Unique&Easy Micro-Encapsulation Solutions

Product Overview - 4900-01

SalSphere® Benzoyl Peroxide (BPO)

A cornerstone in acne treatment due to its multifaceted actions

Benzoyl Peroxide treats acne by killing bacteria, exfoliating the skin, reducing inflammation, and preventing the development of antibiotic resistance. SalSphere BPO utilizes advanced encapsulation to enhance the efficacy of BPO and minimize irritation, aligning with the demand for innovative, gentle skincare.

Figure 1: SalSphere® BPO is available a suspension

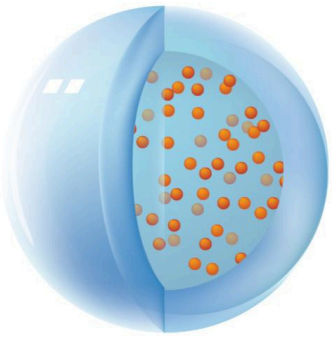

Figure 2: SalSphere® BPO is made with a solid core containing the BPO and a Hydrophilic shell.

Key benefits

- **Easy to use** in cosmetic and pharmaceutical formulations. Formulators avoid the challenges of handling raw BPO, which is highly reactive and prone to oxidation. Add SalSphere® BPO during the cool-down phase (<40°C). SalSphere® BPO is a liquid form that disperses easily into water-based or emulsion systems (e.g., O/W microemulsions, gels, or washes), requiring minimal mixing compared to raw BPO, which can clump or require high shear.
- **Enhanced Stability:** SalSphere® BPO protects BPO from degradation, extending shelf life and maintaining efficacy in formulations.
- **Controlled Release:** The encapsulation technology reduces the risk of over-exposure and minimizes irritation, a common issue with free BPO, making it suitable for consumers with sensitive skin.
- **Reduced Skin Irritation:** By encapsulating BPO, SalSphere minimizes direct skin contact with high concentrations, thereby reducing side effects such as dryness, redness, and peeling. This is particularly valuable in brands that prioritize gentle formulations for sensitive skin.
- **Improved Experience:** SalSphere BPO enhances the delivery of BPO to target comedones, effectively clearing pores and eradicating Propionibacterium acnes (P. acnes), the bacteria that cause acne. This leads to better treatment outcomes for mild and severe acne.

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The structure of SalSphere® BPO

The structure of SalSphere® encapsulated Benzoyl Peroxide (BPO), developed by Salvona Technologies, is a sub-micron encapsulation system designed to enhance the delivery and performance of BPO for acne treatment.

Composition: SalSphere® BPO is a lipid-based, sub-micron encapsulation system that encases benzoyl peroxide within a semi-solid core and a protective shell. The shell is typically used to stabilize the suspension by forming a hydrophilic shell around the hydrophobic core (Figure 2).

: The system features sub-micron particles (mainly smaller than 3 micrometers), which facilitate penetration into the hair follicles (follicular delivery) and target blackheads.

Unique Delivery System:
Unlike traditional microsponges or silica-based carriers, SalSphere® utilizes a proprietary semi-crystalline lipid-based technology (distinct from liposomes) to protect BPO from premature degradation. This advanced system enables time-released delivery, effectively addressing challenges such as poor water solubility and sensitivity to environmental factors.

Benefits of the Structure

- The sub-micron lipid matrix forms a stable suspension in liquid form, allowing for low-temperature mixing and simplified formulation. It is compatible with Sephora Clean standards and delivers a non-irritating, cosmetically elegant product experience for consumers.
- The sub-micron lipid matrix enables a controlled, slow release of BPO, which helps reduce skin irritation and enhances user compliance—particularly for individuals with sensitive skin.
- The structure enhances BPO stability, mitigating risks of premature degradation.

Encapsulation Mechanism: Benzoyl peroxide (BPO) is encapsulated at a 25% load within a lipid-based matrix composed of natural lipids. Through hydrophobic interactions, the encapsulated core adheres to lipid-rich areas such as sebum and blackheads. Gradually, the microspheres partition into the skin's lipid layers, releasing BPO in a controlled manner. This targeted delivery minimizes direct contact with the skin, thereby reducing irritation.

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The functional ingredients:

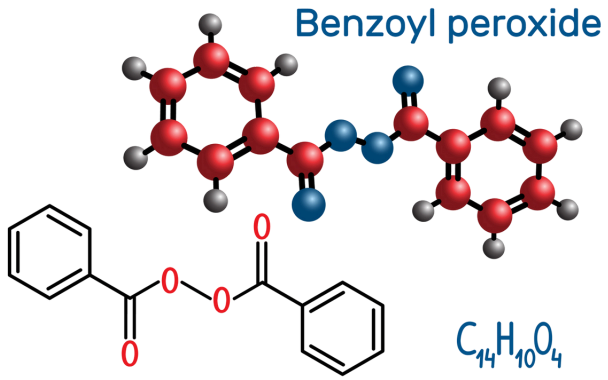

Figure 3: Diagram of Benzoyl Peroxide BPO

BPO consists of two benzoyl groups (C6H5CO−) linked by a peroxide bond (−O−O−). The symmetrical molecule, with the peroxide bond being the key reactive site. It appears as a white crystalline powder poorly soluble in water but in organic solvents like acetone or ethanol.

The −O−O—bond is weak, making BPO highly reactive. It readily decomposes to form free radicals, which are critical to its anti-acne function.
Decomposition is triggered by heat, light, or skin contact, producing benzoyloxy radicals and phenyl radicals.

BPO's chemistry hinges on its reactive peroxide bond, which generates free radicals that kill P. acnes, oxidize sebum, and exfoliate skin, making it a potent anti-acne agent. Encapsulation, as in SalSphere® BPO, mitigates its instability and irritation potential, enhancing stability and delivery.

Oxidizing Agent

- BPO's strong oxidizing properties disrupt bacterial cell membranes and oxidize proteins, enhancing its antibacterial effect.
- It also oxidizes sebum components, reducing oiliness and aiding in pore clearing.

Keratolytic Action

- BPO's radicals promote desquamation by breaking down keratin in dead skin cells, preventing pore clogging, and reducing comedones (blackheads/whiteheads). This is a mild chemical exfoliation process.

Stability and Challenges

- **Instability:** BPO is sensitive to heat, light, and moisture, leading to degradation and reduced efficacy. Under certain conditions, it can also form benzene, a concern advanced encapsulation addresses.
- **Irritation:** Free BPO's reactivity can cause skin irritation (redness, dryness) due to non-selective oxidation of skin lipids and proteins.
- **Solubility:** Poor water solubility (insoluble in aqueous environments) complicates formulation, necessitating delivery systems like SalSphere® BPO

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Role of Encapsulation

- **Structure:** Salvona's SalSphere® BPO encapsulates BPO in a sub-micron lipid matrix, protecting the peroxide bond from premature decomposition.

Suspensible Forms of Benzoyl Peroxide (BPO):

- Benzoyl Peroxide is inherently poorly water-soluble, making it challenging to formulate in water-based or low-irritation systems. To address this, several suspensible forms have been developed to improve dispersion and compatibility.
- Micronized or Submicron BPO: These are finely milled particles with increased surface area, allowing better dispersion in aqueous gels when combined with appropriate stabilizers. While not truly soluble, they create a more uniform distribution within formulations.
- However, SalSphere® BPO goes a step further. The BPO is encapsulated in a semi-solid, lipid-based sub-micron structure (Figure 4), providing a smooth suspension that is easy to use, with enhanced physical stability, targeted delivery, and a time-released mechanism. This results in an elegant product featuring gentler and more effective formulations—ideal for consumers with sensitive or acne-prone skin.

A

B

Figure 4: Microscopy x600 of A; BPO insoluble particles in water, B: SalSphere® BPO in water.

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Mechanism of release:

The release of Benzoyl Peroxide (BPO) from Salvona's SalSphere® encapsulation system is a sophisticated process designed to optimize acne treatment by targeting pimples and blackheads with precision while minimizing irritation. Below are the steps for releasing a BPO from SalSphere.

1. **Adhesion with High Affinity to Pimples and Blackheads:**

- **Mechanism:** SalSphere® BPO is encapsulated in a sub-micron lipid matrix that mimics skin lipids, allowing selective adhesion to sebum-rich areas like pimples and blackheads (Figure 5).
- **Chemistry:** The hydrophobic nature of the lipid matrix interacts with sebum (lipids like triglycerides and squalene) on the skin's surface, particularly around comedones. The specific adhesion ensures targeted delivery to areas with high Propionibacterium acnes (P. acnes) activity.
- **Advantage:** Unlike free BPO, which disperses non-selectively, SalSphere®'s adhesion enhances localized delivery, reducing waste and irritation.

2. **Dissolution within the Lipid Domains of the Skin, Especially in Hair Follicles:**

- **Mechanism:** Once adhered, SalSphere® gradually dissolves within sebum-rich follicles, breaking down through interaction with skin lipids and natural enzymes (Figure 6).
- **Chemistry:** The follicular sebum, composed of natural lipids, allows the core to integrate and gradually dissolve to release the encapsulated BPO.

Advantage: This step ensures BPO is delivered directly to the follicular environment where P. acnes thrives, unlike unencapsulated BPO, which may remain on the skin surface.

Figure 5: Infmammed acne pimples and white heads, pimples, and the surrounding area are reached with lipids, making it ideal for SalSphere® BPO deposition.

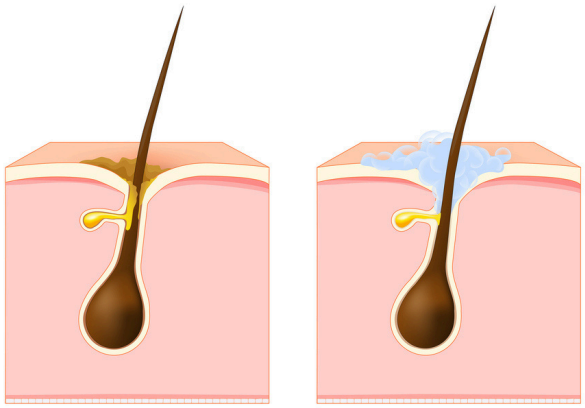

Figure 6: Illustration of sebum oil accumulation at the opening of the hair follicle. This spot becomes the target of SalSphere® BPO adhesion.

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Mechanism of release:

3. **Follicular Delivery:**
Mechanism: The sub-micron size of SalSphere® particles enables deep penetration into hair follicles, where acne originates (Figure 7). The small and lipid compatibility allow the spheres to navigate the follicular canal, delivering BPO to the site of bacterial activity and clogged pores.

Chemistry: Once in the follicle, the lipid matrix breaks down, positioning BPO for targeted action.

Advantage: This targeted follicular delivery enhances BPO's antibacterial and keratolytic effects, directly addressing comedones and inflammatory acne.

4. **Gradual Release as the Core Dissolves:**
Mechanism: As the lipid matrix dissolves, the BPO core is released gradually into the follicular environment. The controlled-release mechanism ensures a steady, low-concentration delivery of BPO, preventing sudden high-dose exposure.

Chemistry: Upon release, BPO decomposes into benzoyloxy radicals and reactive oxygen species via cleavage of the peroxide bond. These radicals kill P. acnes by disrupting bacterial cell membranes, oxidizing sebum to reduce oiliness, and promoting exfoliation by breaking down keratin.
Advantage: The gradual release minimizes irritation, a common issue with free BPO, and reduces the risk of benzene formation by stabilizing the molecule until delivery. This is critical for sensitive skin types.

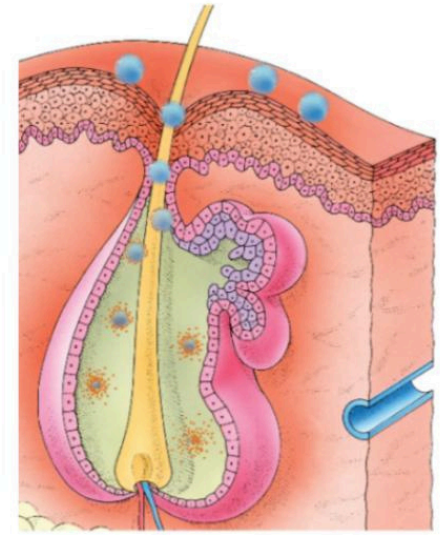

Figure 7: Penetration pathway into the hair follicles where acne is initiated.

Chemistry of Benzoyl Peroxide (BPO) Degradation:

Benzoyl Peroxide is an organic peroxide with the structure $(C_6H_5CO)_2O_2$
Its degradation produces free radicals:
The primary pathway based on radical decomposition :
At skin temperature or in the presence of light, heat, or metals:

- $(C_6H_5CO)_2O_2 \rightarrow 2\ C_6H_5CO\bullet$

(Benzoyloxyl radicals)
These benzoyloxyl radicals rapidly decarboxylate:

- $C_6H_5CO\bullet \rightarrow C_6H_5\bullet + CO_2$

(Forming phenyl radicals and releasing carbon dioxide)
These radicals are responsible for:

- **Antibacterial activity (oxidizing bacterial proteins/lipids)**
- **Comedolytic effect (breaking down keratin plugs).**

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Technical Data

Composition of SalSphere® Benzoyl Peroxide (BPO),
PID: #4900
Water/Aqua/Eau, Benzoyl Peroxide, Butyrospermum Parkii (Shea) Butter, Hydroxyethyl Behenamidopropyl Dimonium Chloride, Hexylene Glycol, Euphorbia Cerifera (Candelilla) Wax/Euphorbia Cerifera Cera/Cire de candelilla, Citric Acid

Visual appearance
SalSphere® BPO appears as a white semi-liquid with a light, non-greasy texture (figure 8). It is water-dispersible and can be easily incorporated into lotions and creams during the cool-down phase of formulation.

Figure 8: SalSphere® Benzoyl Peroxide (BPO) in a tube, ready for use.

Particle size distribution
The particle size of SalSphere® Benzoyl Peroxide (BPO) is essential for several key reasons related to its effectiveness and usability in acne treatment formulations (Figures 5 and 9) :

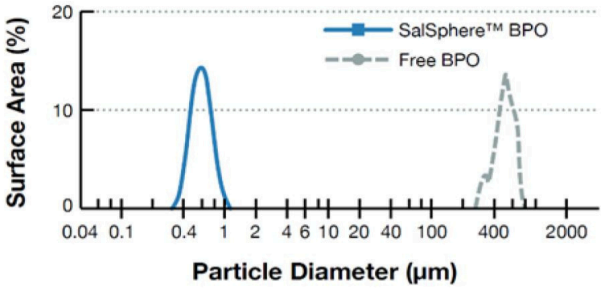

Figure 9: (A) Free BPO and (B) SalSphere® BPO dispersed into identical lotion bases (5% BPO). A liquid diffraction module performed a particle size distribution analysis on the Beckman Coulter LS13320 Laser Diffraction Particle Size Analyzer.

Reduced size of SalSphere® Benzoyl Peroxide (BPO) is beneficial:

- **Enhanced Penetration:** Smaller particle sizes, such as the sub-micron spheres used in SalSphere® BPO, allow for better penetration into hair follicles and pores where acne-causing bacteria reside.

- **Improved Cosmetic Elegance:** Particle size affects the texture and feel of the final product. Microspheres larger than 30 microns can feel gritty or rough, leading to a less pleasant user experience. SalSphere BPO's smaller particles contribute to a smoother, more aesthetically pleasing formulation, thereby enhancing the user experience.

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Technical Data

Specfications:

Table 1: Specification of SalSphere® Benzoyl Peroxide (BPO)

Appearance @ 20°C	While Semi-liquid
Color	White to off-white
Odor	Characteristic
pH (1% Solution)	4.5 ± 1.5
BPO Assay (HPLC) (Wt.%)	22-27
Shelf Life (Months)	18
Usage Level (Wt.%)	10-40
Storage (°C)	Closed container, at 12-28**° C**

The effectiveness of SalSphere® Benzoyl Peroxide (BPO) against P acne

Propionibacterium acnes (P. acnes) is the primary bacterium associated with acne, papules, and pustules.

No Bacterial Resistance: Unlike antibiotics, P. acnes does not develop resistance to BPO, making it a reliable long-term treatment option. This is critical given the increasing prevalence of antibiotic-resistant strains of P. acnes.

Clinical Efficacy: Clinical studies demonstrate that BPO at 2.5% to 10% effectively reduces both inflammatory and non-inflammatory acne lesions. For example, a 2.5% BPO formulation can reduce lesion counts by 40-60% over 4-8 weeks, with higher concentrations (e.g., 5% or 10%) showing similar or slightly greater efficacy but with an increased risk of irritation. Encapsulated forms like SalSphere® BPO enhance efficacy by improving delivery and reducing irritation.

Limitations: While highly effective, BPO's impact depends on formulation, concentration, and patient compliance. Side effects like dryness, peeling, or irritation can reduce adherence, though encapsulated versions like SalSphere® BPO mitigate these issues. Additionally, for comprehensive acne management, BPO is most effective when combined with other agents but not in the same package (e.g., retinoids or antibiotics).

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Qualifications of SalSphere® Benzoyl Peroxide (BPO)

Effective Against P Acne
Encapsulated and very effective

	P. Acne Kill Rate (%)
SalSphere® Benzoyl Peroxide (BPO)	82.22
Free BPO	76.09

Table 1: In-Vivo Bacterial Kill Study:
An 8-hour in-vivo study evaluated the ability of SalSphere® BPO versus free BPO (2.5%) to kill P. acnes.

Results showed that SalSphere® BPO was more potent, confirming that its encapsulation and slow-release mechanism not only preserve but effectively enhance its antibacterial efficacy.

Figure 11: Method for skin extraction

Enhanced Deposition from Rinse-off

SalSphere® enhances the deposition of BPO on the skin from rinse-off products, a critical feature in prolonging treatment and increasing efficacy.

The deposition of BPO from SalSphere® was compared to that of free BPO as used in a market competitor's product for a rinse-off application. Each product was applied to the forearms, rinsed off and extracted Figure 11.

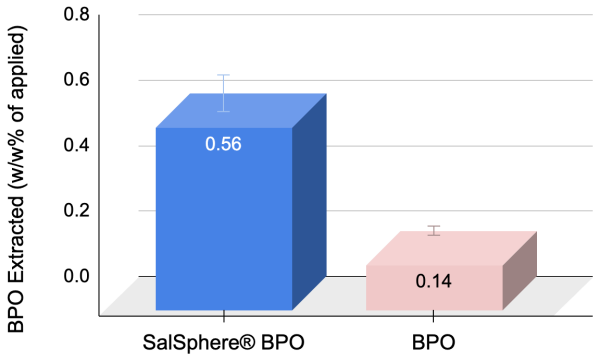

Figure 10: BPO extracted from the skin after a rinse-off application containing SalSphere® BPO versus free BPO used in competitor products. The level of BPO in the product is 2.5%.

Three and a half (3.5) times more BPO resides on the skin from SalSphere® BPO than from the market competitor, demonstrating that the technology enables time release of BPO for a more potent and effective acne treatment.

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Qualifications of SalSphere® Benzoyl Peroxide (BPO)

Stability, Shelf life

The stability of Benzoyl Peroxide (BPO) is critical for several reasons, as it directly impacts its effectiveness, safety, and usability in acne treatment formulations

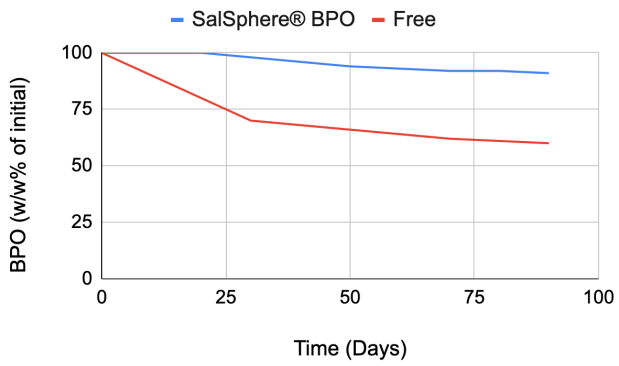

Figure 12: BPO content of samples stored at 42 C for 90 days The initial level was 10% BPO.

SalSphere® technologies enhance the stability of BPO. This is critical to ensure sustained efficacy, minimize irritation, extend shelf life, enable consistent delivery, and maintain compatibility with other ingredients, all contributing to effective and user-friendly acne treatments.

Stability is critical because:

- **Maintaining Efficacy:** BPO is a highly reactive oxidizing agent that can degrade when exposed to air, light, heat, or certain chemicals. If unstable, BPO breaks down into inactive byproducts, reducing its antibacterial activity against Propionibacterium acnes (P. acnes) and its ability to reduce acne lesions. Stable formulations, like SalSphere® BPO, ensure consistent potency over time, delivering the intended therapeutic effect.

- **Preventing Irritation:** The degradation of BPO can produce free radicals or other reactive compounds that may increase skin irritation, leading to side effects such as redness, dryness, or peeling. Stable encapsulation, as in SalSphere® BPO, minimizes these byproducts, reducing irritation and improving patient tolerance.

- **Extended Shelf Life:** Stability ensures a longer shelf life for BPO-containing products. Unstable BPO degrades faster, shortening the product's usability and potentially leading to wasted medication or reduced efficacy if used past its effective potency.

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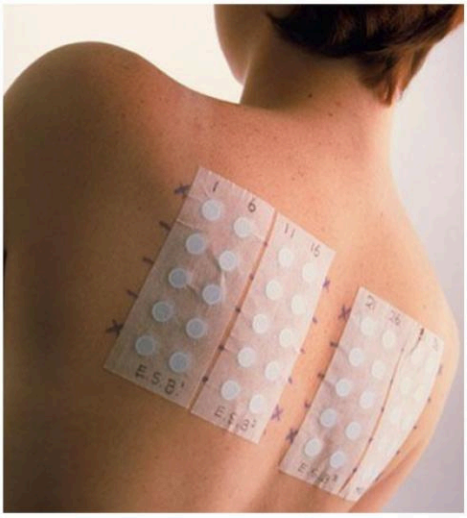
Clinical Studies

Repeated Insult Patch Test.

This is a standardized dermatological test used to evaluate the potential of a substance, such as a topical formulation, to cause skin irritation or allergic reactions (sensitization) after repeated applications.



Results from RIPT testing:
Level of SalSphere® BPO = 5% w/w
number of testing points = 50

Non-primary Irritant
Non-primary Sensitizer

The Repeated Insult Patch Test is the most relevant meaning, as it directly pertains to evaluating the safety and tolerability of topical acne treatments.

Meaning and Importance of RIPT:

Purpose: The RIPT assesses a product's safety by determining whether it causes cumulative irritation or induces allergic contact dermatitis over time. It is crucial to ensure that products like SalSphere BPO formulations are safe for consumer use, particularly when used for prolonged periods in acne treatments.

Process: During a RIPT, the test substance (e.g., SalSphere® BPO) is repeatedly applied to the skin of volunteers under occlusive or semi-occlusive patches over several weeks. The skin is monitored for signs of irritation (redness, swelling) or sensitization (an allergic response).

Relevance to BPO: BPO can irritate some users, particularly in unencapsulated forms. Technologies like SalSphere® aim to reduce irritation, and RIPT results help confirm whether the encapsulation improves skin tolerance. A successful RIPT (resulting in minimal to no irritation or sensitization) indicates that the formulation is gentler and safer for long-term use.

Regulatory and Consumer Trust: RIPT results are often required by regulatory bodies and are used by manufacturers to support claims of **“dermatologist-tested” or “non-irritating”** products, enhancing consumer confidence.

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Technical Data

Appearance @ 20°C	Opaque Fluid
Applications	Creams, lotions, spot treatments.
Color	White to Off-White
Odor	Characteristic
pH (1 % solution)	4.5 ± 1.5
BPO Assay (HPLC) (Wt.%)	≥ 24.0
Shelf Life (months)	12
Usage Level (BPO, wt%)	2.5-5 %
Storage (°C)	Closed container, at 12° – 32°C

No Additional Efficacy Testing Required:
Since BPO's efficacy against Propionibacterium acnes (P. acnes) and acne vulgaris is well-established and covered by the monograph, manufacturers do not need to conduct new clinical trials to demonstrate anti-acne activity for OTC products using BPO within the approved range.
This applies to SalSphere® BPO, as its encapsulation enhances delivery and stability but does not alter BPO's fundamental mechanism as an antibacterial and comedolytic agent.

FDA Regualtions

According to FDA regulations, benzoyl peroxide (BPO) is recognized as a safe and effective over-the-counter (OTC) active ingredient for acne treatment under the OTC Acne Monograph (21 CFR Part 333.310).
This means that if you formulate with BPO within the monograph's guidelines, you generally do not need to conduct additional testing to prove its anti-acne activity for regulatory approval. However, there are important nuances to consider to ensure compliance and product safety. Below is a detailed explanation:

Key Points on FDA Regulations and BPO Testing:
OTC Acne Monograph:
The FDA's OTC Acne Monograph classifies BPO as a Category I (safe and effective) ingredient for topical acne treatment at concentrations of 2.5% to 10%.
Products formulated under this monograph, including those using delivery systems like SalSphere® BPO, are considered compliant for anti-acne claims without requiring new clinical efficacy studies, provided they adhere to the monograph's specifications (e.g., concentration, labeling, and usage instructions).

Special Considerations for SalSphere® BPO:
SalSphere® BPO's encapsulation enhances stability, reduces irritation, and improves delivery without altering its FDA OTC Acne Monograph status (2.5%-10% BPO), requiring no additional efficacy testing. A Repeated Insult Patch Test (RIPT) conducted by Salvona confirms reduced irritation, supporting "gentle" marketing claims and consumer safety, though not mandatory for FDA approval.

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Synergistic Mechanisms of SalSphere® Even Skin and SalSphere® BPO:

SalSphere® Even Skin (encapsulated salicylic acid, SA) and SalSphere® Benzoyl Peroxide (BPO) are proprietary delivery systems developed by Salvona Technologies, designed to enhance the stability, efficacy, and tolerability of SA and BPO in acne treatments. These encapsulated actives work synergistically to target multiple aspects of acne pathogenesis, offering complementary benefits that improve treatment outcomes.

Below is a detailed explanation of their synergy, compatibility for combined use, and considerations for formulation, incorporating relevant information from web sources and aligning with FDA regulations.

Synergistic Mechanisms of SalSphere® Even Skin and SalSphere® BPO:
Complementary Acne-Targeting Mechanisms:

SalSphere® Even Skin:
Comedolytic Action: SalSphere, with Salicylic acid, targets the comedones of blackheads and whiteheads to exfoliate dead skin cells and dissolve sebum, breaking down the blockages that form comedones (blackheads and whiteheads). By clearing follicular hyperkeratosis, SA opens clogged pores, exposing the anaerobic environment inside to air. This is critical because P. acnes, an anaerobic bacterium, thrives in low-oxygen conditions within comedones.

Anti-inflammatory Effect: SA reduces redness and inflammation in acne lesions, particularly in early-stage comedones.
Gentler Profile: Encapsulation reduces SA's irritation potential, making it more transparent, smoother, and non-irritating

SalSphere® BPO:

- Antibacterial Action: Once SalSphere® Even Skin opens comedones, air (containing oxygen) can penetrate the follicle. P. acnes cannot survive in oxygen-rich environments, so this exposure begins to inhibit bacterial activity.
- SalSphere® BPO: The sub-micron spheres (1-3 microns) in SalSphere® BPO enhance penetration into opened pores, ensuring targeted delivery of oxygen to the deeper layers. SA's exfoliation and pore-opening action amplifies BPO's antibacterial efficacy by improving access to P. acnes. This combination accelerates the reduction of both comedonal (non-inflammatory) and inflammatory acne lesions (papules, pustules).
- Studies on non-encapsulated SA and BPO have shown a 40-60% reduction in lesion size over 4-8 weeks, and encapsulation likely enhances this effect due to improved delivery and tolerability.

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Formulation Tips

Formulating with SalSphere® Benzoyl Peroxide (SS BPO) requires careful consideration of its unique properties as an encapsulated, stabilized delivery system for benzoyl peroxide (BPO) designed to enhance stability, reduce irritation, and improve targeted delivery.

Below is a concise guide on how to formulate SalSphere® BPO:

- Understand SS BPO Properties:

Composition: SalSphere® BPO is an odorless, white liquid containing about 25% BPO.

- **pH Sensitivity:** BPO is most stable at a pH of about 3 or lower, so formulations should target this range to maintain efficacy and shelf life.

- **Concentration:** SS BPO typically delivers 2-10% active BPO in final formulations, depending on the desired potency (e.g., 2.5%, 4%, or 10% BPO).

- **Formulation Types:**

SalSphere® BPO is versatile and can be incorporated into creams, gels, lotions, or cleansers for acne treatment.

- SS BPO's pre-encapsulated form simplifies formulation compared to raw BPO, which is challenging due to its reactivity and instability.

Cosmetic Elegance: The small particle size ensures a smooth, non-gritty texture, enhancing user experience.

Formulation Steps:

- **Select a Base:** Choose a compatible base (e.g., oil-in-water emulsion for creams or a gel matrix for gels). Ensure the base is stable at low pH (around 3) to prevent BPO degradation.
- **Incorporate SalSphere® BPO:** Add SalSphere® BPO during the cool-down phase of formulation (below 40°C) to avoid heat-induced degradation. SalSphere® BPO's encapsulation simplifies incorporation, as it is pre-stabilized and disperses easily.
- **Adjust BPO Concentration:** Calculate the SalSphere® BPO needed based on its 25% BPO load. For example, to achieve a 2.5% BPO final concentration, use 10% w/w SalSphere® BPO (since 25% of 10% = 2.5% BPO).
- **Add Stabilizers and Emollients:** Include ingredients like hydroxyethyl behenamidopropyl dimonium chloride to enhance texture and reduce irritation. Avoid ingredients that react with BPO, such as potent antioxidants.
- **Test pH and Stability:** Adjust the formulation to a pH of ~3 using buffers (e.g., citric acid and sodium citrate). Conduct stability testing to ensure BPO potency over time, as SalSphere® BPO's encapsulation helps maintain shelf life.

Storage: Store formulations in opaque, airtight containers to protect against light and air, which can degrade BPO despite SS BPO's enhanced stability.

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Unique&Easy Micro-Encapsulation Solutions

SalSphere® Benzoyl Peroxide (BPO)

A cornerstone in acne treatment due to its multifaceted actions

Formula: Sephora Clean Facial Wash and Gel with SalSphere® BPO

Rationale for Ingredients:

- SalSphere® BPO (10% w/w): Delivers 2.5% BPO for effective antibacterial and comedolytic action against acne.
- Decyl Glucoside and Cocamidopropyl Betaine: Mild, plant-derived surfactants for gentle cleansing, compliant with Sephora Clean standards, producing low foam suitable for a wash/gel.
- Glycerin and Aloe Vera: Hydrate and soothe skin, counteracting potential dryness from BPO.
- Hydroxyethylcellulose: Provides a smooth, gel-like texture for easy application and rinsing.
- Sodium Citrate/Citric Acid: Maintains pH ~3 to stabilize BPO and minimize benzene risk.

Manufacturing Process:

- Aqueous Phase: In a clean vessel, combine water, glycerin, aloe vera juice, and hydroxyethyl cellulose. Heat to 40°C and mix until the mixture is fully hydrated and clear.
- Add Surfactants: Cool to <35°C, add decyl glucoside and cocamidopropyl betaine, and stir gently to avoid excessive foaming.
- Incorporate SalSphere® BPO: Add SalSphere® BPO (10% w/w) at <35°C to prevent degradation. Mix slowly to ensure even dispersion without disrupting encapsulation.
- Adjust pH: Add citric acid and sodium citrate to achieve pH ~3, verifying with a pH meter to stabilize BPO and minimize benzene formation.

Ingredients	(% w/w)
Water	q.q to 100
SalSphere® BPO	10.0% (yields 2.5% active BPO)
Decyl Glucoside	5.0
Cocamidopropyl Betaine	3.0
Glycerin	3.0
Aloe Barbadensis Leaf Juice	2.0
Hydroxyethylcellulose	1.0
Sodium Citrate	0.5
Citric Acid	q.s to pH 3

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Clinical Studies and Reviews on BPO Efficacy for Acne Treatment:

1. **Clinical Efficacy and Safety of Benzoyl Peroxide for Acne Vulgaris**: Comparison Between Japanese and Western Patients

Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC5697687/
Description: This review compares the efficacy and safety of BPO in Japanese and Western patients, confirming its effectiveness in reducing both inflammatory and non-inflammatory acne lesions across populations. BPO (2.5%-10%) significantly reduced lesion counts, with no notable differences in efficacy between groups. The study supports BPO's role as a standard acne treatment, relevant for formulations like SalSphere® BPO.

2. **Efficacy and Safety of Microencapsulated Benzoyl Peroxide and Tretinoin**
Link: https://www.sciencedirect.com/science/article/pii/S0190962222001560
Description: This study confirms that microencapsulated BPO/tretinoin provides statistically significant improvements in the Investigator's Global Assessment (IGA) scores and lesion counts (both inflammatory and non-inflammatory) in acne patients. It highlights the enhanced efficacy of encapsulated BPO, relevant to SalSphere® BPO's sub-micron delivery system.

3. Advancement in Benzoyl Peroxide-Based Acne Treatment
Link: https://jddonline.com/articles/advancement-in-benzoyl-peroxide-based-acne-treatment-S1545961622P0001X/
Description: This review discusses BPO's proven track record in acne treatment, reducing lesion counts by 40-60% at concentrations of 2.5%-10%. It emphasizes BPO's antibacterial and anti-inflammatory effects and its ability to decrease reliance on antibiotics, aligning with SalSphere® BPO's role in modern formulations.

4. Single-Blind and Comparative Clinical Study of the Efficacy of Benzoyl Peroxide 4% vs. Adapalene
Link: https://www.tandfonline.com/doi/full/10.1080/09546634.2020.1740312
Description: This study compares BPO 4% to adapalene, finding BPO superior in reducing inflammatory and non-inflammatory lesions at weeks 2 and 5. The rapid lesion reduction supports BPO's efficacy, particularly relevant for encapsulated forms like SalSphere® BPO, which may further enhance results.

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Clinical Studies and Reviews on BPO Efficacy for Acne Treatment:

5. A Double-Blind Comparison of the Efficacy of a Salicylic Acid (0.5%) vs. Benzoyl Peroxide (2.5%) Acne Treatment Regimen
Link: https://www.jaad.org/article/S0190-9622(15)01715-9/fulltext
Description: This study shows BPO (2.5%) outperforms SA (0.5%) in reducing non-inflammatory lesions, but combining both (as with SalSphere® Even Skin and BPO) could leverage SA's comedolytic effects and BPO's antibacterial action for synergistic results. This supports their combined use in formulations.

6. A Systematic Review of Clinical Trials on Retinoid and Benzoyl Peroxide Combination
Link: https://www.cureus.com/articles/148927-a-systematic-review-of-clinical-trials#!/
Description: This review evaluates the efficacy and safety of BPO combined with retinoids, showing significant reductions in acne lesions (both inflammatory and non-inflammatory) and improved IGA scores. The findings support BPO's role in combination therapies, relevant to its synergy with SA in SalSphere® systems.

7. Evaluation of the Efficacy, Tolerability, and Safety of Benzoyl Peroxide
Link: https://jddonline.com/articles/evaluation-of-the-efficacy-tolerability-and-safety-of-benzoyl-peroxide-S1545961622P0001X/
Description: This review confirms BPO's efficacy at 2.5%-10% for acne treatment, reducing lesion counts by up to 60% in clinical trials. It highlights BPO's role as a cornerstone therapy, supporting its use in advanced delivery systems like SalSphere® BPO.