

Greener Alternatives to Dimethylformamide Use in Polyurethane Synthetic Leather

Partnered with Nike, Inc.

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Greener Solutions: A Safer Design Partnership

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Executive Summary

Dimethylformamide (DMF) has been used for decades to produce polyurethane (PU) synthetic leather materials for the textiles industry. Studies have demonstrated a myriad of health hazards posed by DMF to factory workers, primarily related to hepatotoxicity. In this work, we considered three categories of interventions to facilitate the phasing out of DMF in PU synthetic leather production: drop-in solvent replacement, PU process changes, and functional material changes.

We identified five promising polar aprotic candidate drop-in solvents which met our technical performance criteria, and which all represent a substantial improvement in human health and environmental hazard performance over DMF. The recommended solvents are Cyrene™, dimethyl isosorbide, γ -valerolactone, cyclopentyl methyl ether, and glycofurol. Replacing DMF with any of these solvents would likely constitute a major improvement to worker health, as well as fulfill several of Nike's sustainability goals.

The most promising PU process change was a move to water-borne PU dispersions which eliminates the need for DMF use. Although there are health concerns for some additives in these dispersions, the significantly smaller volume of their use may produce a substantive reduction in their risk. The extant problems associated with a poor color palette available with dispersions may be solved by using a CO₂ dyeing process to greatly increase the usable color space.

With regard to material changes, mycelium-based leathers are currently gaining traction within the industry, but concerns over scalability due to longer growth times leads us to recommend synthetic leather made using the crosslinking of natural oils through a safe, green process. We expect this strategy to scale well and operate with short processing times. The human health and environmental hazard profile is particularly good, and this strategy also meets many of Nike's other sustainability goals while producing material akin to natural leather.

All of the strategies considered in this report are expected to be promising in the replacement of DMF-PU synthetic leather, and could all make a large contribution in mitigating risk to workers during production of synthetic leather. Our primary recommendation is to replace DMF with one of our suggested drop-in solvents, or to change the material from PU to synthetic leather produced by the crosslinking of natural oils. The former is expected to carry a relative ease of implementation, while the latter is a more disruptive strategy (but likely an even greater contribution to safety and sustainability). Both should substantially reduce the health risks of producing synthetic leather, as well as meet many of the sustainability goals desired by Nike for their products.

Background

From natural to synthetic leathers

Leather has been produced by humans for at least 4,000 years for use as clothing and as a functional material such as in toolmaking. More recently, concerns of exposure to highly toxic hexavalent chromium during the tanning process have driven the search for alternative tanning agents, as well as for different kinds of “leather” materials. Synthetic or artificial leathers are leather-like materials intended to provide the look and/or feel of natural leather, and may be produced from natural or synthetic feedstocks. One of the first examples of a synthetic leather was Presstoff, which was derived from layered paper pulp in 19th century Germany. It gained popularity during the Second World War due to German rationing of natural leather, but was unsuitable for footwear due to delamination caused by repeated material flexing.

Polymeric materials have been the preferred synthetic leather option since their rise to prominence in the 20th century due to their superior material properties over pulp synthetic leathers. Both polyurethane (PU) and polyvinyl chloride (PVC) have been used since the 1960s, but PVC was often preferred due to its lower cost despite having much lower breathability. More recently, PVC has faced increased scrutiny for consumer exposure to phthalate plasticizers and unpolymerized vinyl chloride monomers, and due to dioxin pollutants that are produced during PVC combustion. In response to these concerns, Nike switched from using PVC to PU in their synthetic leather products in 1998. The PU is produced in a process reliant on the solvent N,N-dimethylformamide (DMF), and which pervades the textiles industry.

Nike’s sustainability commitments

Heightened awareness of the hazards of DMF use can be traced back to when Greenpeace launched its Detox Campaign in 2011. The Detox Campaign aims to expose the environmental issues from using hazardous chemicals in textile and apparel manufacturing. One report put out as part of the campaign specifically called out Nike and other apparel brands for having measurable levels of DMF in products sold as part of the FIFA World Cup 2014 tournament. Most football boots were manufactured in South Asia and contained DMF at levels above the 10 mg/kg limit set by the German Committee on Hazardous Substances, showing that DMF was widely used in the manufacture of World Cup merchandise by major brands (Cobbing & Brodde, 2014).

Due to human health concerns and the resulting regulatory challenges of using DMF solvent, Nike has committed to phasing out DMF use for synthetic leather by 2025. In 2014, Nike developed the first industry-aligned manufacturing restricted substances list (MRSL) with the ZDHC Coalition – an industry group aiming for Zero Discharge of Hazardous Chemicals, detailing chemicals restricted from use in the manufacturing process. Additionally, in 2016 Nike publicly announced

its “moonshot”: double its business while halving its environmental impacts. These impacts include carbon emissions, freshwater withdrawals, and the use of controversial chemicals (Figure 1). Eliminating DMF will have a large impact on Nike’s chemical footprint, as it consists of ~10% of the total hazardous chemical usage (Hackenmiller-Paradis, 2019). While phasing out DMF presents a sizable challenge to Nike and the footwear industry, it also provides an opportunity to make large strides toward overall sustainability within the industry.

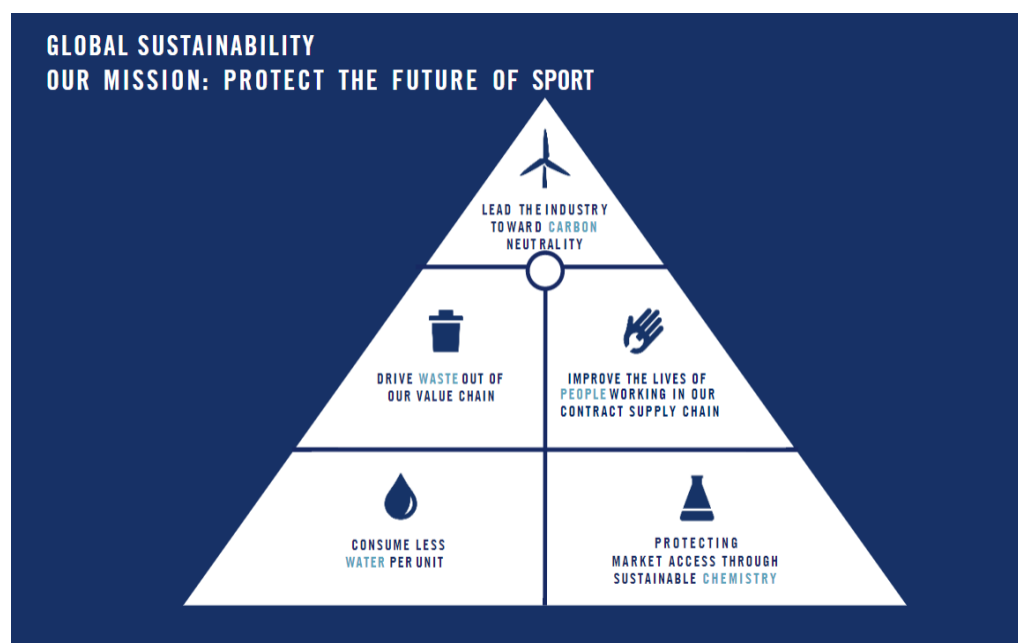


Figure 1. Global sustainability goals set forth by Nike to guide product innovation.

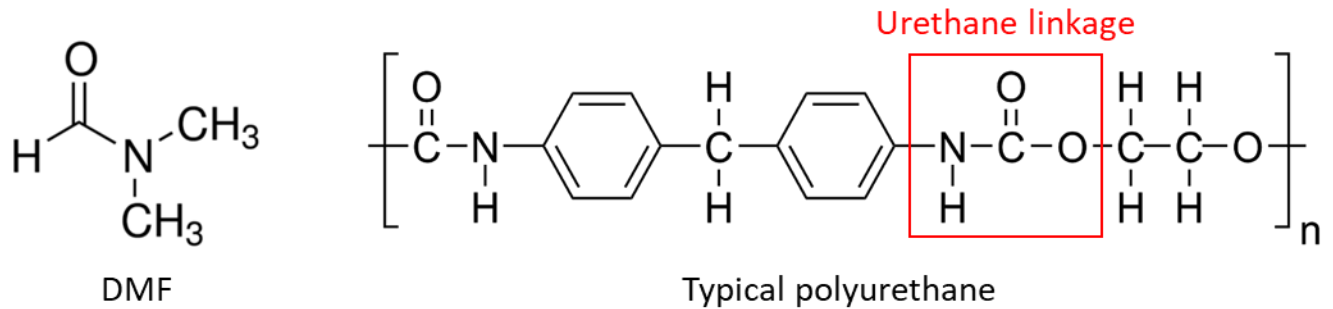
Dimethylformamide and polyurethane synthetic leather

DMF (Figure 2a) is a polar aprotic solvent which is miscible with water as well as many organic molecules, and possesses a high boiling point and relatively low vapor pressure. The versatility of DMF as a solvent has led to very high production volumes and consequently to very low cost. It has found extensive use over many decades in the manufacture of synthetic leather throughout the textile industry supply chain. Nike states that DMF is used in a variety of cleaning processes, but is predominantly used with synthetic leather production, where it acts as a solvent and foaming agent (NIKE, Inc., 2018). Many companies, including Nike, use DMF in the production of PU synthetic leather for use in footwear. A polyurethane typically used in the textiles industry is shown in Figure 2a, and is formed from the reaction of methylene diphenyl diisocyanate with ethylene glycol.

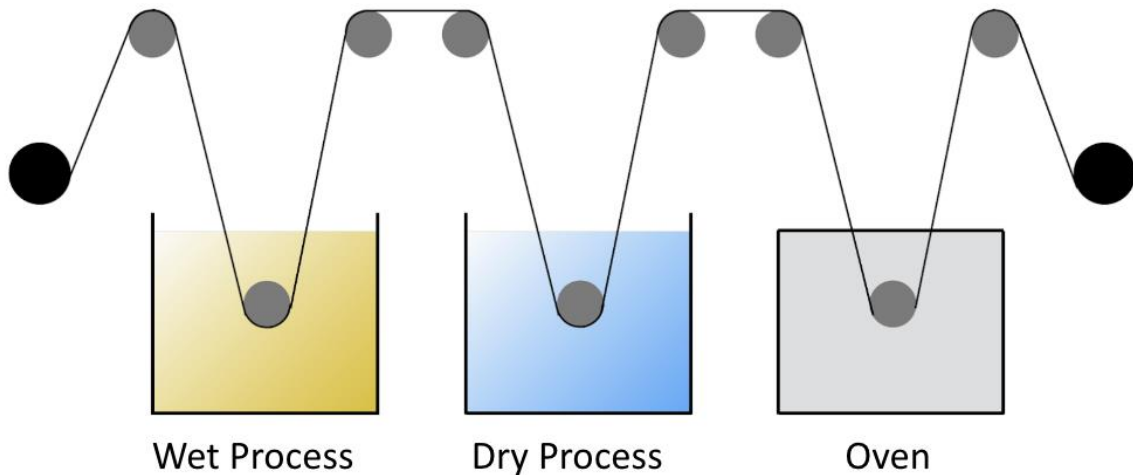
The process to make PU synthetic leather used in Nike products uses DMF as a solvent at multiple process steps (Figure 2b). The process starts with a woven fabric where layers of polymeric material are added to meet strength and aesthetic criteria. This is done through wet and dry

processes (with and without water). First, the fabric goes through a series of baths to build up the PU layers. Then, the fabric is washed with water to remove excess DMF. Finally, ovens cure and bake off any residual DMF on the fabric. The final product can have multiple layers of adhesive and PU backing (Figure 2c). A key aspect of these processes is the repeated reliance on DMF as a solvent for components of the PU synthesis formulation, including PU resin, pigments, catalysts, and filler materials.

a)



b)



c)

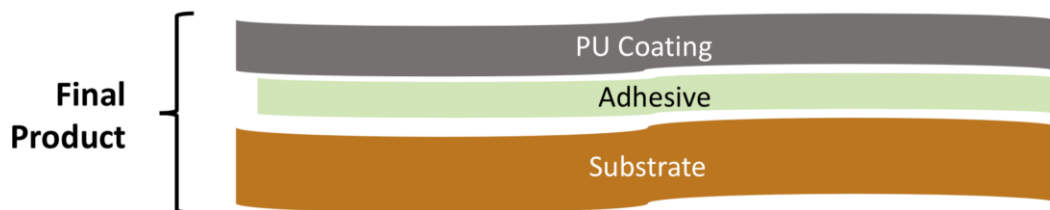


Figure 2. (a) DMF and PU molecular structures, (b) Schematic of roll-to-roll PU production using the wet and dry processes, and (c) schematic cross-section of a final product consisting of PU coated onto a substrate.

Health hazards of DMF

DMF is a known liver toxicant and is associated with several other severe health outcomes (Figure 3). DMF can be easily absorbed by the dermal and respiratory systems, whereafter the liver is the primary target organ. As such, hepatotoxic mechanisms of acute and subchronic exposure have been widely studied in humans and other animals. While the exact mechanism of toxicity has not been established, there is evidence that activation by cytochrome P450 (CYP2E1) catalyzes the stepwise conversion of DMF to methyl isocyanate (MIC) through N-hydroxymethyl-N-methylformamide (HMMF) and N-methylformamide (NMF) intermediates (Gescher, 1993; Kim and Kim, 2011). Metabolism of DMF could lead to the depletion of glutathione (GSH) upon MIC adduct formation. These currently available studies provide solid evidence for the involvement of oxidative stress in the onset of DMF-induced liver injury. In addition, some pilot studies have indicated the involvement of caspase-mediated apoptosis, disturbance of cellular Ca^{2+} homeostasis leading to cell necrosis, and the alteration of gut microbiota community (Li & Zeng, 2019). The International Agency for Research on Cancer (IARC) Monographs Working Group has classified DMF as a Group 2A probable carcinogen to humans based on human evidence that exposure of DMF lead to testicular cancer as well as sufficient animal studies (IARC, 2018).

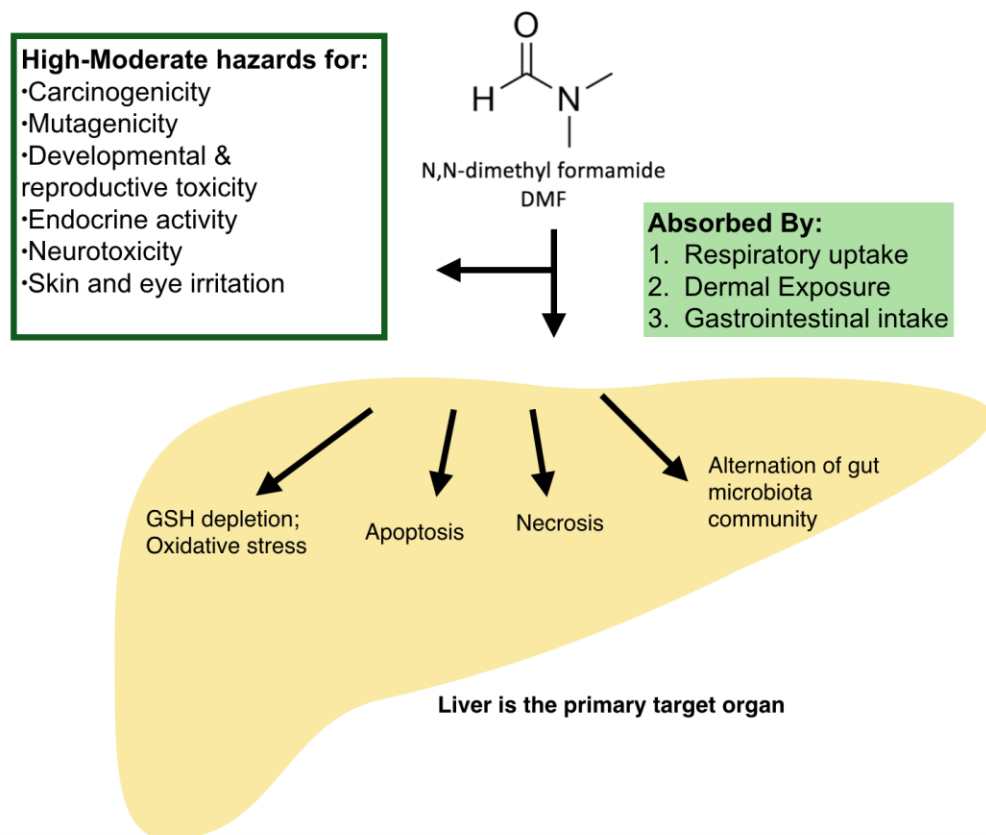


Figure 3. Primary toxicological action of DMF in humans (adapted from Li & Zeng, 2019).

Other human health endpoints for which DMF is a concern include reproductive and developmental toxicity, endocrine activity, acute mammalian toxicity, systemic toxicities, neurotoxicity, skin/eye irritation and corrosivity (based on classification in the Pharos database [Pharos, 2019]). Overall, DMF is a high or moderate hazard for the endpoints of carcinogenicity and mutagenicity, developmental and reproductive toxicity, endocrine activity, neurotoxicity, and skin and eye irritation.

Occupational exposure to DMF

A relatively recent review contains information about exposure to DMF from various populations spanning nearly two decades, including the major health impacts (Table 1) (Kennedy, 2012). The predominant outcome of DMF exposure across these studies was liver damage, with occasional instances of hormonal or cellular shifts/irregularities and disorders of the nervous and digestive systems. In some cases the liver damage was temporary, and some populations were found to be more susceptible to DMF-induced health issues based on specific genotypes. Considering the toxicological pathways, toxicity primarily results from dermal and respiratory exposure to DMF. Consumer exposure to DMF is of generally low concern because stringent regulations ensure almost all DMF is removed during the production process. Exposure to DMF in occupational settings is the foremost concern around DMF use in PU leather production, as workers are exposed through direct dermal and respiratory contact (Wu et al., 2017).

Although exposure guidelines exist in China and the US, they are insufficient to prevent issues related to DMF toxicity in workers exposed to the solvent. Liver injury occurs at exposure levels 3-4 times below the recommended limits set by the Chinese Ministry of Health and the US Occupational Safety and Health Administration, and in practice workers can experience up to thirteen times the permitted exposure limits (Figure 4) (Luo et al., 2001; He et al., 2010; Qi et al., 2017). Although some of these studies may highlight extreme cases, most studies report levels of exposure above the annual cumulative dose that has been linked to increased risk for liver injury. At the highest levels, exposures can range between 13.1-199.8 mg/m³ in the wet process and 14.9-72.4 mg/m³ in the dry process. Workers that are involved with the wet process are exposed on average to higher concentrations of DMF. Since various human health issues are expected to arise even at the permitted exposure limits, eliminating DMF use in occupational settings is considered a high priority in the interest of protecting worker health.

Table 1. Health endpoints associated with human exposure to DMF (from Kennedy, 2012).

Exposure	No. involved	Duration	Finding	Reference
General population	2	1 day	Liver damage, survived suicide	Hantson et al., 2010
General population	1	1 day	Liver damage, survived suicide	Buylaert et al., 1996
Patient	2	?	Transient liver damage	Poelmans et al., 1996
General population	1	1 day	Liver damage, recovered in 3 wks	Stedtler et al., 2003
Occupational	64	2 years	Liver damage, identified susceptible genotypes	Xu et al., 2007b; 2009
Occupational	13/44	?	Liver damage, identified susceptible genotypes	Luo et al., 2005
Occupational	?/136	?	Liver damage associated with redox changes	Zhang et al., 2007b
Occupational	27	?	Lowered WBC, % eosinophils	Situ et al., 2007
Occupational	573	Chronic	Liver damage greater with higher exposures	Zhang, 2009
Occupational	16/75	>1 year	Liver damage	Fiorito et al., 1997
Occupational	?	Chronic	Liver damage, alcohol synergized	Wrbitzky, 1999
Occupational	?	>1 year	Liver damage	Qian et al., 2007
Occupational	1	2 month	Liver damage	Hou et al., 2002
Occupational	60/243	?	Liver damage, coexposure to toluene	Zhang et al., 2007a
Occupational	30	?	Liver damage, from dermal contact	Garnier et al., 1992
Occupational	165/1394	Chronic	Liver damage, in 2005	Gu, 2007
	224/1230	Chronic	Liver damage in 2006	
Occupational	?/1296	Chronic	Liver damage, digestive & nervous system disorders	Yang et al., 2006
Occupational	242	>1 year	Digestive system impairment	Yang et al., 2000
Occupational	43	>1 year	Minor liver function changes	Kim et al., 1996
Occupational	38	2 years	Digestive system impairment	Bianco et al., 1994
Occupational	100	?	Testosterone levels increased	Zhang et al., 2005
Occupational	49	?	Testosterone, estradiol levels increased	Li et al., 2004
Occupational	12	?	Normal sperm counts & morphology, motility reduced	Chang et al., 2004
Occupational	1	2 month	Liver damage	Hou et al., 2002

? = Value not known (not reported).

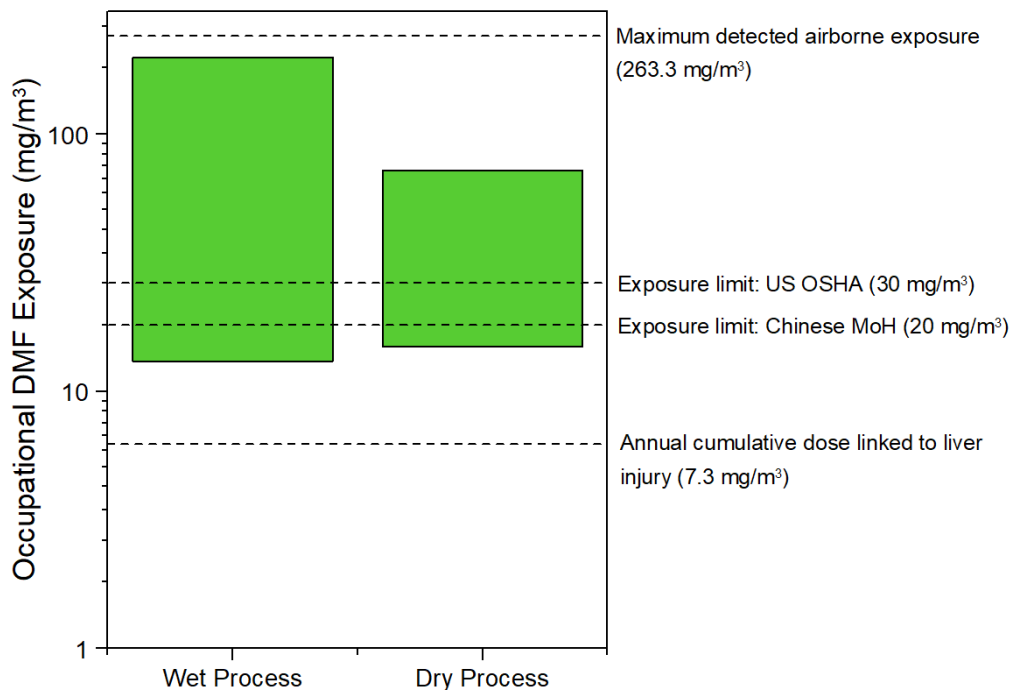


Figure 4. Range of airborne exposures of DMF measured in synthetic leather production plants for the wet and dry processes, and maximum level and its comparison to regulatory limits. Note the use of a logarithmic scale for exposure levels.

Environmental exposure to DMF

Environmental exposure to DMF does exist, mostly in air, from sources such as manufacturing plants. Other avenues of DMF exposure are of less concern because, DMF has relatively rapid biodegradation in water or soil with a half-life of 18-36hrs (IARC, 2018). In the city of Longwan, the synthetic leather capital of China, the airborne concentration of DMF has been identified to range between 0.18-0.565 mg/m³. Exposure in the local residents were measured through air samples and urinary samples to identify the levels of the NMF urinary metabolite. The authors concluded that there was a positive correlation between the exposure and liver disease hospitalization for residents. To understand the hazard of exposure at these concentrations, comparison can be made to the Chinese standard for short-term exposure to DMF is 0.15 mg/m³, in this city even the lowest concentration measured exceeded this standard. While this is not even close to what workers at these factories are exposed to, it is still important to understand there could be health effects on those who experience long-term low dose DMF environmental exposure (Wang et al., 2014).

Challenge statement

Given the health concerns of occupational exposure to DMF and with Nike's moonshot goal for reducing its impact in mind, our challenge was to identify inherently safer alternatives to synthetic leather made with DMF. This is done to support Nike's commitment to phasing out the use of DMF in an effort to safeguard worker health. To meet our challenge, we assess potential alternatives such as a drop-in solvent replacement, a change in polyurethane processing methods, and a change in the synthetic leather material. We consider both the final product performance and toxicological endpoints wherever possible in this rich opportunity landscape.

Approaches

Opportunities for intervention

There are many places intervene in the production of Nike products to reduce or eliminate DMF (Figure 5). This spectrum represents a continuum of options based on time, scalability, capital investment, and rethinking of conventional leather shoes. Perhaps the least disruptive option for intervention is implementation of a drop-in replacement. This would entail switching out DMF with a greener, more environmentally friendly solvent. Another less disruptive point of intervention would be a PU process change, which would entail changing the process in which PU synthetic leather is created. Changing the material shoes are made from could also lessen or eliminate the use of DMF. This can occur by finding alternative artificial leathers, by a more radical changing of the material, or even by moving away from materials that look and feel like leather. An example of this would be Allbirds shoes, which are made from Trino™, a combination of tree fibres and merino wool. The most radical change could be a fundamental ‘Swoosh’ change, reframing the way consumers recognize a Nike shoe in a way that would not rely on a piece of functional material (e.g. using paint).



Figure 5. Multiscale depiction of intervention opportunities for removing DMF from Nike products.

Overall design goals

Although the types of solutions may be very different depending on which level in production the intervention is staged, we wanted to establish a set of broad criteria that any proposed solution would ideally meet. While there were many factors to consider, a pared down list of four general design criteria for all of our proposed solutions was chosen as follows:

1. Reduce or eliminate DMF from production lines
2. Meet Nike’s other sustainability goals (Figure 1)
3. Maintain or exceed current performance in strength, durability and aesthetics
4. Avoid toxic substitutions that lead to future problems

In meeting the goal of reducing or eliminating DMF, the solution should ideally meet some of Nike's other sustainability goals, which include carbon neutrality and reducing waste and water usage. The solution should also be as strong, durable, and aesthetically pleasing as existing products, or ideally outperform them. To avoid toxic substitutions, the solution should not have a similar or worse hazard profile compared to DMF. As an example, some manufacturers are switching to using dimethylacetamide (DMAc) due to regulatory concerns about DMF. However, Nike recognizes that the toxicological considerations are not enough of an improvement to justify replacing DMF for DMAc (Hackenmiller-Paradis, personal communication, 2019). Similar toxicity of DMAc and DMF is not very surprising given the biological mechanism of DMF toxicity. As with DMF, metabolism of DMAc is likely to be largely mediated through cytochrome P450 enzymes in the liver, leading to the same MIC metabolite suspected as being responsible for the majority of DMF toxicity.

Evolution of performance metrics

With any DMF replacement, the quality of the final synthetic leather product must be maintained. Current PU synthetic leathers meet performance metrics for mechanical properties and aesthetics. They have the strength and durability to be stitched on shoes and flexed during athletic use. It is also important for the colors to be bright, to not rub off onto other materials (color fastness), and to be resistant to ultraviolet light exposure. Additionally, the PU should have a leather-like appearance and have a good hand-feel, which is a more subjective criterion. The aesthetic criteria may represent the greatest potential opportunity for change, as other leathers that have historically been used have a variety of textures and aesthetics.

Hazard assessment methods

In our approach for selecting a solution, we consider the inherent hazard of different chemicals used during the points of intervention as well as the likelihood of exposure based on physical properties. For inherent hazard assessments, we gathered the data primarily from authoritative lists and from academic literature sources.

One database that we found especially useful was the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) database, which is a regulation from the European Chemicals Agency (ECHA) of the European Union (EU). The regulation requires all substances manufactured or imported into the EU in quantities of 1 ton or more per year to register information on the properties of the substances. These are used to perform an assessment of the hazards and risks that substance may pose and how those risks can be controlled. Another authoritative list we used was from the International Agency for Research on Cancer (IARC). IARC coordinates and conducts epidemiological and laboratory research into the causes of human cancer and classifies agents with monographs. If other sources lacked information, we also looked at the Safety Data

Sheet of a chemical, which provides standardized information on occupational safety and health. We searched for a chemical's hazard through Pharos, which summarizes hazard, use, and exposure information from authoritative lists. From Pharos, we could identify sources of the data, including Globally Harmonized System (GHS) categorizations or hazard statements from a variety of countries. The GHS categories are a system for standardizing the classification and labelling of chemicals. Finally, we did a broad literature search to identify any additional information relevant to human and environmental health and safety.

To compare solutions as part of our assessment it was important to standardize the information located using the resources described above. We first standardized our data to GHS categories whenever possible to have numerical values for each endpoint. For acute mammalian toxicity, we used the Hodge-Sterner index, which gives a ranking of 1-6 from "Extremely toxic" to "Relatively harmless" based on an appropriate LD50 value.

GreenScreen® for Safer Chemicals (GreenScreen), developed by Clean Production Action, is a publicly available and transparent chemical hazard assessment method designed to promote the adoption of greener and safer chemicals. We used GreenScreen for designating high, medium, or low hazards in our hazard assessment. When GreenScreen highlighted a category with a "very high" concern designation, we grouped it instead under the "high" hazard for simplicity. We color-code hazards in our assessment as red for high hazard, yellow for medium hazard, and green for low hazard. When an authoritative source showed potential concern for a particular endpoint (for example based on modeled data, but lacking experimental data for comparison), we designated it as a "potential concern" and color it purple in our hazard table.

Drop-In Replacement

Benefits of a drop-in solvent

Drop-in solutions are the first and the simplest recommend strategy at this time. Compared to our other strategies of process change and material change discussed in subsequent sections, drop-in replacements require considerably lower capital investment. A drop-in solution could also offer broader cross-industry impacts, as DMF is also used in various industries outside of synthetic leather manufacturing. While this solution may represent an incremental change, it is important to reiterate that DMF consists of ~10% of Nike's overall hazardous chemical usage. By utilizing a drop-in substitution that is more environmentally and health friendly, this solution would make a large difference in Nike's chemical footprint. This solution should also be easy to implement within the current PU process, enabling the possibility of maintaining currently used suppliers.

The space of potential solvents is very large, so to begin to narrow our possible solutions we started with three promising categories: bio-based solvents; solvents exploited in solid-phase peptide synthesis; and a catch-all category for inspiration from other sources (Figure 6). These categories are used to broadly orient the reader, and are not meant to be used as rigid classifiers. From the large space of solvents spanned by these three solvent categories we select a small number of (often representative) molecules, which we assess more rigorously in order to produce a final short list of recommendations.

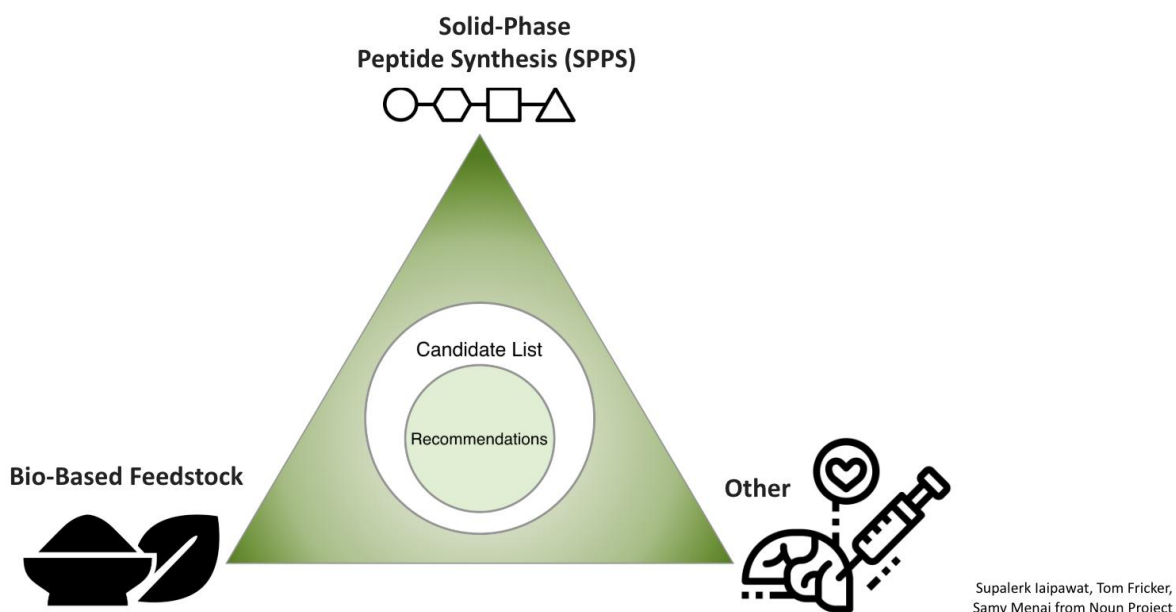


Figure 6. Solvent categories used in this work, of which our candidates comprise only a subset.

Bio-based solvents

Many plants, animals, microorganisms, and fungi are promising feedstock sources for obtaining bio-based small molecules and polymeric materials. A key feature of biologically-derived feedstocks is their renewability; however, this can raise issues over competition for land allocation between bio-based feedstock generation versus food production, use of water for irrigation, and environmental impact (e.g. pesticide/fertilizer use and habitat destruction). While bio-based feedstocks currently comprise a small percentage of feedstocks used by the polymer industry, their utilization is growing faster than that of petrochemical feedstocks, demonstrating their increasing importance (Bicerano, 2018). Lack of efficient industrial transformation pathways has rendered most chemicals derived from bio-based feedstocks unable to compete with their petrochemical counterparts in numeracy and cost, but increased research and development is making progress towards a profitable transition (Jenck et al., 2004; Mülhaupt, 2013; Zhou et al., 2018). This has been spurred by growing pressure on companies, in response to environmental concerns, to incorporate safer and most sustainable chemicals into their products through innovation.

For our bio-based drop-in solvents, we selected molecules which can be derived within a few chemical transformations from glucose, which is produced by plants in enormous quantities. Figure 7 shows a schematic derivation of three chemicals starting from glucose molecules. Many of the selected chemicals were highlighted in the academic literature as potential DMF replacement solvents and/or advertised explicitly as such by companies that market them, which were used here as an initial indicator for feasibility (van Es, 2017).

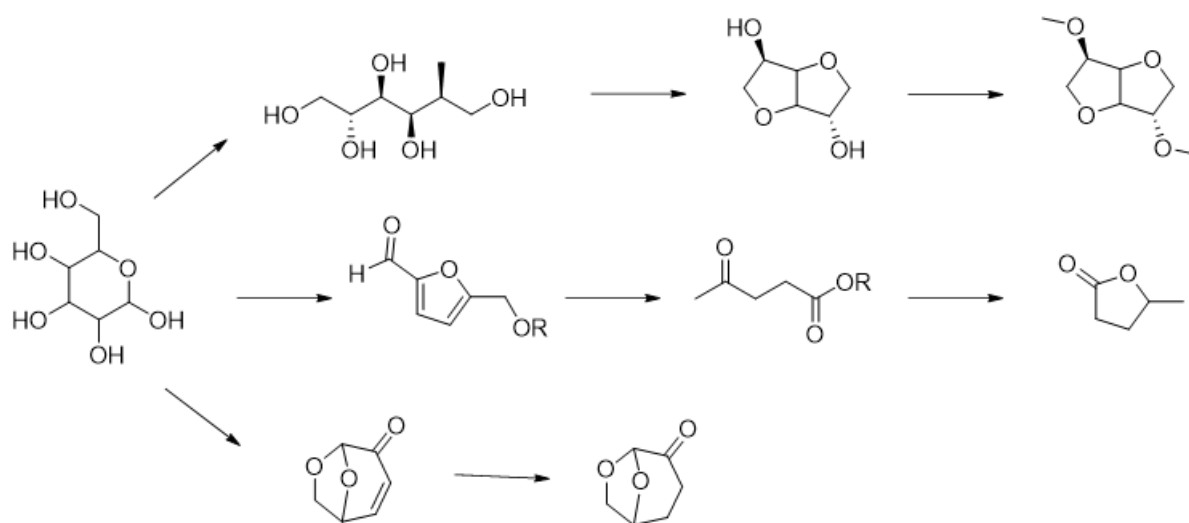


Figure 7. Schematic synthesis of (top to bottom) dimethyl isosorbide, γ -valerolactone, and dihydrolevoglucosenone starting from glucose.

Solid-phase peptide synthesis solvents

The field of solid-phase peptide synthesis (SPPS) has a strong focus on finding greener solvents that efficiently dissolve oligo- and polypeptides. SPPS typically involves many chemical transformations each followed by extensive washings that use copious amounts of polar aprotic solvents, such as DMF (Lawrenson et al., 2017). This class of polymers is challenging to efficiently solvate, and contains amide linkages between monomers that are structurally very similar to the urethane linkages in PU polymers. Due to this similar chemistry, good solvents for SPPS applications are also assumed to be promising candidates for effectively solvating PU materials.

Other solvents

We considered several other drop-in candidates that did not fall into either the bio-based or SPPS categories, but which we wanted to highlight as they also showed promise as solvents for PU. These candidates were typically found through literature searches.

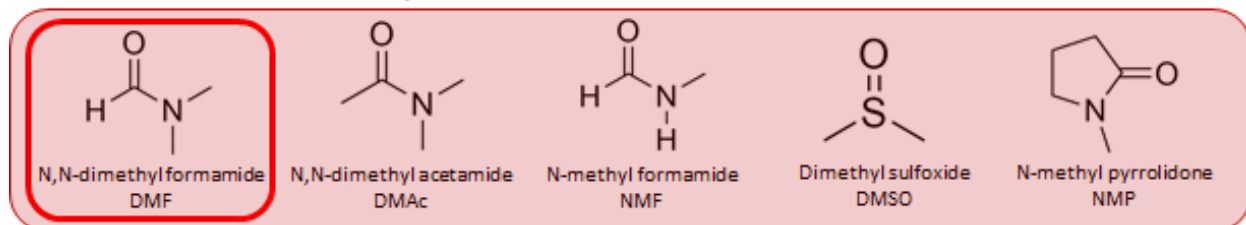
From these categories, we came up with a list of candidates. For several solvents such as ionic liquids and levulinic ketals we selected a representative molecule. We then removed obvious red flags, including any chemicals flagged as a 1 in GreenScreen (corresponding to very high hazard). The list of candidate solvents considered in this work is shown in Figure 8, where the nomenclature used to refer to these molecules is also defined. Included for comparison are DMF and several other examples of more traditional polar aprotic solvents, many of which can be used for PU synthesis.

Design criteria for drop-in replacements

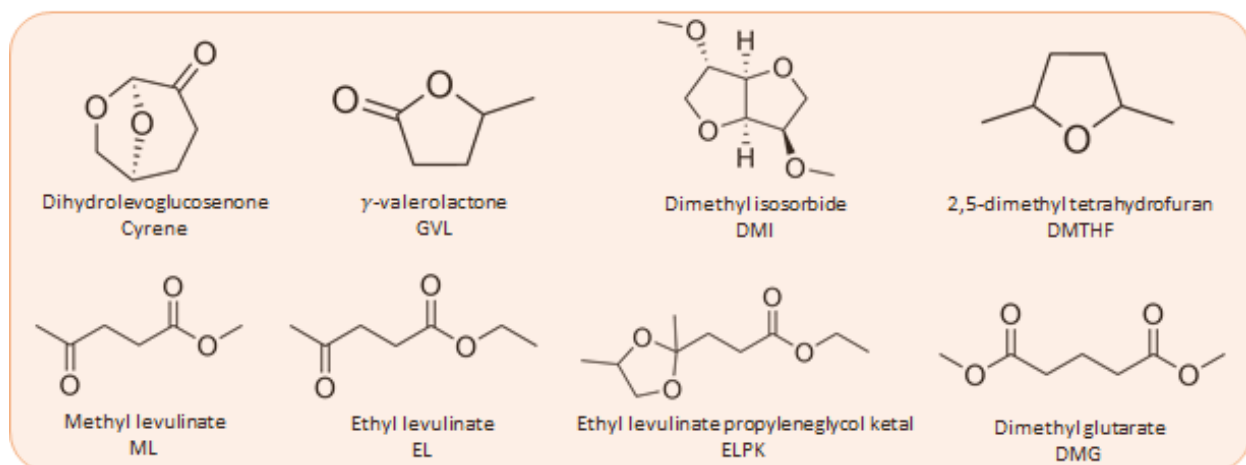
In order to recommend solvents from the candidate list, both technical performance and inherent hazard were considered. There are no examples of any of the solvents in the candidate list being used in the production of PU or synthetic leather, so for the technical performance criteria alternative metrics were used to assess performance. Given these constraints, we focused on three specific design criteria, two for technical performance and one for inherent hazard (Figure 9). The drop-in solvent replacement must dissolve PU, be compatible with the current manufacturing process, and reduce inherent hazard over DMF.

Dissolving PU is critical to the function of the solvent because the PU resins are difficult to dissolve and harder to replace than typical dyes or additives (Hackenmiller-Paradis, 2019). In order to be compatible with the current production line, we highlight various key physical properties of the solvents. For example, physical properties such as vapor pressure and boiling point indicate how readily this solvent would evaporate out of the process baths and the energy required to bake out any residual solvent in the final product. The solvent should also be miscible with water so that residual amounts can be washed out of the product after it leaves the reaction baths. For

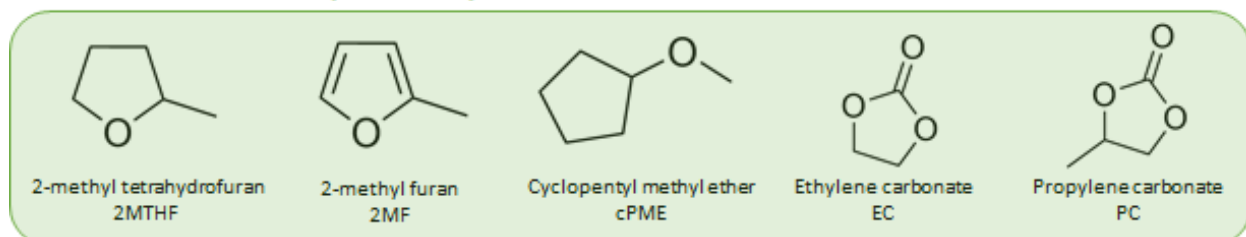
Traditional Polar Aprotics



Bio-Based Renewables



Solid-Phase Peptide Synthesis



Other

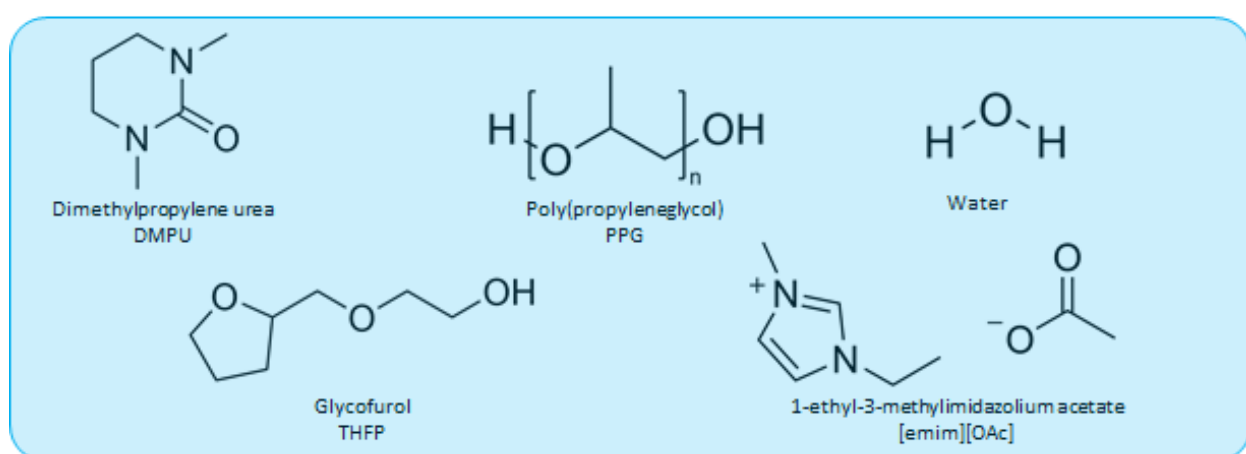


Figure 8. Drop-in solvents considered in this work, compared to some traditional polar aprotics.

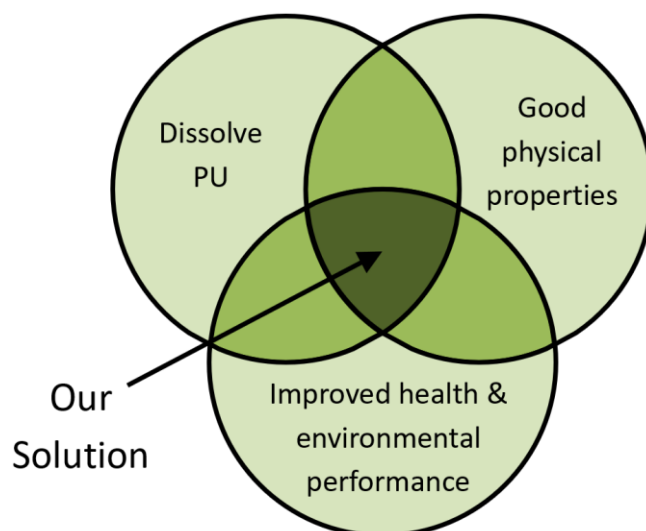


Figure 9. Design criteria used to assess drop-in replacement solvents.

the inherent hazard criteria, a full hazard assessment, as described in the approach, was used to compare the various candidate solvents.

Narrowing through physical properties

A large list of physical properties for each candidate is located in the appendices (Table A1). In order to work in the manufacturing process, the physical properties of the solvent must be considered. Low vapor pressure is required so that the solvent stays in liquid form in the baths and does not vaporize to a great extent. A low vapor pressure typically means a high boiling point, but higher boiling points require more energy to evaporate residual solvent in the oven baking stage of the process. Additionally, the solvent should be miscible with water so that it can be effectively washed out following processing. The physical properties given the most consideration in this study were therefore the boiling point, vapor pressure, and water solubility. Candidates are sorted in Table 2 into two lists depending on whether they have favorable physical properties, particularly for those highlighted above.

Narrowing through PU solvation capability

Given the uncertainties of the exact PU synthetic formulation, we focused on the ability to dissolve PU as the most important technical performance metric for a drop-in replacement solvent. In order to predict the solubility of PU in a given solvent candidate we consider the Hansen solubility parameters of PU and each candidates. A thorough description of Hansen solubility parameters is included in the Appendices. Briefly, the interaction energy between molecules of the same kind are split into contributions from three parameters corresponding to dispersion forces (δ_D), dipolar interactions (δ_P), and hydrogen bonding (δ_H) (Hansen, 1967; 2004). Solvents are situated in this three-dimensional Hansen parameter space according to the

Table 2. Filtering solvent candidates by physical properties.

Candidates meeting physical property criteria	Candidates that did not meet physical property criteria
<ul style="list-style-type: none"> ● 1-ethyl-3-methylimidazolium acetate ([emim][OAc]) ● Cyclopentyl methyl ether (cPME) ● Dihydrolevoglucosenone (Cyrene) ● Dimethyl isosorbide (DMI) ● Ethylene carbonate (EC) ● γ-Valerolactone (GVL) ● Glycofurol (THFP) ● Propylene carbonate (PC) ● Water 	<ul style="list-style-type: none"> ● 2,5-Dimethyl tetrahydrofuran (DMTHF) ● Dimethyl glutarate (DMG) ● Dimethylpropylene urea (DMPU) ● Ethyl levulinate (EL) ● Ethyl levulinate propyleneglycol ketal (ELPK) ● 2-Methylfuran (2MF) ● 2-Methyltetrahydrofuran (2MTHF) ● Methyl levulinate (ML) ● Polypropyleneglycol (PPG)

value of each of the Hansen parameters. This theory assumes that molecules which have similar values of their solubility parameters will interact with each other in a very similar fashion, and are therefore likely to be miscible (i.e. it assumes that the adage “like dissolves like” is valid).

Empirical determinations of the solubility of a given material in many different solvents typically yields a roughly spherical volume of radius R_o in this three-dimensional Hansen solubility parameter space. The distance R_a between two points in this space is given by

$$R_a^2 = 4(\delta_{D2} - \delta_{D1})^2 + (\delta_{P2} - \delta_{P1})^2 + (\delta_{H2} - \delta_{H1})^2$$

Any solvent situated within this volume (i.e. $R_a < R_o$) is therefore expected to be a suitable solvent for the material of interest.

Hansen solubility parameters for various polyurethane polymers can be found in the literature, and are summarized in Table A2 in the Appendices. From these data we expect the PU polymer class to be roughly situated at point $(17.6 \pm 0.6, 6.0 \pm 3, 9.0 \pm 2)$ MPa^{1/2} with an expected solubility interaction radius of 9 ± 4 MPa^{1/2}. In order to assess the viability of candidate solvents their position relative to PU polymers in this parameter space must be determined. Solvents with $R_a < 9$ MPa^{1/2} are expected to be promising candidates for DMF replacement, and those with $R_a < 13$ MPa^{1/2} (corresponding to the upper bound set by the standard deviation) are deemed worthy of further investigation.

The linear distance in Hansen parameter space of each solvent candidate from PU as well as from DMF is shown in Figure 10. The light gray region encompasses the upper error bound associated with the mean PU solubility sphere obtained from the literature, and the dark gray region represents areas of space that are larger than the solubility sphere. The dashed line represents equidistance from DMF and PU. The majority of solvent candidates are within the solubility

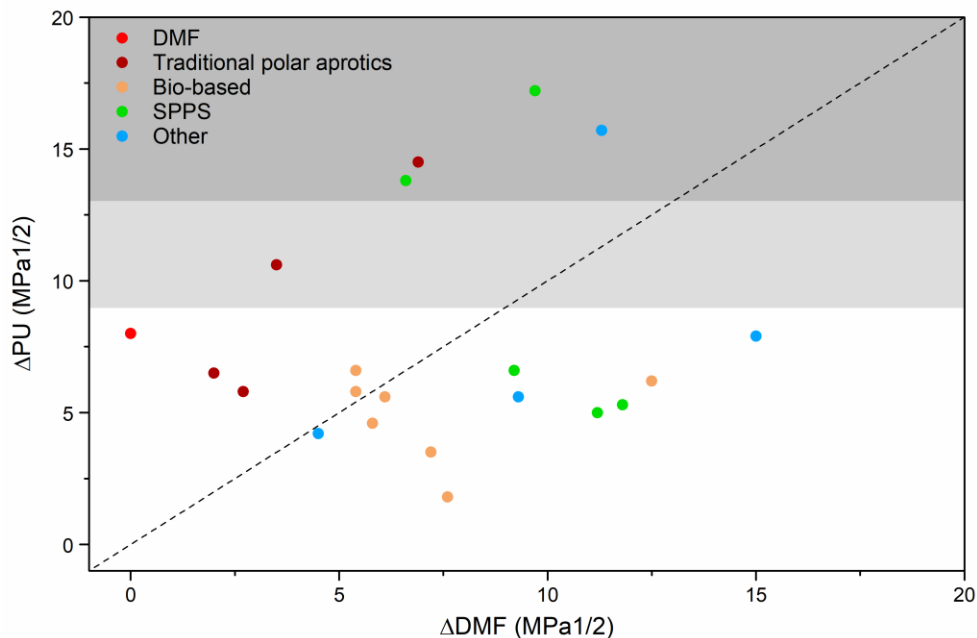


Figure 10. Distance of each solvent candidate in Hansen parameter space from PU and DMF.

sphere, and therefore expected to work effectively for PU solvation. Given the uncertainties about other components of the PU formulation, one might choose to further limit candidates that are not very far from DMF, which is known to dissolve all components. We do not take such a stringent approach in this assessment. Table 3 shows the solvent candidates filtered to those which satisfy both the physical properties and PU solvation criteria, and those which do not satisfy at least one of these criteria.

Table 3. Filtering solvent candidates by physical properties and PU solvation.

Candidates meeting PU solvation and physical property criteria	Candidates not meeting either PU solvation or physical property criteria
<ul style="list-style-type: none"> ● Cyclopentyl methyl ether (cPME) ● Dihydrolevoglucosenone (Cyrene) ● Dimethyl isosorbide (DMI) ● γ-Valerolactone (GVL) ● Glycofurol (THFP) 	<ul style="list-style-type: none"> ● 1-ethyl-3-methylimidazolium acetate ([emim][OAc]) ● 2,5-Dimethyl tetrahydrofuran (DMTHF) ● Dimethyl glutarate (DMG) ● Dimethylpropylene urea (DMPU) ● Ethyl levulinate (EL) ● Ethyl levulinate propyleneglycol ketal (ELPK) ● Ethylene carbonate (EC) ● Methyl levulinate (ML) ● 2-Methylfuran (2MF) ● 2-Methyltetrahydrofuran (2MTHF) ● Polypropylene glycol (PPG) ● Propylene carbonate (PC) ● Water

Drop-in solvent health and environmental performance

When considering the inherent hazard endpoints for a drop-in solvent, we focused on major human endpoints such as carcinogenicity/mutagenicity and developmental/reproductive toxicity, as well as endpoints for which DMF is particularly hazardous, such as dermal and respiratory irritation. We wished to include neurotoxicity and endocrine disruption data as these are a concern for solvents broadly, but there are major data gaps in these categories for virtually all of our list of drop-in candidates, so we excluded them from the hazard assessment tables shown here.

One endpoint we were concerned with was the potential for persistence and bioaccumulation (P/B). We used the n-octanol/water partition coefficient ($\log K_{ow}$) values for all of our drop-in candidates to screen for bioaccumulation potential. We found that all of our candidates are below the commonly accepted bioaccumulation threshold of 4.5, and are therefore not expected to bioaccumulate (Figure 11). To understand the potential for these solvents to persist in the environment, we used authoritative lists when available, and then filled in additional data gaps very broadly with chemical intuition. For example, comparisons of the typical hydrolysis rates of ethers vs. esters can be found in the literature. We categorized our P/B data as low hazard if it was not expected to persist or be bioaccumulative, moderate if either was expected, and high if both were expected. Based on the $\log K_{ow}$ data none of our solvent candidates have a high P/B categorization.

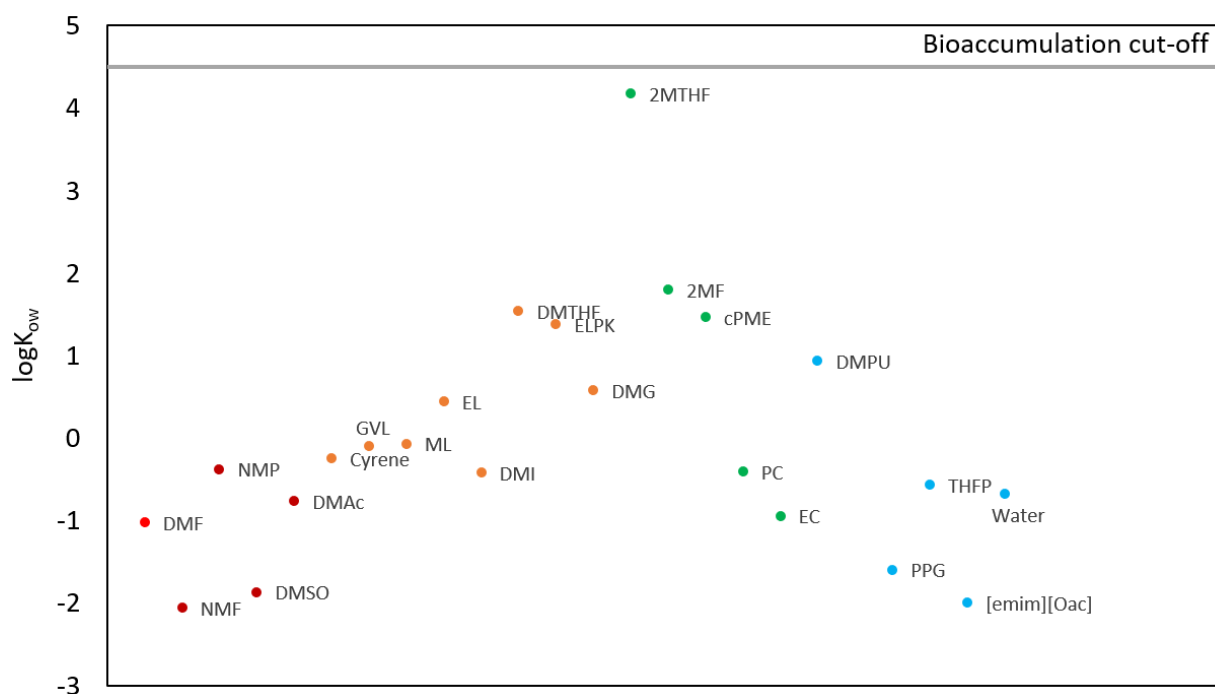


Figure 11. Bioaccumulation potential of solvent candidates. The x-axis simply displaces solvents for ease of viewing, and carries no physical significance.

A word on hazard modeling

For small molecules, like many on our list, modeling may help determine whether a chemical will be a hazard for a given endpoint without any experimental data. However, we were not able to use modeling to add data beyond our authoritative sources for a number of reasons. The drop-in solvent replacements were modeled using the EPA Comptox, Vega, and OECD software toolboxes/packages. These models usually rely on data from similar molecules to make accurate predictions, and in general they lacked suitable analogs for our solvent candidates, sometimes even using DMF as the analog species. Because of this, estimates of toxicity could range by many orders of magnitude between models and relative to experimental data when it existed. However, DMF is toxic primarily due to its MIC metabolite, so metabolite modeling may be a useful endeavor for future work on the solvent candidates discussed in this work. Such a task was deemed to be beyond the scope of the present work.

Hazard analysis of the recommended solvent list

Based on the technical performance, our most promising candidates are Cyrene™, DMI, GVL, cPME, and THFP. The hazard profile of each of these recommended solvents is compared to DMF in Table 4 in an abridged form. The unabridged hazard table for the full list of solvents considered as drop-in candidates is in Table A3 in the Appendices. Details of each candidate on the recommended list are included below, but all show a substantial improvement in human health and environmental endpoints compared to DMF.

Table 4. Abridged hazard table for the recommended solvents list. More details can be found in the unabridged Table A3 in the Appendices.

Solvent	C/M/R	Systemic	Irritation	Acute	Aquatic	P/B
DMF	H	M	M	M	L	M
Cyrene	L	L	L	M	L	L
DMI	L	-	L	L	L	M
GVL	pC	-	L	L	-	L
cPME	L	L	M	M	L	M
THFP	-	-	-	M	-	M

Dihydrolevoglucosenone (Cyrene™). REACH determined that Cyrene did not require classification for carcinogenicity, mutagenicity, developmental/reproductive toxicity, or systemic toxicity. Cyrene is an eye irritant, but REACH determined that it did not require classification as a skin irritant. REACH also determined Cyrene did not require classification for aquatic toxicity and is not expected to be persistent. There was some evidence of acute mammalian toxicity. Cyrene has been cited in the literature as demonstrating significant promise as a polar aprotic solvent

with similar properties to DMF (Sherwood et al. 2014). As Cyrene is derived from glucose, it has a fully renewable feedstock. While, it is not widely available at present by industrial/commercial production on a large scale, it is expected to be commercially feasible (Waijers-van der Loop et. al 2018).

Dimethyl isosorbide (DMI). REACH determined that DMI did not require classification for carcinogenicity, mutagenicity, and developmental/reproductive toxicity. It is not expected to be a skin or respiratory irritant, but it is an eye irritant. Based on the literature, DMI is not expected to be acutely toxic (Moity, 2012) or aquatic life. There is evidence that it could be persistent in the environment. DMI was the solvent with the closest Hansen Solubility Parameters to PU. It is currently advertised as a high purity solvent and carrier which offers a safe, effective delivery enhancement mechanism for active ingredients in personal care products. At present, DMI is available for commercial production and at industrial scale (Waijers-van der Loop et. al 2018).

γ -Valerolactone (GVL). Based on modelled data in REACH, GVL is of potential concern for carcinogenicity, mutagenicity, or developmental/reproductive toxicity. These endpoints should be prioritized for further research. REACH determined that GVL did not require classification for skin, eye, or respiratory irritation. It is also not expected to be acutely toxic or persistent in the environment. There is some evidence of toxicity to aquatic life. GVL has been recommended as a green solvent and solvent precursor (Alonso, D. M., Wettstein, S. G., & Dumesic, J. A. 2013) and is expected to be fully degradable and non-toxic (Shen et al., 2019). Polymerization of biomass-based diol precursors, which were obtained from the ring opening of GVL with amine compounds, also resulted in novel polyurethanes (Chalid, 2015). Specifically, GVL was used as polyol in the polyurethane backbone (Chalid, 2015). It is also one of the volatile flavor constituents in mango and honey (Wilson, C., et al., 1990; Guyot, C., 1999). While it is not widely available at present by industrial/commercial production, it is expected to be commercially feasible (Waijers-van der Loop et. al 2018).

Cyclopentyl methyl ether (cPME). REACH determined that cPME did not require classification for carcinogenicity, mutagenicity, developmental/reproductive toxicity, or systemic toxicity. cPME is a skin irritant but not respiratory irritant and is a level 3 on the Hodge-Sterner acute toxicity scale. There was some evidence of low toxicity to aquatic life which did not reach the threshold for REACH classification. cPME is not expected to bioaccumulate in tissue, but could be persistent in the environment due to its ether group. cPME has been identified as a greener option for ether solvents based on its favorable environmental, health and safety characteristics based on its chemical and physical properties (Musaimi et al., 2018).

Glycofurol (THFP). There is a dearth of toxicity data for glycofurol, but the available data is promising. BIBRA Toxicity Profile of glycofurol states that no skin irritation was found after applying as a dilute solution to the skin of mice (BIBRA, 1992). Glycofurol is a level 3 on the Hodge-Sterner acute toxicity scale and is not expected to bioaccumulate in tissue, but could be persistent in the environment due to its ether groups. Glycofurol is used as a solvent in parenteral pharmaceutical formulations and is generally regarded as a relatively nontoxic and nonirritating material at the levels used as a pharmaceutical excipient (Weller, 2002).

Additional candidates and assessment resources

Two additional tools for ranking solvents are helpful for future direction and for identifying “honorable mentions” to our recommended list. Work on updating the GlaxoSmithKline (GSK) solvent guide, includes a robust list of solvents, adjusts the way in which multiple health, environment, safety, and waste categories are combined to reach a single composite score and color assignment; and has updated data behind all scores (Alder et al., 2016). This solvent guide is a great resource for considering additional sustainability criteria that we did not quantitatively analyze, such as life cycle analysis or recyclability, or other risk factors that we did not include in our hazard assessment, such as potential for exposure.

In addition, the US EPA’s Safer Chemical Ingredient List (SCIL) includes many of the chemicals evaluated through the Safer Choice Program, and has a specialized criteria assessment for solvents (US EPA, 2014). Two solvents from our candidate list that did not meet the technical performance criteria that we set as part of this project do meet EPA’s highest rating - “green circle.” We recommend that these solvents, propylene carbonate (PC) and dimethyl glutarate (DMG), be tested for the ability to dissolve PU because of their strong health and environmental performance. PC was only excluded from the recommended solvent list due to falling very slightly outside of the solubility sphere for PU. However, given the large uncertainty associated with the size of this sphere, PC may be feasible in practice despite this position.

Process Change

PU dispersion

How it works. Polyurethane dispersions (PUD) are a polyurethane polymer resin dispersed in water rather than an organic solvent. This process is referred to by several names, including aqueous polyurethane dispersion, waterborne polyurethane dispersion, and solvent-free process. The PUD market size is expected to grow from USD\$2.4B in 2019 to USD\$3.4B by 2024, driven by increasing demand from automobile, textile and leather industries (Research and Markets 2019). In fact, Nike has already begun using PUD in its natural leather production (Hackenmiller-Paradis, 2019).

The water-based process for PU artificial leather uses foamed, water-based polyurethane dispersions as a coating material during leather production. In conventional synthetic leather production methods, DMF is used to create a porous product that provides similar microporosity as natural leather. In the water-based process, this step is substituted with the formation of a frothed foam by incorporating air into the waterborne PU dispersion. The solvent-free process uses a reactive polyol-isocyanate mixture as a coating material or applied to release layer, then curing these polyurethane system components to form the polymer (Ritter, 2014). This solvent-free or water-based processes would eliminate not just DMF, but other toxic solvents like toluene and methyl ethyl ketone. It does not utilize organic solvents and is able to produce products that perform similarly to conventionally produced synthetic leather. Several companies including TFL, Bayer, and Evonik already have promising PU dispersion for artificial leathers.

Bayer MaterialScience claims that their water-based manufacturing technology uses significantly less energy and only a fraction of the water consumed in the conventional process. Energy consumption is reduced by nearly 55% by avoiding the need to heat water, implement multiple drying steps, and perform solvent recovery and purification. It also eliminates worker exposure to DMF. Although the new process is a water-based method, it still uses ~95% less water than the DMF process since washing steps are no longer required (Ritter, 2014).

Hazard Profile. However, to improve performance, aesthetics, and production speeds, additives are used which may pose their own health risks (Table 5). The company Evonik has developed a series of additives specifically for use in the production of water-based and solvent-free PU leathers. Polycat, an amine catalyst used in PU foam, had data gaps across many human endpoints, but is a skin and eye irritant. There is evidence of moderate acute mammalian toxicity modeled data shows there is potential concern to aquatic life. Dabco, another amine catalyst, is a moderate hazard for developmental/reproductive and systemic toxicity. It is a skin, respiratory and eye irritant. Similar to Polycat, there is evidence of moderate acute mammalian

Table 5. Hazard profile of some additives used in PUD formulations.

Molecule	C/M/R	Systemic	Neuro	Irritation	Acute	Aquatic	P/B
Polycat	-	-	-	H ¹	M ¹	pC ²	-
Dabco	M ³	M ⁴	-	H ^{1,4}	M ¹	pC ²	-
KOSMOS	M ^{3,4}	pC ⁴	-	H ⁴	H ⁴	H ³	-

¹(New Zealand EPA, 2019)

²(Danish EPA, 2019)

³(Japanese GHS, 2019)

⁴(ECHA, 2019)

toxicity modeled data shows there is potential concern to aquatic life. KOSMOS[®] 19 by Evonik is a dibutyltin dilaurate with moderate hazard for carcinogenicity, mutagenicity, and developmental/ reproductive. Based on modeled data, it is of potential concern for systemic toxicity. It is a skin and eye irritant and has high acute and aquatic toxicity. We selected these additives as representatives for potential health concerns of constituents used in the PUD process. It is important to note that as various companies have different PUD processes, they have different additives as well. As such, a careful inspection should be made of each available process before passing judgement.

PU dispersions have the potential to reduce or completely eliminate DMF, along with many other toxic chemicals used currently in the production of PU synthetic leather. They could also provide additional water and energy savings. Despite being a water-based process, it actually results in water and energy savings by eliminating the need to wash or bake DMF out of products. There is also literature on improved abrasion resistance (European Coatings Journal, 2009). Potential concerns of this process are its higher costs and the health and safety of additives. Furthermore, there is the potential that some PUD processes does not completely eliminate DMF. A PUD process alone may not produce the color and quality standards that Nike requires, however, the PUD could be combined with other processes such as the CO₂ dyeing to bolster the available color palette.

Alternative backbone chemistry

The need for a strong solvent, such as DMF, in the PU process is driven by the isocyanate in the polymer backbone. Isocyanates themselves are a health hazard and can cause sensitization and acute toxic effects to the mucus membranes (CDC). One potential process change would involve moving to a less hazardous backbone chemistry for the PU. There is some research into isocyanate-free PU, which instead uses diamines (Besse, 2013). This process would still require a solvent to enable polymerization. However, DMF could perhaps be replaced with a less

hazardous solvent that may not be feasible in the current process. While we wanted to highlight alternative backbone chemistries here as an interesting option to consider, and for which some work in the literature has already been done, it was considered beyond the scope of the current investigation.

Material Change

Grown leathers

Recent interest in using biological feedstocks to produce functional materials has led to a myriad of strategies to produce leather materials from many different organisms. The primary attraction to biological feedstocks is the ability to grow the raw materials used in product fabrication, rather than to rely on extractive resource acquisition (petroleum in particular). Many of these strategies were deemed by us to have issues with scalability or market readiness/availability, and in general technical and health performance data are not available. As such, we only provide a brief overview of the current bioleather landscape.

Pineapple leather. Piñatex is making pineapple leather from pineapple leaf fibers, an agricultural waste. This was developed through a process called decortication, removing the surface layer of the pineapple leaves to extract the long fibers within. These fibers are then degummed and undergo an industrial process to become a mesh, which is the base of the material. This non-woven mesh then goes through specialized (petroleum-based) finishing, which gives its leather-like appearance (Piñatex, 2019). Since the exact processes are unknown, this leather production process may still utilize solvents like DMF. Pineapple leather is commercially available and has been used by retailers such as H&M in their clothing (The Independent, 2019).

Cactus leather. Desserto is a company making alternative leathers from cactus leaves. Cactus leather is made from mature cactus leaves. Cactus plant that can withstand the cold weather are selected as raw materials. Plant fibers are refined once picked. A protein extracted from the plant is used to help the molecular binding between the organic components and chemicals. It is unclear what chemicals are being used in this process (Desserto, 2019).

Collagen from yeast. Collagen proteins are the primary constituent of connective tissues such as skin, and are cross-linked during tanning in the production of natural leather. Genetically engineered yeast and bacteria are able to produce collagen through a fermentation process, which can then be extracted and assembled into bioleather. Companies such as Modern Meadow are currently exploring products made in this way (Modern Meadow, 2019).

Mycelium leather

How it works. Mycelium leather is another bioleather alternative to traditional PU-based synthetic leathers. We chose to highlight mycelium-based leather products separately from other grown leathers because they are used more widely used in the fabrication of consumer goods, and because more information on their performance is available. Mycelium is the vegetative tissue of the fungi, composed of hyphae, a root-like structure that allows for nutrient absorption.

Fungi grow based on a symbiotic relationship with its feedstock which could be saw dust and other agricultural waste or byproducts to form the entangled network of fiber (Haneef et al., 2017). This network of fibers can then undergo various processes such as those outlined below to be transformed into a leather-liked material.

Technical performance. Companies such as Bolt Threads and MycoWorks are two leading innovators in this production method. MycoWorks has described its product as matching conventional leathers in flexibility, strength and durability with the additional qualities of natural antimicrobial action and water-resistance. They claim that the texture and performance of their leather is customizable as a direct result of growth and processing condition variation. The feedstocks for their mycelia are agricultural waste materials such as corn cobs, hemp hurds, paper pulp waste, rice hulls, and saw dust. By providing mycelia different “foods” and mediating the environment, temperature, humidity, amount of light and the exchanges of gases, mycelium leather is grown to possess various properties. Even adhesives can be grown inherently into the leather. According to MycoWorks, their raw material can be grown in two weeks compared to two years for the same amount of cow hide for traditional leather production. MycoWorks have declared its product to be fully biodegradable, carbon neutral and free from the addition of industrial chemicals (MycoWorks, 2016).

Bolt Threads also creates their products from mycelia. Their process starts with the mycelium cells, that are introduced to a bed of feedstock that also includes agricultural waste. Once the mycelium grows large enough, it is compressed, tanned and dyed to make the mycelium leather. Bolt Threads have collaborated with designers to create soon-to-be commercially-available handbags that range from USD\$400 to several thousands of dollars (Bolt Threads, 2019).

Hazard profile. Due to proprietary information the exact processes of used by both companies remain unknown. Prior Greener Solutions project have worked on improving the performance of MycoWorks’ mycelium leather and also making the process less toxic (Deeg et al., 2017). Unfortunately, it is unclear whether the recommendations set out in this previous report are currently in use. It is also unclear what kind of tannins and dyes are used by Bolt Threads. While claiming to be more environmentally friendly, there may be potentially toxic chemicals involved with either company’s processes. Despite being promising solutions, a hazard assessment of the current processes are necessary to determine whether the material is as safe as claimed.

Crosslinked plant-based oils

How it works. The overwhelming majority of modern synthetic polymers are derived from petrochemical feedstocks. More recently, increased focus has been placed on functionalization of plant-based renewable chemicals. Many plant-based fatty acids contain unsaturated C=C

double bonds that are susceptible to chemical functionalization. Epoxidation of these bonds leads to particularly reactive sites on these molecules, broadening their utilization potential. Epoxidized soybean oil (ESBO) is typically used due to its commercial availability, but any other unsaturated fatty acid can be similarly functionalized.

ESBO molecules can be crosslinked in a fully renewable process using polybasic acids and alcohol solvents (Liu, 2017). Typical alcohols include ethanol, butanol and isopropanol; citric acid is often used as the polybasic acid since it is generally recognized as safe (GRAS). As an example, ESBO and citric acid dissolved in isopropanol and heated to ~50-80 °C crosslink to form an elastomeric material (Figure 12). Unfortunately, the reaction takes up to 24 hours at 80 °C, and residual alcohol has to be extracted by vacuum filtration. These issues severely limit the economic viability of this material due to issues with scalability and energy resource costs. Furthermore, the resultant elastomer contains many air bubbles produced during alcohol solvent evaporation that lead to unfavorable mechanical properties.

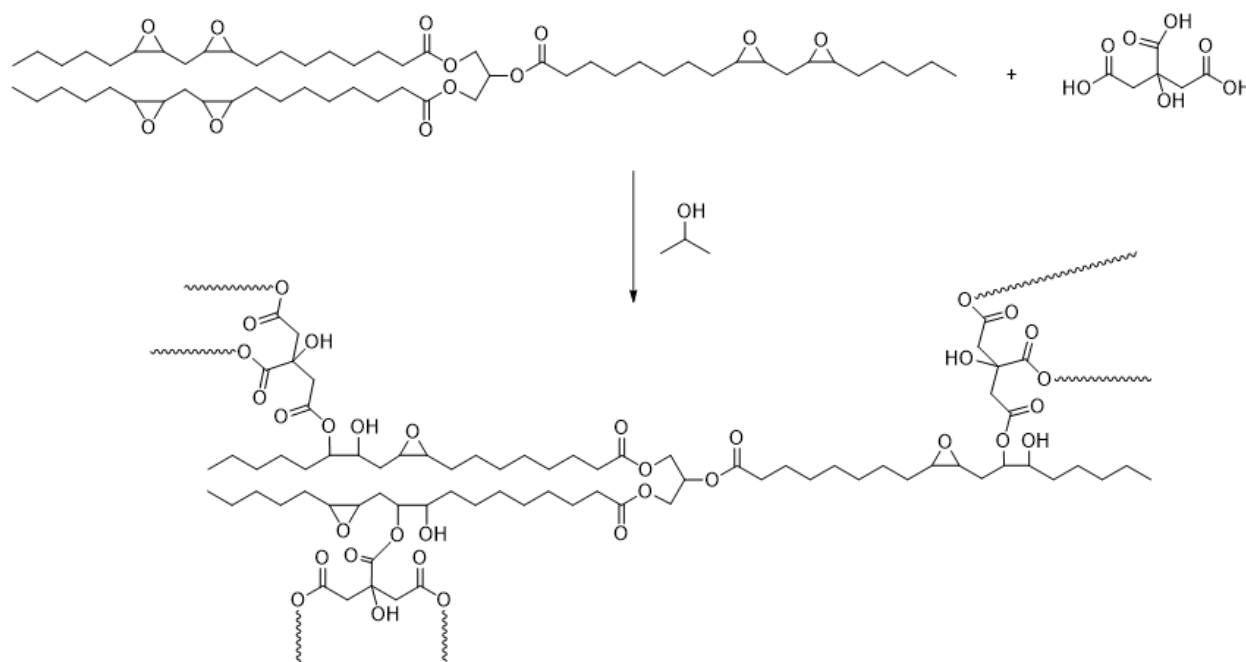


Figure 12. Crosslinking of ESBO using citric acid in isopropanol. Crosslinks between fatty acid molecules are illustrated with wavy lines.

While synthetic leather production by fully crosslinking ESBO as described above is unsatisfactory, extensions to this technique have led to large improvements in the feasibility of producing artificial leather (Amstutz, 2019). A pre-polymer “curative” is first produced using the method described above. Citric acid and ESBO are dissolved in a small alcohol with an excess of citric acid, which prevents gelation of the pre-polymerized material. The alcohol solvent reacts

with some of the carboxylic acid groups in citric acid molecules to form ester linkages which decrease the average functionality of the citric acid molecules and leads to less branching in the pre-polymer. Varying the ratio of alcohol and another unreactive solvent molecule can be used to tailor the physical properties of the final product. The result of this reaction is a viscous liquid oligomeric curative composed of ester linkages between fatty acid molecules, citric acid, and small alcohols whereupon excess alcohol can be readily removed by heating. This curative is miscible with unreacted and epoxidized vegetable oils, and used for further processing.

For fabric coatings the curative is mixed with additional epoxidized fatty acid, applied to a non-stick surface, and fabric is layered onto the liquid resin. Curing the material in a heated hydraulic press at 100-150 °C takes 15-45 minutes. Curing can be accelerated by various catalysts including quaternary ammonium or phosphonium molecules, imidazoles, or zinc salts of organic acids. For materials that need to perform under very cold conditions the curative is added to epoxidized natural rubber (ENR). Additives in these materials include clays or silica particles, additional epoxidized oils, essential oil deodorants, and vitamin E as a natural antioxidant. Color may be introduced in a variety of ways, but black and brown variants are readily formed by adding coconut charcoal and cork powder respectively.

Technical performance. Varying the synthesis conditions can lead to a variety of material finishes and appearances. Color, texture, and embossed patterns can all be added to the final product, which is described as having appearance, texture, and mechanical performance very similar to natural leather (Figure 13). It is able to be cut and sewn or otherwise assembled by conventional means. It has a Shore A hardness of 50-90, a Young's modulus up to ~35 MPa, and a high tear strength, similar to natural leather. Curing these materials in a hydraulic press requires much lower applied pressure, since the excess alcohol solvent is evaporated from the curative and does not form vapor during the curing process. This requires less expensive production tools, and improves the overall energy efficiency of manufacturing.



Figure 13. Synthetic leather produced from plant-based oils, and a purse made from this leather (from Natural Fiber Welding, Inc.).

Hazard profile. This natural fatty acid crosslinking process has a substantially safer toxicological profile than the current DMF-based PU synthetic scheme (Table 6). There are no known health hazards associated with raw soybean oil. The high reactivity of epoxides is usually a health and safety concern, but their incorporation into large fatty acid molecules like ESBO mitigates their risk substantially. ENR is also known to have only ~2-4% of the latex allergen activity of untreated rubber. Ethanol and isopropanol, and to a slightly lesser extent n-butanol, have a very favorable profile across virtually all endpoints, and citric acid is a common constituent of citrus foodstuff that is designated GRAS. Acetone is included in the formulation as a solvent mixture with the alcohol in order to alter the functionality of citric acid in the curative, and therefore change the final properties of the product. Acetone has high volatility and is the substance of most concern in this formulation. It is used in the formation of the curative, so it could be easier to have engineering controls in place that minimize exposure to acetone vapors until they are removed by heating. The essential oil deodorants, vitamin E antioxidant, and silica/clay fillers would not be expected to present significant health hazards.

Table 6. Hazard classification of molecules used to produce leather from plant-based oils. Soybean oil and quinoline are used as representative examples of a natural fatty acid and a catalytic species respectively.

Molecule	C/M/R	Systemic	Irritation	Acute	Neurotox	Aquatic	P/B
Soybean oil	L ¹	L ¹	M ¹	L ¹	-	-	L ¹
ESBO	L ^{2,3}	L ^{2,3}	L ^{2,3}	L ^{2,3}	-	L ²	L ²
Citric acid	L ²	L ²	L ²	L ²	-	L ²	L ²
Ethanol	L ²	L ²	L ²	L ²	L ²	L ²	L ²
n-Butanol	L ²	L ²	H ²	M ²	L ²	L ²	L ²
Isopropanol	L ²	L ²	H ²	L ²	M ²	L ²	L ²
Acetone	L ²	L ²	H ²	L ²	L ²	L ²	L ²
Quinoline	H ²	pC ²	H ²	M ²	L ²	M ²	L ²

¹(Toxnet, 2019)

²(ECHA, 2019)

³(Hatlelid, K., 2019)

Crosslinking between carboxylic acids and epoxides in this method can be catalyzed by various substances, usually nitrogen-containing species. Quinoline is included here as a representative example of a catalyst for this reaction. It is implicated in many unfavorable health endpoints and should be avoided whenever possible. Synthesis of the artificial leather in a heated hydraulic press already reduces processing times to the order of many minutes rather than hours, so it may be possible to avoid such catalytic species.

Discussion

In this work, we considered three general opportunities for intervention to facilitate the phasing out of DMF in PU synthetic leather production. We screened a reasonably large list of novel polar aprotic solvents, often derivable from bio-based feedstocks, for potential use as drop-in replacement solvents. We also considered the possibility of making changes to the PU process chemistry that could enable reductions or elimination of DMF use in these processes. Finally, we explored several material changes that would eliminate the need for DMF by disposing of PU as a functional material altogether.

For drop-in solvents, all candidates would represent a substantial improvement in the hazard profile of the PU synthetic process compared to DMF. We narrowed our list down to only a few top candidates, taking the conservative route when uncertainties arose. We therefore encourage further testing of any candidate on our long list of drop-in solvents that may appear suited to a given process. We believe that Cyrene, GVL, DMI, cPME and THFP are excellent starting points for further work on this project by Nike, and encourage the addition of PC and DMG as honorable mentions that were struck from consideration due to conservative approaches, but which otherwise represent very promising candidates.

It is worth mentioning that we only consider pure solvents in this study, but solvent properties can be widely tuned by changing the ratios of different solvents mixed together. Consider a simple example in which cPME is deemed to be too volatile and PC too far from PU in Hansen parameter space to solvate PU. A 2:3 mix of cPME:PC would necessarily have a much lower vapor pressure according to Raoult's Law, and would have a distance from PU of only 7.9 in Hansen space, sitting within the solubility sphere as well as being extremely close to DMF itself. While beyond the scope of this work, exploring solvent mixtures may represent the key to finding an optimal drop-in replacement solution.

In our assessment of process change, we found the alternative backbone chemistry solution to be an interesting avenue for further exploration, but generally beyond the scope of this work. The PU dispersions seem to be a much more promising option, although issues remain with the color palette currently available with this process. Many catalysts used in this process have several negative health outcomes, although they are likely used in smaller volumes than DMF and may also have a lesser potential for exposure. Given the large uncertainties surrounding some of these formulations, we would encourage Nike to gather more information through industry contacts, if possible. If this results in a fair outcome, we would suggest considering this process for its many benefits despite issues with the color palette.

There are several options for material changes, with varying levels of available information and potential produce at scale. Information about several bioleathers is very sparse, and we cannot recommend them as solutions at this time. Mycelium leather was the focus of a previous project in the Greener Solutions course, but we were unable to verify whether or to what extent the recommendations put forth in that report were incorporated into production. There are also concerns with the requirement for growth times on the order of days-weeks. The crosslinking of natural oils process patented by Natural Fiber Welding, Inc. shows great promise, as do the renewable nature of the feedstocks, relatively short processing times on the order of minutes, and the very favorable hazard analysis.

We recommend that Nike look into utilizing some of its existing capital investments to achieve or enhance our recommended material and process changes. For example, Nike has an existing relationship with vendors using polyurethane dispersions for some products (Nike, 2018), and should consider expanding this further. In addition, Nike has an existing 'ColorDry' process, developed in collaboration with Far Eastern and DyeCoo. DyeCoo's website specifically claims the ability to dye and material into which CO₂ can penetrate. Expanding the use of the ColorDry process could address a primary concern with both the material change and process strategies by enabling the bright and fluorescent color palette desired by Nike.

Our primary recommendations include replacing PU with synthetic leather based on crosslinked natural oils, and replacing DMF with one of our recommended drop-in solvents. A material change to synthetic leather produced by the crosslinking of renewably sourced natural oils has the scalability and health profile to meet production demands and accomplish many of Nike's sustainability goals while mitigating risk to workers and consumers. Given the relative ease of implementing a drop-in solvent replacement, this strategy is also highly recommended for consideration at Nike.

Appendices

Physical properties of drop-in solvent candidates

Table A1. Physical properties of drop-in replacement candidate solvents. Values shaded grey are indicate predicted or modelled results. Values in purple are inferred from comparisons to similar molecules when data does not exist for the candidate.

	Molecular Weight (amu)	Melting Point (K)	Boiling Point (K)	Vapor Pressure (Torr)	Density (g/cm ³)	log(K _{ow})	Aqueous Solubility (g/100 mL water)	Polar Surface Area (Å ²)	Dipole Moment (debye)	Dynamic Viscosity (cP)	δ _D (MPa ^{1/2})	δ _P (MPa ^{1/2})	δ _H (MPa ^{1/2})	Distance from DMF (MPa ^{1/2})	Distance from PU (MPa ^{1/2})
DMF	73	213	426	3.9	0.948	-1.03	∞	20.3	3.86	0.92	17.4	13.7	11.3	0.0	8.0
NMF	59	269	456	0.808	1.011	-2.064	∞	29.1	3.83	1.681	17.4	18.8	15.9	6.9	14.5
NMP	99	249	476	0.3	1.028	-0.38	∞	20.3	4.09	1.686	18.0	12.3	10.6	2.0	6.5
DMSO	78	292	462	0.42	1.100	-1.87	∞	36.3	3.96	1.996	18.4	16.4	10.2	3.5	10.6
DMAc	87	253	438	2.3	0.937	-0.77	∞	20.3	3.72	0.945	16.8	11.5	10.2	2.7	5.8
Cyrene	128	255	476	0.062	1.26	-0.25	∞	35.5	3.4	11	18.8	10.6	6.9	6.1	5.6
GVL	100	242	481	4.87	1.05	-0.096	∞	26.3	5.3	2.18	17.1	11.9	6.2	5.4	6.6
ML	130	242	469	0.41	1.05	-0.072	6.2	43.4	3.22	1.916	16.6 ¹	9.8 ¹	7.3 ¹	5.8	4.6
EL	144	<298	479	0.249	1.01	0.438	10-100	43.4	2.58	1.93	16.6 ¹	9.8 ¹	7.3 ¹	5.8	4.6
DMI	174	203	507	0.07	1.15	-0.42	∞	36.9	1.74	6.41	17.6	7.1	7.5	7.6	1.8
DMTHF	100	173	390	62.1	0.83	1.54	0	9.32	1.67	0.485	16.4 ²	4.1 ²	3.6 ²	12.5	6.2
ELPK	202	<298	516	0.038	1.012	1.38	0.048	44.8	3.3	-	16.5 ³	11 ³	7 ³	5.4	5.8
DMG	160	231	487	0.091	1.0876	0.571	5.9	52.6	2.3	2.5	16.1	7.7	8.3	7.2	3.5
2MTHF	86	137	353	102	0.86	4.17	14	9.32	1.38	0.46	16.9	5.0	4.3	11.2	5.0
2MF	82	186	337	176	0.913	1.791	0.3	13.1	0.72	0.378	15.8	5.7	14.5	9.2	6.6
cPME	100	133	379	34.6	0.86	1.467	1.1	9.23	1.27	0.57	16.7	4.3	4.3	11.8	5.3
PC	102	224	515	0.035	1.21	-0.41	24	35.5	4.98	2.47	17.0	19.8	9.0	6.6	13.8
EC	88	310	516	0.0246	1.321	-0.946	21.4	35.5	4.9	1.919	18.4	23.1	10.4	9.7	17.2
DMPU	128	253	520	0.039	1.024	0.933	∞	23.6	4.17	2.934	17.4	10.2	8.5	4.5	4.2
PPG	-	333	575	<0.01	1	>2	∞	10-20	1.69	>100	15.0	6.9	7.2	9.3	5.6
THFP	146	<298	529	0.002	1.06	-0.566	∞	38.7	3.4	13	18.0 ⁴	1.6 ⁴	2.5 ⁴	15.0	7.9
[emim][OAc]	-	256	646	0.0009	1.21	-2.71	∞	-	-	154	23.0	19.0	10.0	12.5	16.9
Water	18	273	373	23.8	0.997	N/A	∞	25.3	1.85	0.89	15.5	16.0	42.3	31.3	35.0

¹Me/Et levulinate assumed halfway between GVL (1 fewer ether) and DMG (1 additional ether)

²2MTHF ≅ TMTHF, so assume DMTHF is 1/3rd of the distance from 2MTHF to TMTHF

³ELPK is loosely based on similar molecules: assume dD = 1,2-methylisobutylidene glycerol; dP estimated from a plot of dipole moment vs dP data herein; assume dH = 7 based to similar structures

⁴Assume THFP is the same as a glycofurol molecule with a slightly longer ether chain

Hansen solubility parameters

For a condensed phase molecule to evaporate, it must possess sufficient energy to overcome the forces of attraction binding the molecules together. This same cohesive energy density (ced) must also be overcome by solute-solvent interactions if the solute molecules are to be successfully separated from one another and fully solvated by the solvent species. Hildebrand suggested in 1936 that the square root of the ced would be a good estimate of the solubility of different substances

$$\delta = (ced)^{1/2} = \left(\frac{\Delta E_v}{V_m}\right)^{1/2}$$

$$\Delta E_v = \Delta H_v - RT$$

where ΔH_v is the latent enthalpy of vaporization, V_m is the molar volume, R is the universal gas constant and T is the temperature (Hildebrand and Scott, 1950). Substances with similar solubility parameters are expected to be mutually soluble within one another in this model. The Hildebrand solubility parameter has been found to work best for relatively non-polar compounds that do not exhibit hydrogen bonding. In 1967 Charles Hansen improved upon this theory by dividing the solubility parameter into three separate parameters corresponding to dispersion forces (δ_D), dipolar interactions (δ_P), and hydrogen bonding (δ_H) (Hansen, 1967; 2004). This theory is predicated on the assumption that molecules which interact with each other in a similar fashion to the desired solute will likely be good solvents. Solvents are thus situated as three-dimensional points in the Hansen solubility parameter space. It is typically found that there exists a roughly spherical volume of radius R_o around a solute of interest within which solvents are found to perform adequately. The distance R_a between points in this space is given by

$$R_a^2 = 4(\delta_{D2} - \delta_{D1})^2 + (\delta_{P2} - \delta_{P1})^2 + (\delta_{H2} - \delta_{H1})^2$$

where doubling the contribution from the dispersion parameter is found experimentally to convert spheroidal volumes in this parameter space to more spherical ones.

The Hansen solubility model has found widespread popularity due to its simplicity, and since the three parameters typically have values that align with chemical intuition based on molecular structure (for example, molecules with larger permanent dipole moments have larger dipolar parameter values). Due to this simplicity, these solubility parameters are available for a very large number of potential solvent molecules. Hansen solubility parameters for various polyurethane polymers can be found in the literature, and are summarized in Table A2. Solubility parameters in this work have the SI units of $\text{MPa}^{1/2}$, which differ from those in units of $(\text{cal}/\text{cm}^3)^{1/2}$ by essentially a factor of 2. From these data we expect the PU polymer class to be roughly situated at point $(17.6 \pm 0.6, 6.0 \pm 3, 9.0 \pm 2) \text{MPa}^{1/2}$ with an expected solubility interaction radius of $9 \pm 4 \text{MPa}^{1/2}$. In order to assess the viability of candidate solvents their position relative to PU polymers in this parameter space must be determined. Solvents with $R_a < 9 \text{MPa}^{1/2}$ are expected to be promising candidates for DMF replacement.

Table A2. Hansen solubility parameters for various polyurethane polymers. The nomenclature in the original sources are used, and are explained in the table footnotes.

Sample	δ_D (MPa ^{1/2})	δ_P (MPa ^{1/2})	δ_H (MPa ^{1/2})	R_o (MPa ^{1/2})
PU1 ¹	17.6	3.5	9.0	-
PU2 ¹	16.8	4.4	6.8	-
PU3 ¹	17.2	4.5	9.3	-
NOP-PUD ²	18.7	11.4	9.5	10.5
PU ³	18.0	6.3	6.3	3.1
SCP ⁴	17.6	4.4	8.7	9.7
P-450 ⁴	17.2	7.8	13.3	13.1
Average	17.6	6.0	9.0	9
St. Dev.	0.6	3	2	4

¹(Mieczkowski, 1992): PU1-3 made respectively from the reaction of polyethylene oxide, polypropylene oxide, and polyethylene adipate polyols with 1,6-hexamethylene diisocyanate.

²(Oh, 2011): NOP-PUD made by the reaction of soy oil polyester polyols, acid containing diols such as 2,2-bis(hydroxymethyl)propionic acid, and optionally short chain diols with isophorone diisocyanate.

³(Latnikova, 2012): PU made by the reaction of polyvinyl alcohol with poly[(phenyl isocyanate)- co-formaldehyde] (isocyanate prepolymer)

⁴(Zhang, 2015): SCP is a natural oil-based PU prepared using soy-castor oil-based polyol (formed in a reaction between epoxidized soybean oil with castor oil fatty acids) and diphenylmethane- 4,4'-diisocyanate (PMDI). P-450 is a petroleum-based PU made by the reaction of polyol 450 (a reaction product of propylene oxide and glycerol) with PMDI.

EPA's safer choice criteria for solvents

To identify safer solvents, EPA Safer Choice focuses on the characteristics (hazard endpoints) that are relevant to solvents and that distinguish safer solvents from those of greater concern. With cleaning solvents, there are potential concerns for the following hazards: carcinogenicity, acute mammalian toxicity, reproductive and developmental toxicity, repeated-dose toxicity, neurotoxicity, and environmental fate and toxicity. The Safer Choice Criteria for Solvents were developed for the alcohol, ester, ethylene glycol ether, and propylene glycol ether solvent classes.

Criteria generally rely on not being GHS classified for the above endpoints. Carcinogenicity includes listings on other authoritative lists (IARC, NTP, EPA); neurotoxicity allows for data gaps; acute mammalian toxicity is based on median lethal dose greater than levels listed by route of exposure; and environmental toxicity and fate depends on if the solvent is an acute aquatic toxicant (then it must biodegrade rapidly and not be bioaccumulative). EPA considers the chemicals in this listing as among the safest for their functional use.

Meanings of listing levels:

- Green circle: the chemical has been verified to be of low concern based on experimental and modeled data.
- Green half-circle: the chemical is expected to be of low concern based on experimental and modeled data. Additional data would strengthen our confidence in the chemical's safer status.
- Yellow triangle: the chemical has met Safer Choice Criteria for its functional ingredient-class, but has some hazard profile issues. Specifically, a chemical with this code is not associated with a low level of hazard concern for all human health and environmental endpoints. While it is a best-in-class chemical and among the safest available for a particular function, the function fulfilled by the chemical should be considered an area for safer chemistry innovation.
- Grey square: this chemical will not be acceptable for use in products that are candidates for the Safer Choice label and currently labeled products that contain it must reformulate per Safer Choice Compliance Schedules.

Complete drop-in solvent hazard table

Table A3. Comprehensive hazard table for all drop-in solvent candidates.

Solvent	HS	Carc	Mut	R/D	Syst	Neur	Sk Irr	Re Irr	Ey Irr	Acu	Aquat	P/B ¹
DMF	5 ²	H ³	M ³	H ⁴	H ⁵	-	M ⁴	M ⁴	H ⁴	M ⁴	L ⁴	M ⁴
Cyrene	4 ⁴	-	L ⁴	L ⁴	L ⁴	-	L ⁴	-	L ⁴	M ⁴	L ⁴	L ⁴
DMG	2 ⁴	-	-	L ⁴	H ⁶	-	-	-	-	H ⁴	M ⁴	L ⁴
DMI	5 ⁷	-	L ⁴	L ⁴	-	-	L ⁴	L ⁴	M ⁸	L ⁷	L ⁴	M ⁴
DMTHF	-	pC ⁴	pC ⁴	pC ⁴	-	-	-	-	-	M ⁹	M ⁹	-
EL	≥4 ⁴	-	L ⁴	-	-	-	H ⁴	-	H ⁴	L ⁴	H ⁴	L ⁴
ELPK	≥4 ⁴	-	L ⁴	L ⁴	L ⁴	-	L ⁴	-	L ⁴	L ⁴	L ⁴	M ⁴
GVL	5 ⁷	pC ⁴	pC ⁴	pC ⁴	-	-	L ⁴	L ⁴	L ⁴	L ⁷	-	L
ML	-	pC ⁴	pC ⁴	pC ⁴	-	-	H ⁴	H ⁴	M ⁴	-	H ⁴	L ⁴
2MF	3 ⁴	-	L ⁴	pC ⁴	H ⁴	-	H ⁴	-	H ⁴	M ⁴	L ⁴	M ⁴
2MTHF	5 ⁷	pC ¹⁰	-	-	L ¹⁰	-	H ⁴	M ⁴	H ⁴	L ⁴	M ¹¹	-
cPME	4 ⁷	-	L ⁴	L ⁴	L ⁴	-	H ⁴	H ⁴	H ⁴	M ⁷	M ⁴	M ⁴
EC	4 ⁴	-	L ⁴	L ⁴	-	-	L ⁴	M ¹²	H ⁴	M ⁴	L ⁴	L ⁴
PC	4 ⁷	-	L ⁴	L ⁴	L ⁴	L ⁴	L ⁴	-	H ⁴	L ⁴	L ⁴	L ⁴
[emim][OAc]	3 ⁴	-	L ⁴	-	-	-	H ⁴	-	L ⁴	L ⁴	L ⁴	M ⁴
DMPU	3 ⁴	-	M ⁴	M ⁴	L ⁴	-	L ⁴	-	H ⁴	M ⁴	L ⁴	M ⁴
PPG	6 ⁴	-	L ⁴	-	-	-	-	-	H ⁴	L ⁴	L ⁴	L ⁴
THFP	-	-	-	-	-	-	-	-	-	M ⁹	-	M
water	6 ⁷	L	L	L	L	L	L	L	L	L	L	M

¹No significant bioaccumulation is expected based on the log(K_{ow}) values (Table A1)

²(WHO, 1990)

³(IARC, 2018)

⁴(ECHA, 2019)

⁵(Kennedy, 2012)

⁶(Trela et al., 1992)

⁷(Moity et al., 2012)

⁸(Waaijers-van der Loop et al., 2018)

⁹(Danish EPA, 2019)

¹⁰(Parris et al., 2017)

¹¹(German FEA, 2019)

¹²(Williard et al., 2011)

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