**USANA Health Sciences**
**Sensé Self Preserving White Paper**
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On September 16, 2004, USANA Health Sciences introduced its new Sensé™ skin and hair care products with revolutionary self-preserving technology. The introduction was the culmination of a ten-year odyssey through the forest of 10,000 cosmetic compounds searching for a combination that would result in formulas for 14 superior products that do not require conventional preservatives. The odyssey began innocently enough with a question by USANA Founder Dr. Myron Wentz: is it possible to make a line of personal care products without employing conventional chemical preservatives?

The possibility of removing conventional chemical preservatives from the Sensé formulas was first considered in 1994 by Dr. Wentz. Although the preservation of personal care products is essential for product integrity and the safety of the consumer, Dr. Wentz' view was that some preservatives are known carcinogens and others could present health problems with long-term use.

Notwithstanding the desire to do preservatives in a different way, USANA scientists, after careful review of all preservative strategies available at the time, selected the chemical preservatives with the best safety profile for its first Sensé product line.

When Dr. Wentz founded USANA in 1992, he did so because he intuitively thought that antioxidants held the most promise for nutritional answers to chronic degenerative disease. The past 12 years, in which hundreds of scientific papers have been published on the subject, have proven him right. Early in the company's history, Dr. Wentz was under enormous pressure to include a diet product with the popular herb ephedra. Notwithstanding the pressure, he refused to develop an ephedra product after looking at the mode of action of the herb. He intuitively felt that the herb had the potential of being harmful, even though the scientific data was inconclusive. In hindsight, this decision was clearly the right one. In a similar way, Dr. Wentz has now decided to abandon the use of parabens in Sensé products since USANA has developed technology that permits his taking this action. Dr. Wentz' record of anticipating scientific findings is unblemished, and USANA expects to see future scientific research validate his concerns about long-term application of these substances to the skin.

## The Need for Preservatives

Most personal care products in the market today are water-based and, as such, provide an inviting medium for microbial growth. Potentially dangerous contamination can occur at two points in the supply chain: 1) during manufacturing of the product; and 2) during the customer's use of the product. All manufacturers must ensure that their products are safe and pose no danger to customers due to contamination from either source.

The attitude of the cosmetics industry in the United States before the 1960s was that if a product didn't smell bad and looked all right, it should be good. This attitude changed in the mid-1960s when skin and hair care products were subjected to testing for microbial contamination. The results were astonishing; roughly half of the products consumers purchased were contaminated with microorganisms. This finding spurred manufacturers to look for ways to preserve their products, not only for the safety of their customers, but to extend the shelf life of their products as well. The hunt was on for new chemical preservatives that were cheap and effective in a variety of different formulas. What scientists found to fill this need were complex chemicals that included parabens, formaldehyde, phenoxyethanol, sorbic acid, and other complex organic molecules that came to be referred to as conventional preservatives.

## Parabens

Parabens (methyl, ethyl, propyl, and butyl) were synthesized in 1922 as a class of chemicals that could potentially replace phenol as a disinfectant for hospitals. Parabens are alkyl hydroxyl benzoate preservatives named for their side chains as methylparaben, ethylparaben, propylparaben, and butylparaben. These are the names one will frequently see on the labels of skin care products.

This class of chemicals has long been considered safe and even used universally as food preservatives for the last fifty years. However, the case for paraben involvement in skin sensitization and allergic dermatitis is well founded (1,2). Even with their problems, parabens are still the safest and most effective chemical preservatives known for skin care products. As such, when the Sensé line was originally introduced in 2000, parabens were chosen to preserve the products.

## Formaldehyde

Today, formaldehyde is almost never employed as a preservative in cosmetic formulas. Although formaldehyde is highly effective as an antimicrobial, the fact that it is a known carcinogen with skin-sensitizing properties at 200 ppm makes it undesirable for use in cosmetics. Formaldehyde is also known to be damaging to nervous tissue.

A class of compounds known as formaldehyde-releasing agents is commonly used for preservation of personal care products. These are effective preservatives because they release small quantities of formaldehyde into the product to aid in preservation. It should be noted that Japan has banned formaldehyde completely from personal care products; therefore products which show any traces of formaldehyde are not allowed except for rinse-off products with special warnings. The following chemical preservatives, often seen on product labels, can release formaldehyde or break down into formaldehyde:

- Quaternium 15
- 2-bromo-2-nitropropane-1,3-diol
- Diazolidinyl urea
- Imidazolidinyl urea
- DMDM Hydantoin
- Sodium Hydroxyglycinate

## Phenoxyethanol

This compound is a commonly used preservative but is most often found in combination with other preservatives, such as parabens. Even though the claim is made that it is less irritating than parabens and is used by manufacturers in an attempt to make a “preservative-free” claim or “natural preservative” claim, the reality is that it is a source of sensitization and irritation to the skin(3).

## Sorbic Acid and Potassium Sorbate

Sorbic acid and potassium sorbate have a long history as preservatives in the food industry where they perform well without known serious health consequences. As a preservative for skin care products, the facts are quite different. When applied to the surface of the skin, they become an irritant resulting in skin sensitization. In 1986, Soschin et.al. commented:

> “Sorbic acid concentrations as low as 0.1% produced transient erythema with edema and flare after open or closed application to human skin. Multiple areas of the body were tested. Reactions were most intense on the face but also could be produced on the back, forearm, and deltoid areas”(4).

There are some skin care product lines claiming “preservative-free” or “paraben-free” formulas that employ sorbic acid-based preservatives.

## Methylisothiazolinone & Methylchloroisothiazolinone

These compounds have been shown to be potent sensitizers and bacterial mutagens(5). They are further implicated in allergic contact dermatitis reactions and allergic airborne reactions(6).

## Other preservative strategies

Although not representative of the industry as a whole, some attempts have been made over the past five to ten years to create products that either replace chemical preservatives with "natural" or "alternative" preservatives, or even to eliminate chemical preservatives altogether. In general, USANA's position on these products is that they are inadequately preserved and can not provide robust, broad-spectrum protection to consumers against a variety of contaminating microorganism species.

At least one manufacturer has formulated bath products that consist of a single oil with an antioxidant to prevent rancidity. Such an approach would limit microbial growth, however would not lend itself to the production of crèmes, lotions, or products that require a thicker consistency. Single oil products are therefore of limited use.

A variety of plant-derived essential oils have well known antimicrobial properties. Formulators have taken advantage of this knowledge to make products that lend themselves to high oil concentrations that render unnecessary the requirement for chemical preservatives. The problem with using essential oils as antimicrobials is that unwanted odors and cost offer only limited specialized applications. The most effective antimicrobial essential oils contain significant percentages of allergens according to the EU(7).

Some manufacturers have employed grapefruit seed extract as a preservative which purportedly works by disrupting the cell wall(8). However, it has also been shown that synthetic preservatives may be contributing to the antimicrobial activity of the extract(9), as Sakamoto has found methyl paraben and 2,4,4'-trichloro-2'-hydroxydiphenylether (Triclosan, an antimicrobial used in liquid soaps) in commercial preparation. Many commercial "grapefruit seed extracts" have been shown to contain conventional chemical preservatives such as parabens and polyquaternium compounds that are therefore mislabeled(10).

There are a few products that do not use chemical or alternative preservatives, but the product must be kept under refrigeration and has a shelf life of only six weeks. This should work, but is not practical. Consumers should be wary of other products that employ no preservatives and do not require refrigeration, and treat these products with the same care they would a bottle of mayonnaise.

## The USANA Story

In 1999, USANA scientists, under the direction of Dr. Wentz, began a project to determine if a self-preserving strategy would work with a wide variety of personal care products. In order to be considered viable, the products would have to: a) have no common chemical preservative added to the formulation; b) have a shelf life of two years or better; c) be resistant to microbial contamination; and d) exhibit the esthetics that Sensé customers have come to expect. Only after a number of failures were USANA scientists able to achieve these goals by pursuing the following three major approaches:

- Hurdle technology
- Liquid crystal technology
- Clean manufacturing environment

## Hurdle Technology

Hurdle technology has been known for more than a decade(11) but not commercially developed for self-preserving cosmetics until now. The concept is beautiful but extremely difficult to accomplish. The idea is to block the growth of microorganisms by putting in their path various impediments that would each reduce the microorganism number

but not kill the entire population. Each impediment would permit a diminished surviving population, so that as the number of impediments grew the number of survivors would be decreased and eventually reach zero. Some of the microorganisms can jump over the first hurdle; of those that survived, some can jump over the second and so forth until none survive the last hurdle—thus the hurdle metaphor. This idea contrasts with conventional chemical preservatives, which is that at a certain concentration all of the microorganisms are killed.

Another important advantage of the hurdle technology is that microorganisms tend to develop resistance to conventional chemical preservatives. Resistant organisms are less likely to occur with self-preserving systems than they are with conventional preservatives. Self-preserving formulas are accepted worldwide by all governmental agencies.

Self-preserving technology is composed of six "hurdles":

1. Water Activity. Microorganisms need available water in order to live. Water is not available to the organism if it is bound tightly in the formula. By the judicious use of common cosmetic ingredients, the scientists found that they could make much of the water in the formula unavailable to the organisms. The reduction of water activity then became one of the hurdles placed in the organism's path.
2. pH Control. Hydrogen ion concentration (pH) of the formula is another factor that affects the viability of microbes. This turned out to be a difficult problem for the scientists because the products designed to go on the skin have a narrow effective pH range, while the pH that would put a stumbling block in the path of the organism is at a different range. The scientists were able to solve this problem by adjusting the pH of the product in such a way that it could meet the efficacy requirement of the skin and put another hurdle in the path of the organism.
3. Active Ingredients. Some cosmetic ingredients are by their very nature antimicrobial. For instance, some surfactants have antimicrobial properties. By a careful selection of esthetically desirable compounds, it is possible to erect another hurdle. For example:
    - Biovectors. A biovector is a substance that transports a material into the cell. USANA scientists selected two biovectors, both of which deliver glycine into the cell. Glycine is a major constituent of both elastin and collagen. By getting the glycine into the cell, the two major skin polymers (elastin and collagen) are assured of a readily available source of one of its primary constituents. The two biovectors that were chosen also exhibit strong antimicrobial properties. These biovectors act as another hurdle.
    - Metal chelator. Chelation is the binding of metals so that they do not interfere with surfactants or other ingredients in the formula. A chelating agent is commonly used in almost all formulas. Chelating agents are therefore commonly used in skin care and hair care formulas. Ethylenediaminetetraacetic acid (EDTA) and other chelating agents are weak antimicrobial agents by themselves. However, they can potentiate the activity of many other antimicrobial agents by chelating minerals that would, under ordinary circumstances, be available to the microbe. Chelation of magnesium is the most significant for EDTA's antimicrobial effect(12). By chelating minerals that would be present in the wall of the microbe and removing them, thus injuring the microbe, it becomes susceptible to the antimicrobial properties of other ingredients in the formula. To achieve this result the scientists had to adjust the amount of chelator used to gain the most antimicrobial effect from the formula.
    - Surfactants. The primary roles of surfactants in formulations are production of foam, production of an emulsion, and to provide cleansing action. However, some surfactants also have antimicrobial activity and can be coaxed to do double duty.
4. Packaging. The selection of packaging that reduces the risk of microbial contamination is essential to the integrity of the self-preserving product. To insure this integrity, USANA chose to use pumps in place of jars. Jars can be contaminated by placing a finger or other object into the product that could introduce microbial contamination.
5. Clean Manufacturing Environment. As this new technology developed in the laboratory, it became clear that a unique manufacturing process was required in order to ensure maximum safety of the products. An exhaustive search concluded that no contract manufacturing plants existed with the necessary cleanliness standards, equipment, and procedures to manufacture self-preserving products. For this reason, USANA

Health Sciences purchased a plant and heavily modified the manufacturing area to meet our needs. Major changes included water filtration systems, positive pressure, HEPA filtration, and new standard operating procedures, as well as extensive microbial testing of raw materials and in-process and finished products.

6. Liquid Crystal Technology. Liquid crystals have been described by some scientists as the fourth state of matter. They consist of many types, including those found in cell membranes and diverse inanimate systems. Liquid crystals have the advantage of being able to be used in cosmetics as moisturizers and as a unique vehicle to deliver active ingredients to the skin and hair. USANA scientists recently discovered that botanical extracts, plant-derived lipids, and amino acid derivatives can be combined to form aqueous association structures (liquid crystals) that are capable of delivering the contents of ultra small "quanta packets," which act to preserve the product. Although it is uncertain, it now appears that the packet is an ordered structure of a monoglyceride and water. Research into exactly how the liquid crystal is formed, its internal dynamics, and how it delivers its contents to the cell is ongoing. A secondary characteristic of these crystals is antimicrobial function.

## Patent

USANA has applied for a U.S. patent as well as patent protection in a number of other countries. The patent application covers a self-preserving botanical extract composition in a hydrophilic liquid crystalline state. When the liquid crystalline composition is added to cosmetic systems, the delivery of plant-derived active substances to the cells in the skin is facilitated. The liquid crystal can also be used as a carrier for self-preserving antimicrobial agents. When this patent issues, the liquid crystal technology will give USANA the exclusive rights to this unique arrangement of the constituents that comprise the formula.

## Laboratory Validation of Self-Preserving Technology – "Challenge Testing"

USANA devised vigorous testing protocols to validate the effectiveness of the new technology's contaminant-neutralizing potential. An ultra-conservative strategy was forged whereby all new formulas are subjected to two rounds of "Challenge Testing." A Challenge Test is a deliberate contamination of a sample of each product, followed by measurements to determine the formula's ability to neutralize the contamination. The United States Pharmacopoeia guidelines, the industry standard, suggest a single 28-day test. Many cosmetic manufacturers forego this test, owing to the proven ability of parabens and other preservatives to kill whatever contaminants are introduced into the product. They simply formulate parabens into the product in amounts that are accepted industry norms.

USANA scientists, however, subjected each self-preserving formula to two, back-to-back, 28-day Challenge Studies. Meaning, each sample was deliberately contaminated twice, and the product successfully neutralized both contamination events before being approved for production. This level of preservation efficacy testing across an entire product line is unusual if not unprecedented in the industry.

## Conclusion

What USANA and Dr. Wentz have now accomplished with self-preserving technology is to eliminate the need for any conventional chemical preservatives while at the same time ensuring the safety and integrity of the product. After reviewing dozens of product lines that claim to be preservative-free, formaldehyde-free, and/or paraben-free, USANA has not found any other product lines with a system of self-preservation that can be applied over a broad range of personal care products. This means that in the event that later research shows that some or all of the chemical preservatives listed above have serious health consequences, the USANA customer is not subject to the problem. If the health consequences of chemical preservatives turn out to be minor, then the customer is not exposed even to small risks. Either way, USANA customers are not subject to any of the risks posed by conventional chemical preservatives.

USANA's self-preserving technology is a groundbreaking development without adding conventional chemical preservatives, but the products are esthetically elegant. Nothing has been compromised. USANA has shown leadership with the development of the new technology and made a major contribution to the future of the cosmetic industry.

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