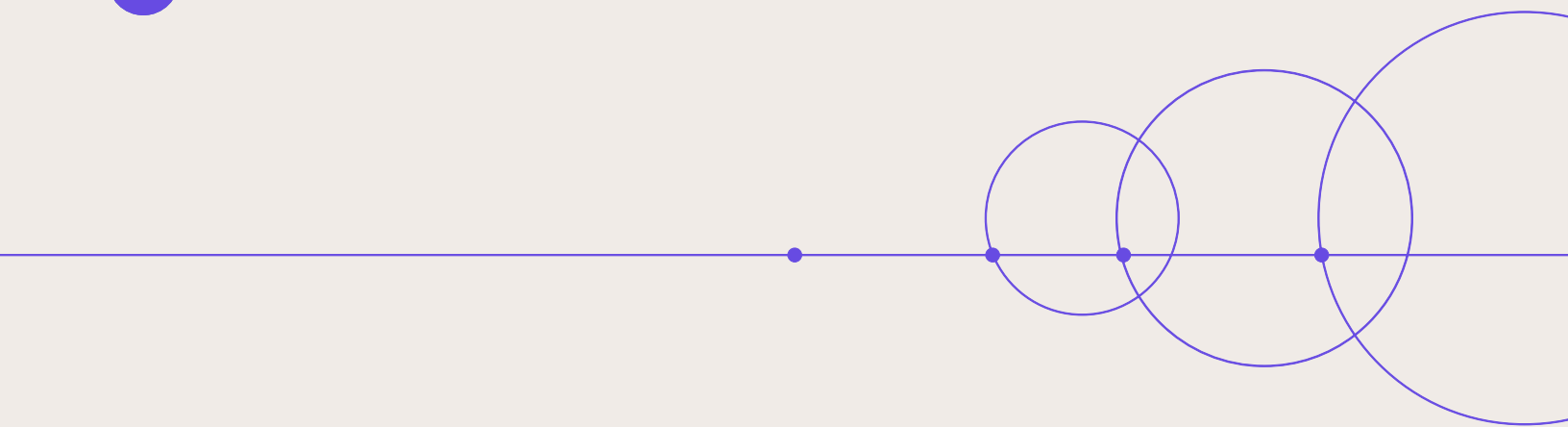




THE FORMULATOR'S GUIDE TO BRINGING PROFESSIONAL-GRADE COOLING TECHNOLOGY TO THE OTC PAIN RELIEF MARKET

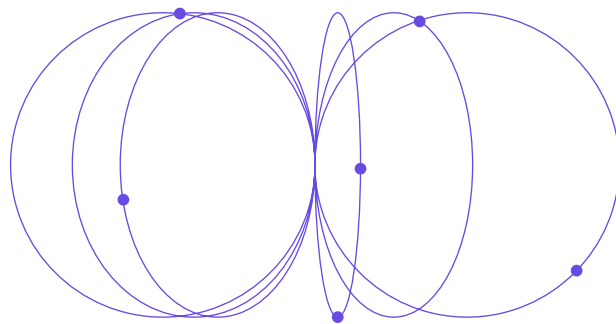


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EXECUTIVE SUMMARY



Demand for over-the-counter (OTC) topical analgesics is growing as consumers increasingly seek fast-acting, non-invasive pain relief that supports self-care. At the same time, brands and formulators face mounting pressure to differentiate products, evaluate documented propellant attributes such as global warming potential (GWP), volatile organic compound (VOC) classification, and flammability, and deliver a premium consumer experience.

This guide explores how Solstice® Propellant, HFO-1234ze(E), can be used in the development of next-generation OTC topical analgesics. Already proven in applications for rapid skin cooling at the point of care (Ref. 1), the technology



can provide an immediate, perceptible cooling sensation before the active pharmaceutical ingredient's (API) analgesic effect, creating a differentiated dual-sensory experience.

Designed for brand owners, formulators and contract manufacturers, this guide examines the formulation science, regulatory considerations and technical support behind Solstice Propellant.

INSIDE THIS GUIDE, YOU'LL DISCOVER:

- 1 The market trends driving innovation in OTC topical analgesics
- 2 Why propellant technology is becoming a key differentiator
- 3 The science behind Solstice Propellant's dual-sensory experience
- 4 Practical considerations for formulating with Solstice Propellant
- 5 Evidence supporting API compatibility and formulation performance
- 6 How Solstice's technical experts help accelerate development from concept to commercialization



ABOUT SOLSTICE ADVANCED MATERIALS

Powered by some of the brightest minds in our industry, Solstice Advanced Materials is a leading specialty materials company that advances science to achieve smarter outcomes with high-performance solutions across refrigerants, semiconductor materials, protective fibers, healthcare packaging, and more. Backed by deep technical expertise across critical industries, we are recognized as a global market leader that partners with customers to solve complex challenges in high-value applications.

At Solstice, innovation is at the heart of what we do—and nothing exemplifies this more than our next-generation propellant solutions. Solstice Propellant is engineered to deliver high performance while offering specific, measurable environmental attributes, including a low 100-year GWP of 1.37 and U.S. EPA VOC-exempt classification (see References).

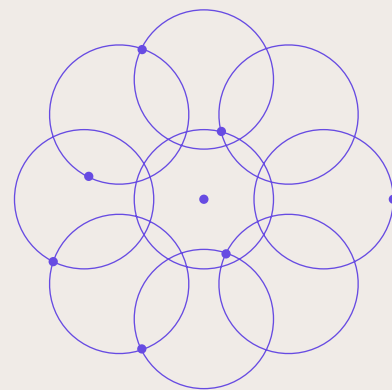
With a low 100-year global warming potential (GWP) of 1.37 — substantially lower than legacy HFC propellants such as HFC-134a (GWP ~1,300) — (Ref. 2), and classification by the U.S. EPA as (VOC)-exempt (Ref. 4), Solstice Propellant is designed to help formulators address specific regulatory drivers such as the HFC phasedown and evolving VOC requirements (see References). It is also classified as non-flammable under EU Test Method A11 and the US DOT standard (ASTM E681) (Ref. 3), offering added confidence for formulators and manufacturers alike.

Solstice Propellant offers an opportunity for differentiation in the OTC topical pain relief spray market due to its sensory performance, tunable cooling profile, and specific properties relative to hydrocarbon alternatives, including higher density and non-flammable classification of the neat propellant (see References).



To learn more about our Solstice® Propellant, [visit our website](#) or talk to our technical team.

INTRODUCTION



The OTC topical analgesics market is evolving rapidly. Driven by growing participation in sport and physical activity, an aging population and increasing consumer preference for self-managed healthcare, demand for effective topical pain relief products continues to grow. Today's consumers expect more than effective pain relief. They expect spray and aerosol products that work quickly, feel comfortable on the skin and deliver a premium user experience from the first application.

At the same time, environmental and regulatory factors inform propellant choice. The phase-down of hydrofluorocarbons (HFCs) under the American Innovation and Manufacturing (AIM) Act may affect the availability of certain HFC propellants, while VOC requirements vary by jurisdiction and product category and may affect traditional hydrocarbon propellants.

Because Solstice Propellant is a hydrofluoroolefin (HFO) and is classified by the U.S. EPA as VOC-exempt (Ref. 4), the propellant is not subject to the AIM Act HFC phasedown and may be excluded from certain VOC requirements, subject to the applicable jurisdiction, product category, and time (Ref. 10). Furthermore, Solstice Propellant can be used to create differentiated OTC analgesic products with a dual-sensory experience, helping formulators evaluate formulation options against applicable requirements.

However, successfully bringing this type of innovation to market requires more than selecting a different propellant. Formulation involves careful consideration of formulation chemistry, hardware compatibility, performance testing and regulatory requirements. Access to the right technical expertise can significantly reduce development risk and accelerate the journey from concept to commercialization.



WHAT'S DRIVING INNOVATION IN OTC TOPICAL ANALGESICS

The over-the-counter analgesics market is forecast to reach USD 37.93 billion by 2031 at a 3.87% compound annual growth rate (CAGR) over 2026–2031 (Ref. 5).

An important share of this growth is attributed to rising demand for topical analgesics, which is fueled by a variety of factors. Firstly, topical gels, patches, and sprays appeal to users who seek localized relief.

Secondly, interest in topical analgesics is also driven by a broader shift toward at-home, non-invasive pain management over clinical intervention, as well as rising participation in sports.

At the same time, the global population is living longer. In the USA, the share of the population age 65 and older increased steadily from 12.4% in 2004 to 18.0% in 2024. (Ref. 6). This growing geriatric demographic is staying active longer, with more age-related physical changes and participation in high mobility activities. Sports injuries in those 65 and older are projected to grow by 123% by 2040 (Ref. 7) and are driving demand for localized, easy-to-apply topical therapies.



WHY PROPELLANT TECHNOLOGY IS DRIVING PRODUCT DIFFERENTIATION



As the OTC topical analgesics market becomes increasingly competitive, product differentiation is extending beyond the active pharmaceutical ingredient (API).

Brand owners and formulators are increasingly looking at every aspect of formulation design to create products that deliver a more compelling consumer experience, making propellant selection an important strategic consideration.

One of the clearest opportunities lies in designing a dual-sensory experience. As demonstrated by Solstice studies (Ref. 8), Solstice Propellant provides immediate physical skin cooling from the moment of application, before the API's analgesic effect. When formulated with an API, this creates a premium two-stage sensory experience:

an immediate cooling sensation followed by the API's analgesic effect. For consumers, this provides an immediate, perceptible cooling sensation on application, while helping brands create a differentiated product experience.

Dual-Sensory Experience Analgesic + Customizable Cooling

Current topical analgesic

Reduces pain by targeting the nerves using APIs that require time to take effect. APIs do not numb the skin.

Our proposal : Dual-Sensory Experience

Solstice Propellant provides immediate physical skin cooling from the moment of application, before the API's analgesic effect.

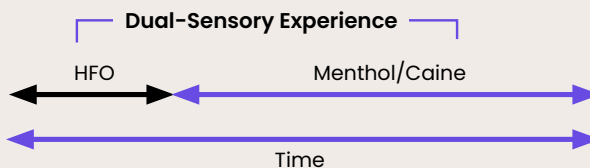
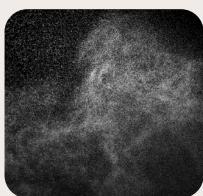


Figure 1: Dual-sensory experience: immediate cooling from Solstice Propellant followed by the API's analgesic effect. (Ref. 8)



Want to dig deeper into the dual-sensory experience?
[Check out our blog for the full breakdown.](#)

Beyond enhanced cooling performance, Solstice Propellant gives formulators greater flexibility to develop premium sensory formats. Compared with hydrocarbon propellants, it enables richer, creamier foams with enhanced spreadability (Ref. 8), while supporting a range of spray profiles, from fine mist sprays to larger stream-like patterns, to meet different product and application requirements.



SPRAY

A variety of spray capabilities can be achieved with HFO-1234ze(E), from small-sized mist droplets to larger stream-like spray patterns.



FOAM

Elevate your foam performance by replacing hydrocarbon propellants with Solstice HFO-1234ze(E).

Deliver a richer, creamier texture, enhanced gloss, and superior spreadability for a premium user experience.

Figure 2: Achieve premium sensory formats by using Solstice Propellant, from fine mist sprays to rich, creamy foams. (Ref. 8)

Solstice Propellant also offers advantages over bag-on-valve (BOV) systems used for topical pain relief sprays. Because BOV systems use compressed gas to expel the formulation from an internal bag, the propellant itself does not contact the skin, resulting in a less pronounced

cooling effect. Spray pressure will also decline as the container empties. As a liquefied gas, Solstice Propellant provides immediate physical skin cooling while maintaining consistent spray pressure and performance throughout the life of the product, helping deliver a more consistent premium sensory experience.

Alongside these formulation benefits, Solstice Propellant is well positioned for an evolving regulatory landscape. The phasedown of HFCs under the AIM Act and New York's phase-out of HFC-152a (Ref. 9) are HFC-specific measures that operate separately from state-level restrictions on VOCs, which vary by jurisdiction and product category. Together, these pressures are prompting formulators to evaluate alternative propellant technologies. Solstice Propellant offers a compelling profile in this context: it has a low 100-year GWP (Ref. 2), is classified as non-flammable under both EU Test Method A11 and the U.S. DOT standard (ASTM E681) (Ref. 3) and is recognized by the U.S. EPA as VOC-exempt (Ref. 4).

SOLSTICE PROPELLANT HFO-1234ze(E) FOR OTC TOPICAL ANALGESICS

Key features of Solstice Propellant relative to hydrocarbons, HFCs, and compressed gas. (Ref. 8)

Attributes		Hydrocarbons (Propane, Isobutane, DME)	HFC (134a, 152a)	Compressed Gas (N ₂ , CO ₂ , Air)	Solstice Propellant HFO-1234ze(E)
Environmental Benefits	Low-GWP (Minimal Impact on Global Warming)	●	●	●	●
	VOC-exempt (Negligible contribution to ground level ozone pollution)	●	●	●	●
Performance Benefits	Non-Flammable	●	● 134a ● 152a	●	●
	Spray Consistency	●	●	●	●
	Aid in Solvency	●	●	●	●

Figure 3: HFO-1234ze(E) propellant advantages versus conventional options.

The attributes in the table describe the neat propellant only and do not establish compliance of any finished product with applicable environmental, health and safety, labeling, warning, or OTC requirements. For HFO-1234ze(E) refer to references 2, 3 and 4 for GWP, non-flammability and VOC exemption, respectively.

THE SCIENCE BEHIND HFO COOLING TECHNOLOGY

Solstice Propellant evaporates when sprayed on the skin, providing immediate physical cooling within a comfortable range without freezing the skin (Ref. 8).

Any analgesic effect in a finished formulation is attributable to the API, not the propellant. Cooling performance is fully tunable and can be optimized through HFO propellant blending, formulation design, hardware selection, and other parameters.

From a compatibility perspective, a three-month stability study (Ref. 8) confirmed that benzocaine, benzethonium chloride, menthol, chlorhexidine digluconate, lidocaine, camphor, and methyl

salicylate remain stable in formulation with Solstice Propellant and ethanol, giving formulators a starting point across some of the most widely used OTC analgesic actives. Because ethanol is a flammable excipient, this stability result does not establish that the finished formulation is non-flammable; finished-product flammability must be independently assessed and tested.

Backed by this formulation, stability, and compatibility data, Solstice is actively working with brand owners and CDMOs to bring Solstice Propellant into commercial OTC topical pain relief products.

SURFACE TEMPERATURE PROFILES:

POPULAR BRANDS VERSUS OTC PROTOTYPE WITH SOLSTICE PROPELLANT

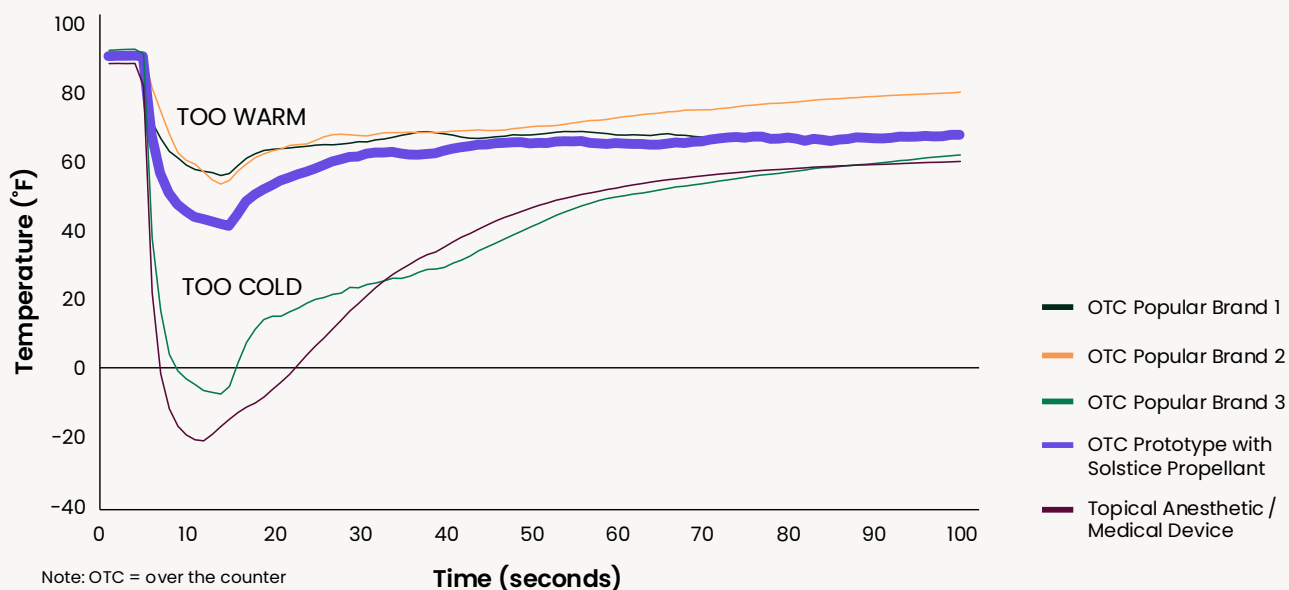


Figure 4: Surface cooling profile of Solstice Propellant compared with leading OTC brands.

CONSIDERATIONS FOR FORMULATING WITH SOLSTICE PROPELLANT

While Solstice Propellant integrates readily into OTC topical analgesic formulations, like any propellant, successful formulation development necessitates careful consideration of key properties, including density, stability, flammability, and toxicity. Solstice's technical team has decades of experience to help customers navigate any formulation modifications needed and ensure smooth early-stage testing.

DENSITY

One of the most important considerations is density.

According to published density values, Solstice Propellant has a density approximately equal to HFC-134a, around 30% greater than HFC-152a and more than twice that of hydrocarbon propellants. These differences influence formulation behavior and aerosol delivery, meaning valve and actuator combinations may need to be optimized to achieve the desired spray characteristics.

Rather than representing a limitation, this provides formulators with greater control over the final product experience. By selecting the appropriate hardware configuration, development teams can tailor spray performance to match the intended application, whether producing a fine mist, targeted spray or rich foam.

Solstice scientists work with customers throughout this process, providing guidance on appropriate hardware configurations and working with established industry partners where required.



STABILITY

Formulation stability is another key consideration during reformulation.

Because HFO-1234ze(E) contains a carbon-carbon double bond, its chemical behavior differs from that of some legacy propellants. As with any formulation program, compatibility between the propellant, active ingredients, excipients, and materials of construction should therefore be assessed during development.

To support this process, Solstice has conducted compatibility testing across common formulation ingredients and materials and can advise on existing compatibility data or undertake additional testing where required. This allows formulation teams to identify potential issues early in development and make informed decisions before progressing towards scale-up.

By combining laboratory data with formulation expertise, Solstice helps reduce uncertainty during product development while supporting robust, stable formulations.

FLAMMABILITY

Flammability testing forms an essential part of aerosol product development, regardless of the propellant selected. A classification of neat Solstice Propellant as non-flammable per EU Test Method A11 and the U.S. DOT standard (ASTM E681) does not establish the flammability profile of a finished formulation, which must be independently assessed and tested, particularly when flammable excipients such as ethanol are present.

To help customers progress efficiently, Solstice offers in-house screening at its Buffalo Research Laboratory. Development programs typically begin with ignition distance testing and, where appropriate, progress to enclosed-space testing before formal assessment by accredited laboratories.

Early screening provides valuable formulation insight, increasing confidence before formal regulatory testing and helping minimize unnecessary redesigns or repeated costly test cycles later in development.

SUPPORTING SAFE PRODUCT DEVELOPMENT

Alongside performance evaluation, product stewardship remains a key part of formulation development. Solstice Propellant has undergone toxicological evaluation to support its intended applications. Combined with formulation guidance, compatibility assessments, and application-specific testing, development teams can evaluate new formulations while following established product stewardship practices.



Solstice's technical team has decades of experience to help customers navigate any formulation modifications needed and ensure smooth early-stage testing.



FROM CONCEPT TO COMMERCIAL PRODUCT

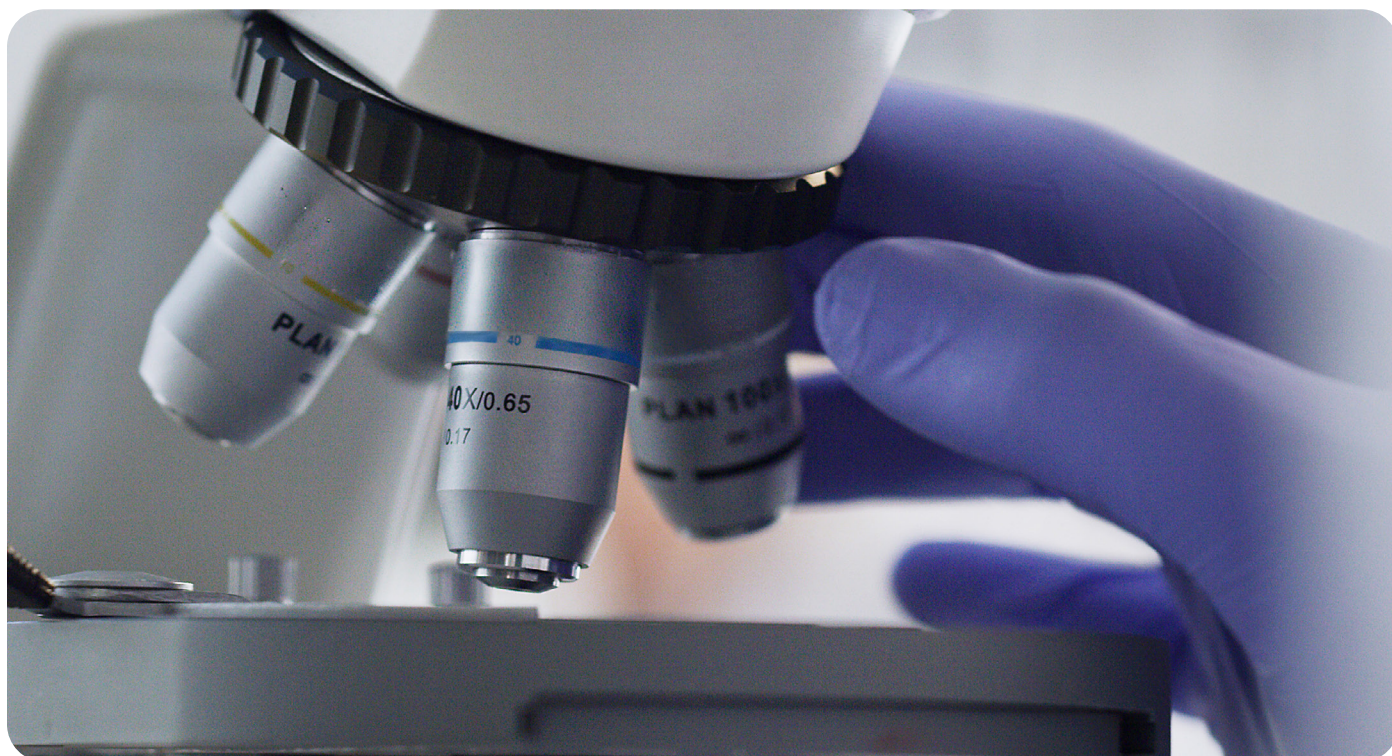
Beyond supplying Solstice Propellant, Solstice brings over five decades of experience in combined advanced propellant innovation to bear to help innovators optimize their OTC formulations.

To that end, we have developed an end-to-end technical support model, encompassing:

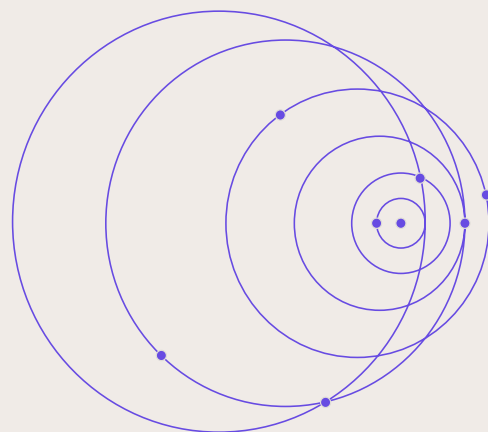
- Custom formulation support, including proof-of-concept, troubleshooting formulation issues, performance evaluation, API compatibility assessments, and stability testing
- In-house flammability testing
- High-level aerosol technology training
- Physical property assessments
- Regulatory considerations

As part of this, we have developed a library of formulation guidelines for different product types incorporating Solstice Propellant to act as a starting point for our customers. Brand owners and formulators can also benefit from our state-of-the-art aerosol lab, which features a spray particle analyzer as well as a myriad of analytical testing capabilities.

The technical support, prototype development, and formulation guidance we provide is entirely independent of the chosen manufacturing partner. Whether you're an established brand owner, a CDMO, or a filler bringing a new product online, the technical groundwork we do together is intended to support subsequent scale-up and manufacturing transfer activities.



REDEFINING WHAT OTC PAIN RELIEF CAN FEEL LIKE



As consumer interest in OTC topical pain relief products continues to grow, formulation innovation is essential to gain a competitive edge in a crowded market. The use of Solstice Propellant enables differentiated OTC topical pain relief sprays that deliver a dual-sensory experience: immediate cooling paired with the API's analgesic effect in a single application.

Backed by an experienced team and end-to-end technical support, Solstice can help to accelerate the development of innovative OTC topical pain relief products that support long-term consumer health and wellness.



SEE WHAT SOLSTICE® PROPELLANT, HFO-1234ze(E) MAKES POSSIBLE



Talk to our technical team to learn how Solstice Propellant can enhance your next OTC topical pain relief product. [Visit our website for more information](#)

REFERENCES

Finished-product safety, flammability, labeling, and compliance with applicable OTC monograph requirements are the responsibility of the brand owner and manufacturer. The properties of the neat propellant do not establish compliance or safety of any finished formulation.

1. There is a commercially available topical anesthetic spray containing Solstice Propellant.
2. <https://www.ipcc.ch/report/ar6/wg1/chapter/chapter-7/#7.6> (Section 7.6.1.1)

Smith, C., Z.R.J. Nicholls, K. Armour, W. Collins, P. Forster, M. Meinshausen, M.D. Palmer, and M. Watanabe, 2021: The Earth's Energy Budget, Climate Feedbacks, and Climate Sensitivity Supplementary Material. In Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change [Masson-Delmotte, V., P. Zhai, A. Pirani, S.L. Connors, C. Péan, S. Berger, N. Caud, Y. Chen, L. Goldfarb, M.I. Gomis, M. Huang, K. Leitzell, E. Lonnoy, J.B.R. Matthews, T.K. Maycock, T. Waterfield, O. Yelekçi, R. Yu, and B. Zhou (eds.)]. Available from <https://www.ipcc.ch/>

The GWP classification applies to the neat propellant under the referenced test conditions only. The GWP of any finished formulation—must be independently assessed and/or tested.

3. Solstice Propellant is classified as non-flammable per EU Test Method A11 and ASTM Standard E681. This classification applies only to the neat propellant and only under the referenced test conditions. The flammability of any finished formulation, particularly one containing flammable excipients such as ethanol, must be independently assessed and tested for actual formulations, equipment and manufacturing processes.
4. The U.S. EPA currently classifies HFO-1234ze(E) as VOC-exempt. The VOC exemption classification applies to the neat propellant under the referenced test conditions only. The VOC exemption of any finished formulation—must be independently assessed and/or tested.
5. Mordor Intelligence: OTC Analgesics Market — Growth, Trends, and Forecasts (2026–2031).
6. U.S. Census Bureau: Older Adults Outnumber Children in a Growing Number of U.S. Counties (2025).
7. Sports Injuries in 65 and Older Significantly Increased Since 2012, Projected to Grow by 123% by 2040 – AAOS 2024 Annual Meeting Press Kit
8. Supporting data from Solstice internal attributes, foam property and feel, temperature and chemical compatibility testing. For more information, contact us at <https://www.solstice.com/us/en/contact-us/sales-inquiry/solvents-propellants>
9. New York Department of Environmental Conservation: Part 494 Fact Sheet.
10. These statements apply only to the neat propellant and are not representations that a customer's finished product complies with applicable requirements.

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