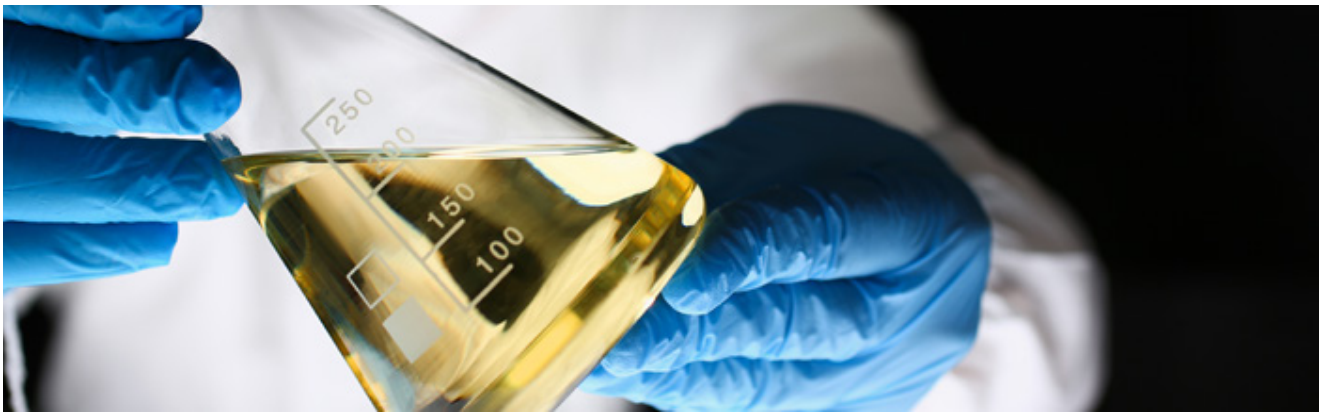
Guest Column: Does putting a label on a 'whole substance' make sense from a public health perspective?

08 October 2021

Nancy Beck of Hunton Andrews Kurth says the US EPA's decision to make the determination of unreasonable risk 'just once for the whole chemical when it is clear the majority of the conditions of use warrant one determination' sounds a lot like a hazard-based approach to chemical regulation



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Whether or not we should regulate chemicals because they are hazardous or because they present a risk has been a longstanding debate. When TSCA was amended by the passage of the Lautenberg Chemical Safety for the 21st Century Act in 2016, the US EPA was given new authorities to evaluate existing chemicals to determine whether or not a chemical substance poses an 'unreasonable risk' under the conditions of use. There is no disagreement about whether or not robust risk evaluations are required for existing chemicals, as directed in section 6 of TSCA*. They are required. One would have thought that the discussion of hazard versus risk was finally over, with the Lautenberg amendments providing clarity, particularly for those chemicals covered by section 6(b) of TSCA. Unfortunately, it seems that is not the case.

Hazard refers to the inherent properties of a substance that make it capable of causing harm. The key word here is capable. A drug is capable of causing injury if you are exposed at a level known to cause adverse effects. However, this harm is only likely to occur above certain levels, which depend on an individual's baseline health. For instance, ibuprofen may decrease blood flow to your kidneys and cause harm. If you have kidney disease, you may want to avoid ibuprofen; however, if you do not have kidney disease, taking the recommended dosage should not cause harm. Unlike hazard, risk includes the exposure

to the substance and a determination of the likelihood that harm could occur within the context of the exposure or use.

Risk tells us how likely it is that harm will occur. Likelihood – also known as probability – is the key concept with risk, and it is a function of the hazard and the level of exposure to that hazard. When talking about risk, there must always be a context of exposure. Without exposure, there is no risk. For instance, a chainsaw can be a deadly tool. However, in the hands of the world-record holding chainsaw juggler, the risk of injury is low. In a different exposure scenario, for instance where a young child finds a chainsaw in an empty yard, the chainsaw may pose a very high risk. The exposure context changes the likelihood of harm.

Consistent with the newfound clarity in the Lautenberg Amendments, in 2016, the EPA began the process of conducting robust risk evaluations. Over the next four years, the agency provided scoping documents, then problem formulation documents, followed by draft and

then final risk evaluations for the first ten chemicals as directed by the statute. In each of these documents, for each chemical, the EPA identified the conditions of use for the chemical. TSCA section 3(4) defines the conditions of use as "the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of".' For some of the chemicals assessed, the agency identified more than 50 different conditions of use. It evaluated each of these use scenarios and presented determinations regarding whether or not each condition of use presented an unreasonable risk.

Change of course

On 30 June, the EPA announced its intentions to change course. It stated:

"EPA will continue to assess and analyse each condition of use, but then the agency plans to make the determination of unreasonable risk just once for the whole chemical when it is clear the majority of the conditions of use warrant one determination. EPA intends to withdraw the previously issued orders for those conditions of use for which no unreasonable risk was found for all the first 10 risk evaluations. The agency then intends to issue revised unreasonable risk determinations for these chemicals as a 'whole substance' and seek public comment on this approach."

There is a lot to unpack in the EPA's statement. The unreasonable risk of a chemical will depend on the findings for the majority of conditions. So if 49% of the conditions of use do not present an unreasonable risk, the chemical as a whole will not present an unreasonable risk? A condition of use for a chemical can be found to present no unreasonable risk, but is it possible that since other uses of the same chemical present an unreasonable risk, a 'safe' use will not be clearly identified and allowed? What if only a minority of uses present an unreasonable risk, but there is a high likelihood of a severe adverse effect for a particular use? Will the chemical as a 'whole substance' be found to present no unreasonable risk?

If you are scratching your head, you are not alone. A 'whole substance' approach sounds a lot like a hazard based approach. It is worthwhile revisiting the longstanding debate about hazard versus risk to ensure that we are all speaking the same language.

In this article we are talking about raw materials, in particular chemicals. By definition, raw materials are used in the production or manufacturing of goods. They can be converted by manufacture, processing, or combination into a new and useful product. Indirect raw materials are used in the production process. Each raw material does have some potential to cause a hazard. To understand whether or not a raw material will cause harm, it is necessary to have an exposure context, also known as the use context.

Chemicals, in many respects, are raw materials. They are essential building blocks and they are used in the context of a specific scenario. In fact, one would be challenged to think of a chemical that has only one use. Chemicals have many uses; some chemicals even have hundreds of uses.

Innate hazard

The innate hazard associated with a chemical never changes, but the chemical's risk will vary with exposure. A chemical can be highly hazardous –consider a highly flammable gas such as chlorine trifluoride – but if you are never exposed to chlorine trifluoride there is no risk. There are scenarios where chemicals with high innate hazards can be safely used.

When the EPA evaluated hundreds of conditions of use for chemicals over the past four years, it always considered exposure. This is what allowed it to make findings regarding unreasonable risk with specificity. The findings could not have been made without an exposure context. The Lautenberg Amendments required an exposure context as they required that the EPA make risk-based findings.

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When Congress updated TSCA, the agency had already created a TSCA work plan which helped to focus and direct the activities of the EPA's existing chemicals programme. Congress did not direct the agency to take risk management on these identified chemicals. Congress directed the EPA to first conduct risk evaluations to determine whether or not these chemicals created an unreasonable risk under their conditions of use. Congress recognised that risk evaluations would be necessary to examine the conditions of use, and that unreasonable risk determinations could not be made without these examinations. Indeed, the mandate for the EPA to consider risk management actions is triggered by the completion of the risk evaluations, with a requirement that proposals be developed not later than one year after finalising the risk evaluations.

The concept of risk is critical to the foundation of the Lautenberg amendments for the existing chemicals programme. Risk management actions are tethered to the risk findings; risk management is required to the extent that it removes the identified unreasonable risks. The Lautenberg Amendments also put an emphasis on the importance of best available science as it is referred to in section 26(h) of the Lautenberg Amendments. This section not only ensures the integrity of the EPA's work, but when followed, gives stakeholders confidence in the agency's evaluations.

As a whole, the Lautenberg Amendments ensured that the EPA would be building a scientifically robust and defendable risk-based chemicals programme.

Whole substance

So what can we expect from a 'whole substance' approach to an unreasonable risk determination? When we look at the 'whole substance' we certainly know a lot about hazard. This information was available before the EPA even began work on the risk evaluations. Hazard information was identified in the 2012 and 2014 TSCA work plan lists. As we have seen in the completed risk evaluations, the majority of conditions of use were associated with findings of unreasonable risk. However, there are also clearly identifiable conditions of use that do not present an unreasonable risk. As is fundamental across all of the EPA's chemical evaluation programmes, depending on the circumstances of use and the exposures, a hazardous chemical can be safely used.

Does putting a label on the 'whole substance' make sense from a public health perspective? Should ibuprofen be advertised as being a hazard? To its many users it is beneficial, but certainly some sensitive subpopulations will experience adverse effects at certain doses. The label for ibuprofen appropriately warns users about potential risks, but the FDA has not tagged ibuprofen with an unreasonable risk classification. What about water? To most of its consumers, water is certainly beneficial, however to ultra-marathon runners over-hydration with water is an identified risk. Yet bottled water does not come with a warning label.

Does putting a label on the 'whole substance' make sense from a public health perspective? Should ibuprofen be advertised as being a hazard? To its many users it is beneficial, but certainly some sensitive subpopulations will experience adverse effects at certain doses

Will removing the exposure context be a step forward or a step back for public health? If one believes that public health decision-making and the private and federal dollars to mitigate concerns should be based on risk, then surely removing the exposure context is problematic. Without the risk context, it is impossible to make appropriate health-based decisions and the associated costs of eliminating all uses of a chemical, even when there is no appreciable risk of harm, could result in significant economic losses without public health benefits.

On the other hand, if you believe that any chemical that has intrinsically hazardous properties should be removed from the market, then on the surface, the exposure consideration is not necessary to protect public health. Products such as antibiotics, pesticides, lithium batteries, hearing aids and pacemakers are all produced with chemicals or metals that have intrinsic hazards. While some backers of a hazard based approach may envision a society without these products, others likely believe that a framework is needed to appropriately evaluate the benefits and the harms. The basis for such a framework has its roots in risk evaluation, a tool which allows us to scientifically and quantitatively evaluate the likelihood of harm. A tool that is fundamental to the three step process – prioritisation, risk evaluation and risk management – identified in TSCA section 6(b). Risk management must follow risk evaluation.

Risk evaluation mandate

The TSCA programme is still in its infancy. While lawyers may argue about what the Lautenberg Amendment drafters meant by 'the chemical substance' there is no debating whether or not risk evaluations are required to evaluate each condition of use. The mandate was for risk evaluations to inform risk management. Labelling, including providing warnings and instructions for use, is a form of risk management. It is fair to ask whether the 'whole substance' approach to labelling a chemical as an unreasonable risk moves us in the right direction for risk-informed public health protection, consistent with the drafting and intent of TSCA section 6.

It has recently been eloquently argued, by a group that includes former scientific leaders from the EPA, that the largest concern with a hazard classification is that it is binary**. In allowing for only two classifications – hazardous or non-hazardous – we create a false dilemma that does not allow for the full spectrum of possible choices that are created by biological responses that span a continuum of severity and potency levels. They argue that categorisation schemes for hazard should appropriately reflect the reality that effects occur over a continuum, and when information exists to inform that

continuum, it should also be used to inform hazard categorisations. If one follows this train of thought, a 'whole substance' approach to a risk classification – which does not allow for a continuum of exposure scenarios and does not consider existing information – would surely be perpetuating a false dilemma and would not be scientifically justifiable.

Once the EPA has released its revised unreasonable risk determinations for chemicals as a 'whole substance', the public health community, regulated stakeholders, and those interested in chemical regulation will have an opportunity to comment and continue the discussion of hazard versus risk in evaluating chemicals.

The views expressed in this article are those of the author and are not necessarily shared by Chemical Watch.

FURTHER INFORMATION
EPA Announces Path Forward for TSCA Chemical Risk Evaluations Author Transparency Statement

*This of course excludes consideration of persistent, bioaccumulative and toxic (PBT) chemicals as those are separately addressed in section 6(h).

** See: Doe et al, Archives of Toxicology (2021) 95:3611–3621

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