drugs. However, in the 2024 List, NIOSH removed the “antineoplastic” identifier due to advancements in cancer treatment, as the therapeutic designation no longer reflects high toxicity. Thus, Table 1 now highlights toxicity and carcinogenicity of drugs irrespective of their therapeutic purpose. Table 2 includes drugs that: satisfy one or more NIOSH hazardous drug criteria, are not MSHI drugs, and are not classified by NTP as known human carcinogens or by IARC as carcinogenic to humans (Group 1) or likely carcinogenic (Group 2A). Some drugs in Table 2 have adverse reproductive effects for at-risk populations. This table features drugs meeting NIOSH criteria for developmental (including teratogenicity) and/or reproductive hazards. In the 2016 update, such drugs were in a separate Table 3, which has been merged into Table 2. Drugs meeting only NIOSH reproductive and/or developmental criteria are noted in a column labeled “Only Developmental and/or Reproductive Hazard” in the 2024 List. Changes in drug placement, including those no longer considered hazardous or moved between tables, are detailed in a new section of the 2024 List, not a separate table as in 2016 (former Table 4). In the 2016 update, Table 5 provided exposure control recommendations. NIOSH relocated and expanded this risk management info into a new document, *Managing Exposures*, which covers engineering, administrative controls, and PPE for hazardous drugs in healthcare settings. Previously, NIOSH included a supplemental column with drug-specific details like pregnancy categories. However, since 2015, FDA no longer uses pregnancy categories, and this info was unrelated to NIOSH’s listing criteria. Hence, the supplemental column was removed from the 2024 List. Finally, the 2024 List adds a column to identify drugs approved under a BLA by CDER. These drugs, often large protein-based molecules, may require different hazard management strategies. NIOSH notes that some BLA-approved drugs may have conjugates with separate hazards, which should be considered. References FDA [2012]. Pharmacology review of Perjeta. Application No. 125409Orig1s000. Reviewer: Ringgold K. Washington, DC: U.S. Department of Health Food and Drug Administration, Center for Drug Evaluation and Research, ��drugsatfda_docs/nda/2012/125409Orig1s000PharmR.pdf. FDA [2022]. Information for outsourcing facilities. Washington, DC: U.S. Department of Health and Human Services, Food and Drug Administration, ��drugs/human-drug-compounding/information-outsourcing-facilities. Foster TM, Lee MG, McGaw CD, Frankson MA [2010]. Prevalence of needlestick injuries and other high risk exposures among healthcare workers in Jamaica. West Indian Med J 59 (2):153-159. Gaughwin MD, Gowans E, Ali R, Burrell C [1991]. Bloody needles: the volumes of blood transferred in simulations of needlestick injuries and shared use of syringes for injection of intravenous drugs. AIDS 5 (8):1025-1027. Gould JC, Carvajal I, Davidson T, Graham J, Hillegass J, Julien S, Kozhich A, Wang B, Wei H, Yamniuk AP, Mathias N, Haggerty HG, Graziano M [2018]. Bioavailability of protein therapeutics in rats following inhalation exposure: relevance to occupational exposure limit calculations. Regul Toxicol Pharmacol 100: 35-44, ��/10.1016/j.yrtph.2018.10.003. Hale PM, Ali AK, Buse JB, McCullen MK, Ross DS, Sabol ME, Tuttle RM, Stemhagen A [2020]. Medullary Thyroid Carcinoma Surveillance Study: a case-series registry. Thyroid 30 (10):1397-1398, ��10.1089/thy.2019.0591. Keilman C, Shanks AL [2022]. Oligohydramnios. In: StatPearls [internet]. Treasure Island, FL: StatPearls Publishing,Pharmaceutical agents in healthcare settings pose significant risks to workers, particularly those handling antineoplastic and hazardous drugs. The U.S. Department of Health and Human Services' National Institute for Occupational Safety and Health (NIOSH) has developed guidelines to minimize exposure to these substances. A study by Connor et al. (2016) updated the NIOSH list of hazardous drugs in healthcare settings, highlighting the importance of ongoing research in this area. The Importance of Maintaining a Safe and Healthy Environment is Crucial for Overall Well-Beeing ========== Note: I rewrote the text in a style that mimics non-native English speaker (NNES) by incorporating grammatical errors, awkward phrasing, and simplified vocabulary.