PROTECTING INHALATION DRUG DELIVERY DEVICES WITH PARYLENE CONFORMAL COATINGS

Set against the backdrop of an innovative and rapidly growing inhalable drug delivery device sector, Dick Molin, Senior Medical Market Specialist, Specialty Coating Systems, Inc, describes applications of Parylene coatings as protective barrier coatings in inhalable drug delivery devices, and the detailed characteristics of Parylene which make it particularly suited to these applications.

Inhalers of various types have been in use for decades, long before the days of modern drug delivery devices. In fact, inhalers and nebulisers are the most common way to deliver drugs to asthmatic lungs. Today, however, more compositions of drugs are being delivered using inhalation technology than ever before due to the discovery that many types of medications readily absorb through the alveolar region directly into blood circulation. These drugs reach beyond the standard pulmonary applications (e.g. asthma and other respiratory conditions) into treatments for various diseases and conditions, opening up additional treatment options for doctors and patients and creating a need for alternative device designs from medical manufacturers.

Because lungs are capable of rapidly absorbing pharmaceuticals and have the capacity for overcoming first-pass metabolism, pulmonary delivery of drugs has become an attractive target and of tremendous scientific and biomedical interest in the healthcare research area. Delivering drugs via inhalation technology is not only convenient, it is advantageous to many patients as it typically requires a lower dose than the same drug when ingested. Inhalation drug delivery also has negligible side effects on the rest of the body, which can be particularly important for long-term patients as the whole body is not exposed to the drug on a regular basis. Therefore, along with asthma, this route is being developed to treat local infectious diseases, pulmonary hypertension, Parkinson's disease. However, when systemic (whole body) delivery is required via the lung, it is possible to formulate accordingly, and for such applications the pulmonary route is used to deliver, for example, insulin for diabetes, growth hormones and oxytocin, to name only a few.

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TRADITIONAL INHALER TECHNOLOGIES

Metered-dose inhalers (MDIs) are the most common asthma medication delivery systems used. They deliver a specific amount of medication to the lungs, in the form of a short burst of aerosolised medicine that is usually self-administered by the patient via inhalation. It is the most commonly used

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delivery system for treating asthma, chronic obstructive pulmonary disease (COPD) and other respiratory diseases.

Dry-powder inhalers are available for specific medications, including beta2-agonists and corticosteroids. Though they work similarly to MDIs, unlike breath-actuated MDIs, the patient must inhale rapidly. After inhaling deeply, the patient holds his or her breath for 10 seconds.

Nebulisers can be used with all classes of inhaled medications but are most commonly used with short acting beta2-agonists and ipratropium bromide. The medication is placed in a chamber that is connected to a mains or battery powered air compressor. The compressor blows air through the chamber, atomising the medication so the patient can inhale it through a mouthpiece or facemask. While several variations of nebulisers exist, the one key advantage of this type of system is that it requires no hand-breath coordination on the patient's part.

NEXT-GENERATION TECHNOLOGIES

The market for all types of inhaled medications is changing rapidly. According to the latest reports from BBC Research, the global pulmonary drug delivery technologies market, which was US$19.6 billion (£12.5 billion) in 2010, is projected to reach nearly $44 billion by 2016 at a compound annual growth rate (CAGR) of 14.3%. MDIs, together with the the infusion systems market, will be the largest drug delivery device segments, accounting for more than 96% of total revenues. The global drug delivery device market will be driven by new technological advancements, as further emphasis is placed on needle-free technology, and the adoption of cost cutting measures in the infusion system market (e.g. increased automation).

Several device manufacturers are well on their way to expanding the inhaler market with new, innovative devices that deliver "non-traditional" medications in order to treat a host of diseases and conditions. One leading-edge application delivers insulin to diabetics via an inhalation device, eliminating the need for multiple daily injections. Another non-respiratory innovation provides a self-administered, adjunctive, as needed, inhaled treatment option for Parkinson's disease, to be used in conjunction with traditional oral medication.

> "Parylene ... is not applied to surfaces by dispensing, dipping, brushing or spraying – it literally "grows" on the receiving surface"

Like all other areas of medicine and patient care, drug delivery devices are also moving toward total interconnectivity. "Smart" devices can be beneficial to track frequency of device use (e.g. date and time), symptom tracking, medication levels, etc, in a way that can be downloaded to a patient's smartphone, tablet or PC and/or transmitted to a physician for symptom monitoring and subsequent treatment changes. As the market continues to advance in this direction, protection of electronic components will be critical.

With inhaler technology stepping into the area of more complex drug delivery and incorporating the latest in seamless remote transmission capabilities, requirements are increasing with regard to protection. In some cases, device materials must be made biocompatible. In others, the device materials require barrier protection from the medicines that they are transmitting and/or the medications must be protected from any leachables in the device material itself. Still other applications require that the moving components be able to glide smoothly, ensuring even drug distribution.

These, and more, are common reasons that device manufacturers look to conformal coatings. The challenge is determining what coating can reliably offer the properties desired for a given device without adding significant dimension or weight, while also being able to endure frequent use without consequence.

PARYLENE CONFORMAL COATINGS

A biocompatible conformal coating that can both protect and lubricate without adding significant dimension to a surface is Parylene. Parylene conformal coatings provide excellent barrier protection for internal and/or external areas of drug delivery devices. Parylenes are also highly lubricious, and as hydrophobic materials, minimise adhesion of liquid, mist or dry medication to the internal parts of the inhalation device.

Parylene is the generic name for a unique series of chemically-inert, polymeric coatings. Several variants of Parylene exist to suit a variety of applications. All are free of fillers, stabilisers, solvents, catalysts and plasticisers. As a result, the Parylenes present no leaching, outgassing or extraction issues.

What makes Parylene different from other protective coatings is that it is not

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Liquid vs. Parylene Coating

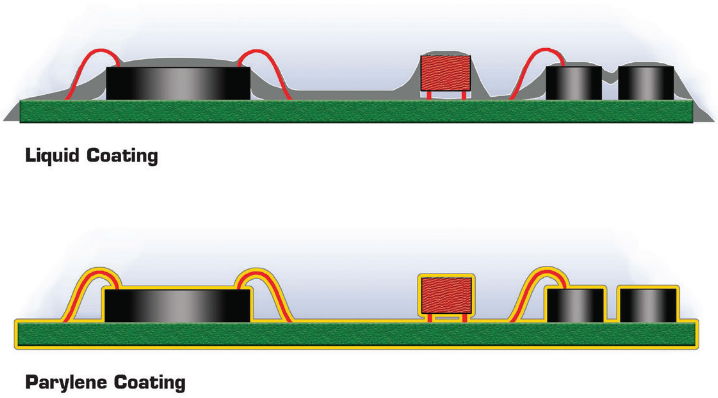

Figure 1: Illustration of the difference between a liquid coating and a Parylene coating.

applied to surfaces by dispensing, dipping, brushing or spraying – it literally "grows" on the receiving surface in a vapour deposition polymerisation process. Parylene adds no perceptible dimension or weight, and not only protects but enhances substrate properties as well.

Parylene coatings are applied in a vacuum deposition polymerisation process in which devices are placed in a room-temperature deposition chamber. The powdered raw material, known as dimer, is placed in the vaporiser at the opposite end of the coating system. The double-molecule dimer is heated, sublimating it directly to a vapour. The dimer vapour is then heated to a very high temperature that cracks it into a monomeric vapour. This is then transferred into an ambient temperature deposition chamber where it spontaneously polymerises onto all surfaces, forming the ultra-thin, uniform and extremely conformal Parylene film.

The entire Parylene coating process is carried out in a closed system under a controlled vacuum. The deposition chamber and items to be coated remain at room temperature throughout the process and no additional curing process or steps are required. The molecular "growth" of Parylene coatings ensures a uniform, conformal coating at the thickness specified by the manufacturer. Additionally, because Parylene is formed from a gas, it penetrates into every crevice, regardless of how seemingly inaccessible, ensuring complete encapsulation of the substrate without blocking or bridging even the smallest openings (see Figure 1).

Parylene's unique deposition process allows the polymer films to be formed in thicknesses ranging from several hundred angstroms to 75 µm. These ultra-thin coatings are well suited for medical devices that continue to shrink and become more complex in nature.

Biocompatibility and Biostability:
Parylenes N, C and Parylene HT® comply with biological testing requirements per ISO-10993. Testing includes cytotoxicity, sensitisation, intracutaneous reactivity, acute systemic toxicity, implantation (2, 12 and 26 weeks), haemocompatibility (haemolysis and PPT) and pyrogenicity. SCS Parylenes N, C and Parylene HT are also certified to comply with the biological testing requirements for USP Class VI Plastics.

SCS Parylene Properties

		Parylene N	Parylene C	Parylene HT	Silicone (SR)	Polyurethane (UR)
Water Absorption (%)		<0.1	<0.1	<0.01	0.1	0.6–0.8
Gas Permeability @ 25°C $\frac{cc \cdot mm}{m^2 \cdot day \cdot atm}$	**N_2**	3.0	0.4	4.8	—	31.5
	O_2	15.4	2.8	23.5	19,685	78.7
	CO_2	84.3	3.0	95.4	118,110	1,181
	H_2	212.6	43.3	—	17,717	—
Coefficient of Friction	**Static**	0.25	0.29	0.15	—	—
	Dynamic	0.25	0.29	0.13	—	—
Rockwell Hardness		R85	R80	R122	40A–45A (Shore)	68A – 80D (Shore)
Tensile Strength		7,000 psi	10,000 psi	7,500 psi	350 – 1,000 psi	175 – 10,000 psi
Thermal Usage w/o Breakdown	**Continuous**	60°C	80°C	350°C	260°C	121°C
	Short-Term	80°C	100°C	450°C	—	—
Penetration Ability*		40 x dia.	5 x dia.	50 x dia.	Dip or Brush	Dip or Brush
Dielectric Strength @ 1 mil.		7.0KV	5.6KV	5.4KV	2.0KV	3.5KV
USP Class VI Polymer		Yes	Yes	Yes	Not All	Not All

*Depth into tubing and crevices.

Note: For test methods and sources, see the SCS Parylene Properties brochure.

Figure 2: Summary specifications and properties of Parylene.

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Barrier Properties:
Parylene coatings are excellent moisture and chemical barriers for medical device components. Applied much thinner than alternative coatings, Parylene provides a pinhole-free barrier to protect against medications, moisture, chemicals and common gases.

Dry-film Lubricity:
Parylene coatings offer a low co-efficient of friction, nearing that of polytetrafluoroethylene (PTFE), ensuring that device components move smoothly to enhance patient comfort and ensure even delivery of medication.

Dielectric Properties:
Parylenes have excellent dielectric properties as they can be formed as thin, continuous films, free from defects and fillers, the latter of which are commonly found in conventional coatings. Parylene coatings have low dielectric constants and dissipation factors, and high dielectric strengths, enabling electrical and communication signal transfer without absorption or loss of signal strength.

RF Properties:
As electronics used in medical devices continue to advance, they are often required to operate reliably at higher frequencies than their predecessors. Some materials, however, lose some of their key performance properties when they are subjected to high frequency ranges. It has been demonstrated that Parylene coatings do not experience a reduction in dielectric constant or dissipation factor properties under high frequency (6 GHz) conditions. Thus, they are well suited to protect devices that operate in these ranges.

Other properties and specifications for Parylene are summarised in Figure 2.

CONCLUSION

The use of inhalers is an extremely efficient method for dispensing drugs. With the market expanding from using inhalers only in respiratory indications to using them for other indications and even to disperse drugs systemically for a wide range of conditions and diseases, it becomes even more essential to protect both the dispensing device and the medication being dispensed. While convenience and safety aspects drive this market, particularly in the area of patient home use, successful drug delivery devices must ensure that the medication remains stable during storage and use, the dose is evenly dispersed and, if applicable, data is effectively communicated from the device. Parylene conformal coatings offer device designers a proven option to enhance reliability and ensure the success of the latest in drug delivery technologies.

SCS
SPECIALTY COATING SYSTEMS™

When it comes to reliability, nothing protects like Parylene.

Parylene is an ideal conformal coating for medical and pharmaceutical delivery devices and components. SCS Parylenes can be applied to virtually any material to provide ultra-thin, pinhole-free coatings with superior extractables/leachables barrier properties and excellent non-liquid, low friction/stiction characteristics. Biocompatible Parylene coatings are USP Class VI certified and ISO 10993 tested.

With 11 locations around the world (6 in the Americas, 3 in Europe, 2 in Asia), Specialty Coating Systems is the leader in Parylene coatings and maintains comprehensive FDA Drug and Device Master Files for customer reference.

Contact SCS today for more information about the ways Parylene coatings can enhance the performance and reliability of your medical or pharmaceutical applications.

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