ADDING COLOUR & FUNCTIONALITY TO PLASTICS USED IN MEDICAL DEVICES

In this piece, Stephen J Duckworth, Global Head of Healthcare Polymer Solutions, Clariant Plastics and Coatings, explains how – with an emphasis on the importance of complying with stringent and changing pharmaceutical regulations – advanced additives in plastics used to make drug delivery devices can significantly enhance the product. Colour is an important example yet, beyond colour, additives for special textures, additives that aid product identification and tackle counterfeiting, and functional additives – imparting lubrication, stabilisation, radio-opacity (shows up on x-rays) or antibacterial properties – are all described.

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Regulations, change control, unique device identifier (UDI) marking, counterfeiting prevention and marketing … there is much more to manufacturing medical devices than simply a functional design and a competent injection moulder. Today's device manufacturers face a bewildering array of issues and challenges. Fortunately, there are ways to simplify things and, in the process, simplify manufacturing and improve the marketability of products.

The medical device industry continues to use plastics with high-performance properties and cutting-edge aesthetics in ever-increasing amounts. These materials must deliver certain performance characteristics, including resistance to sterilisation, chemicals and lipids. They must also meet standards for biocompatibility and toxicity, where even slight changes in the ingredients used could have an impact on leachables and affect the acceptability of the finished device.

For these reasons, regulatory authorities such as the US FDA, EU EMA and other relevant authorities around the world require detailed information on the material components and formulation, manufacturing processes, and extensive supporting data with respect to physical and mechanical properties, biocompatibility and toxicity. Once these materials are properly documented, device manufacturers can use them in their designs and products with the confidence that they will meet regulatory and application requirements. However, the documentation is a point-of-time submission and is material- and formulation-specific. Any material or formulation change over the life-time of the product, and at any point in a sometimes highly complex supply chain, can invalidate previous approvals and, therefore, change control becomes a formidable challenge.

It becomes essential, then, for device manufacturers to select materials that not only meet the necessary criteria, but also are supplied with the appropriate documentation and are sourced from a supplier with the good manufacturing practices and defined procedures to ensure continued compliance over time.

ADDING "SHELF APPEAL"

At the same time, in today's market, success depends on much more than just compliant materials and change-control procedures. Device developers face a growing dilemma – how to make their products not only functional and compliant, but also more distinctive, more user-friendly and more aesthetically appealing to the patient. Indeed, the market has changed so that

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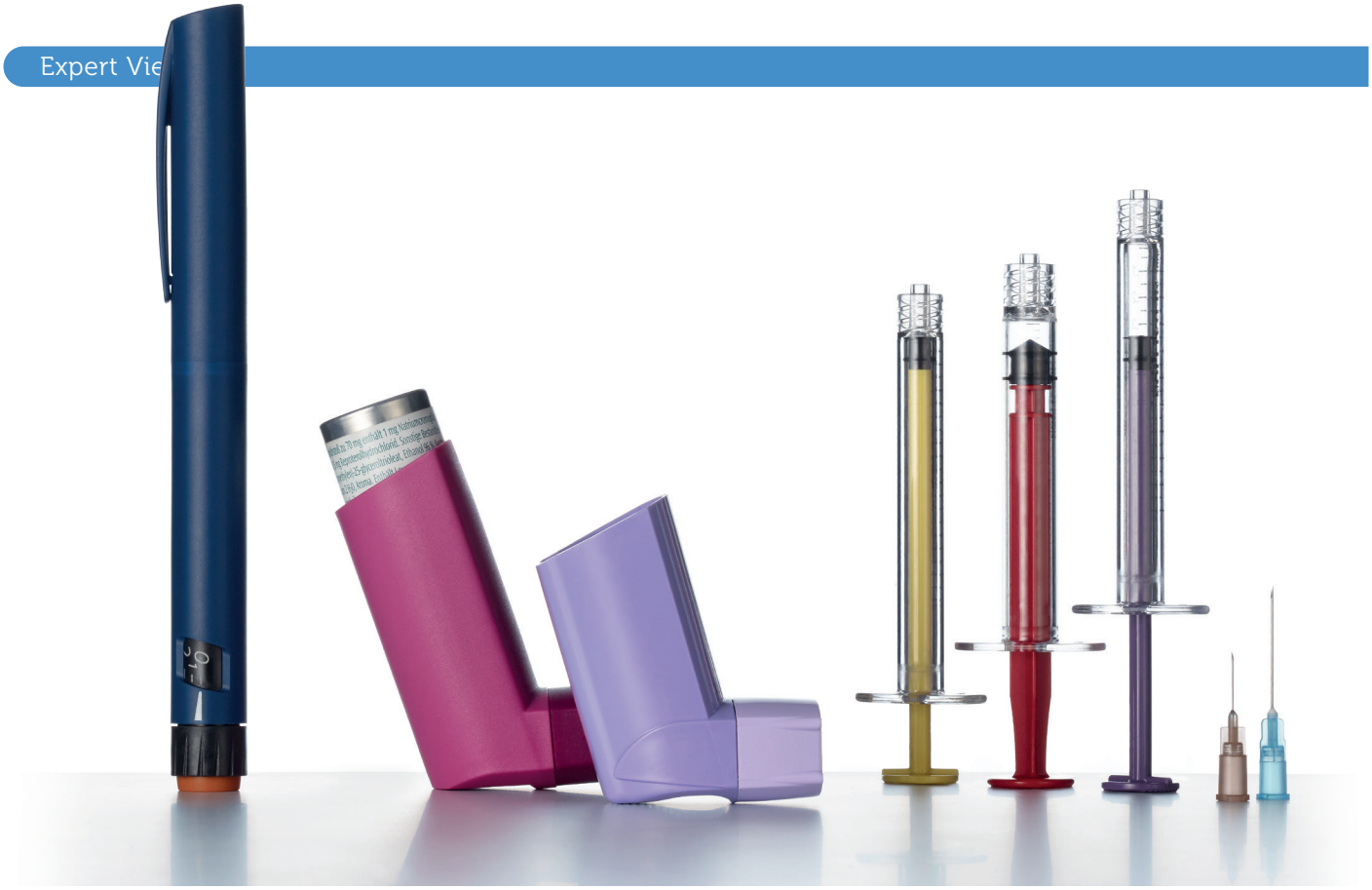

Figure 1: Colour can be used in medical devices for safety identification and to make them more attractive to users.

devices are no longer used exclusively by physicians in a clinical setting, but often by the patient him or herself at home or on the go. Increasingly, treatments are self-administered where compliance to a regular regime is important, and where product branding influences consumer decisions about over the counter (OTC) products. Healthcare designers could learn a few things from the personal care packaging (PCP) and consumer goods sectors and use colour more effectively. They should understand that there are now more options to use colours that support the regulatory compliance needs.

The science of semiotics suggests that colour, just like any sign or symbol, can have a direct effect on emotions and that each one of us responds to the stimulus of colour in a certain way. People tend to be attracted by some colours and repelled or disturbed by others. The differences may arise from deep-seated personality traits, life experiences, basic desires and even subconscious mental processes.

Colour can signal certain subtle differences in familiar scenes, giving us information about what we see. A lush green forest impresses us with its health and vitality, but when the same forest view is tinged with yellow, we see it as unhealthy, even if nothing else has changed. In other situations, a person's response to colour may be conditioned by their culture or national origin. In many parts of the world, red inspires strong feelings of excitement or danger. However, in China, red is all about power, prestige, and happiness, while Koreans are unique in the world in associating red with innovation.

These differences in perception and response are important when it comes to branding and differentiation. They can also be used to boost the success of a medical device by reinforcing the value of a particular brand or by helping patients feel more comfortable about using it. That can potentially go a long way towards treatment compliance.

As diseases such as asthma, COPD and diabetes become more common, and self-administered medication via inhaler or auto injector is becoming the norm, patient compliance becomes extremely important. Yet, US studies indicate only 28% patient-adherence to treatment programmes. The cost of wasted medication and follow-on treatment is estimated in the billions of dollars and companies are looking for ways to make their devices more attractive and easier to use, creating standard device platforms that can be customised with colour and special effects.

Just about any colour imaginable can be developed for medical devices and there is a huge palette of "standard" colours with documented compliance to regulatory standards available and change control policies already in place (Figure 1).

Figure 2: Components and bottle closure that take advantage of pearlescence effect. Ingredients in these new materials conform to medical and pharmaceutical norms.

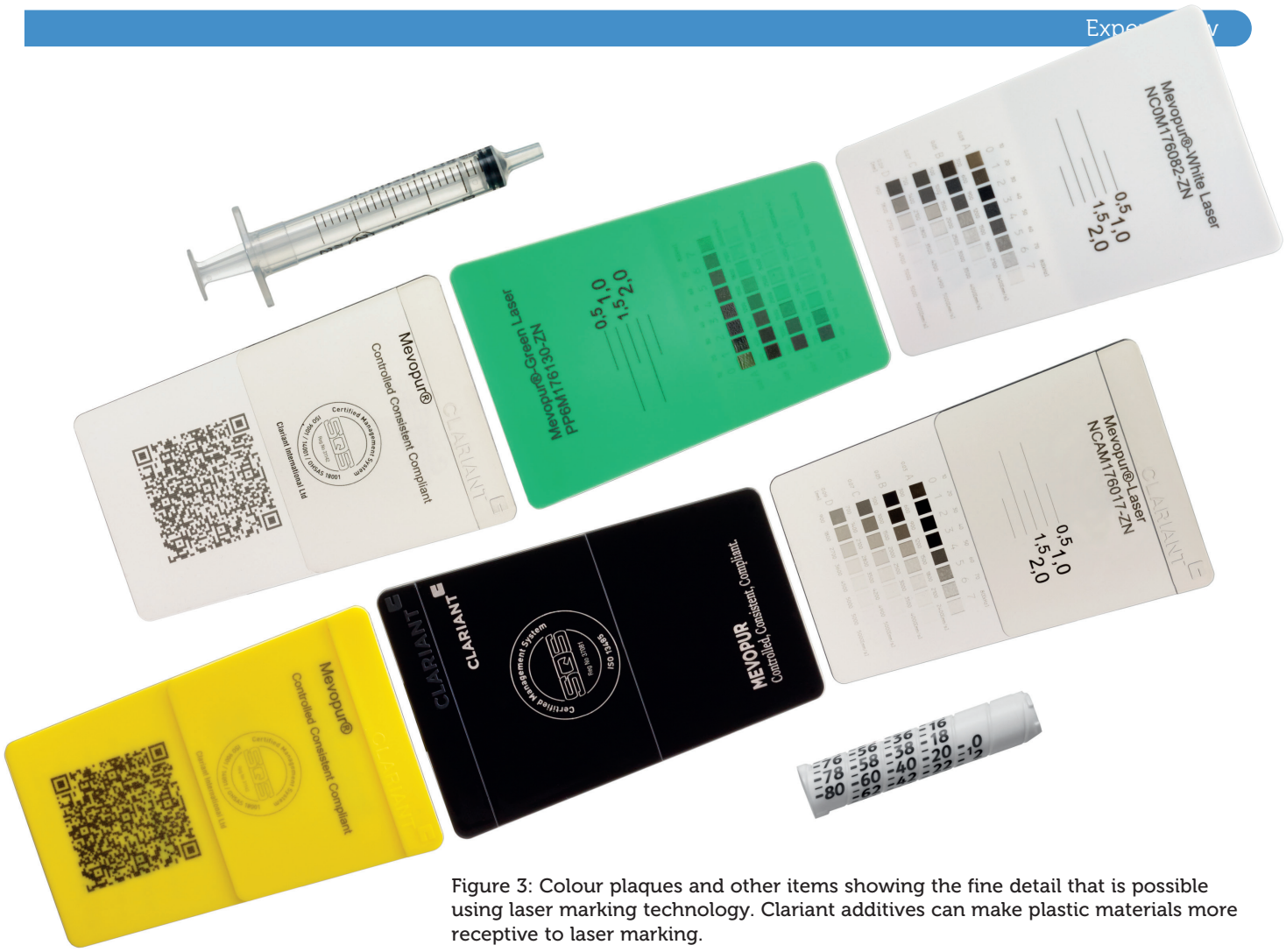

Figure 3: Colour plaques and other items showing the fine detail that is possible using laser marking technology. Clariant additives can make plastic materials more receptive to laser marking.

The same applies to special effects, which have been used for many years to enhance the look and market appeal of personal-care and consumer goods. When added to plastics, these special effect pigments create a singular impression like pearlescence (on previous page Figure 2), sparkle or a metallic look. Testing has been completed to confirm that the ingredients in these new materials conform to medical and pharmaceutical norms.

MORE THAN COLOUR

Colour and special-effect pigments are not the only materials being used to add value and consumer appeal to medical devices. A growing number of functional additives – pre-evaluated using biological evaluation standards ISO10993 / USP23 parts 87 and 88 – are also becoming available to manufacturers.

These include:

- **Lubricants**… reduce the surface friction between plastic components such dial-gauge / actuators for auto-injectors. They make it easier for medical personnel and patients to use these devices.
- **Stabilisers**… provide protection for certain polymers against loss of mechanical properties caused by gamma or e-beam sterilisation. These same stabilisers can sometimes help reduce yellowing caused by sterilisation.
- **Nucleating agents.** When different colours are added to plastics the finished product dimensions can vary even if everything else remains the same. Nucleating agents, which affect how some plastics harden during processing, can help prevent warping due to differential shrinkage. In addition, they can help speed up the process cycle or reduce weight of the component, reducing costs.

Other available functional additives include transparency-enhancing clarifying agents, antimicrobials to limit bacterial activity on devices, anti-stats and radiopaque fillers that make plastic materials more visible to X-rays.

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PRODUCT IDENTIFICATION

Lasers offer a permanent, non-contact marking solution that can survive repeated sterilisation. It opens opportunities for precise and small marking in nearly inaccessible areas, which can be extremely important as unique device identification (UDI) programmes are being rolled out in both the US and Europe over the next few years. When fully implemented in 2020, UDI must be placed on the device label, device packages and, if the device is intended to be used more than once and reprocessed between uses, on the device itself. The permanent label must include the

UDI in human- and machine-readable form.

Laser marking is ideal for direct part marking because it is fast and economical and allows variable data printing for serialisation and on small parts. However many plastics are transparent to the laser energy, and very little marking occurs. Laser-friendly additives, now available with the biological evaluation and supporting regulatory documentation required for medical devices and pharmaceutical packaging applications, make plastic materials more receptive to laser marking (see Figure 3), which offers device makers many advantages over printing or labelling.

> "The covert approach involves the use of taggants – unique ingredients that are incorporated into plastic components to provide immediate and incontrovertible proof of the genuine article."

UDI helps protect patient safety by providing traceability, but is only one weapon against the growing problem of counterfeiting, which impacts both consumable medical devices (insulin pens, inhalers, diagnostic tools, syringes, etc) as well as high-value drugs. Worldwide sales of counterfeit medicines could top US$75 billion (£57 billion) this year, a 90% rise in five years, according to an estimate published by the US Center for Medicine in the Public Interest. According to the WHO, more than 8% of the medical devices in circulation are counterfeit. Clearly, counterfeit medical devices pose a significant liability to their manufacturers and a risk of injury, permanent disability, or even death to both patients and healthcare providers.

One of the most effective ways to address counterfeiting/ brand protection problems is to use multiple level security involving use of covert (hidden) and visible coding on both outside packaging and the device itself. In plastics the covert approach involves the use of taggants – unique ingredients that are incorporated into plastic components to provide immediate and incontrovertible proof of the genuine article (Figure 4). This technology, however, poses a few problems when it comes to its use in medical devices. Most importantly, taggants represent another ingredient in the plastic material and, like all colours and additives, they are subject to compliance and change-control regulations. However, solutions have been developed to address such challenges.

For example, an alliance between Clariant and SICPA SA (Lausanne, Switzerland) announced in September 2016, overcomes several critical roadblocks to successful implementation of taggant technology in medical devices. The companies have launched PLASTIWARD™, a robust integrated protection system for plastic pharmaceutical packaging and medical devices. Specifically, in partnership with SICPA, Clariant is able to provide taggants that meet regulatory requirements for medical and pharmaceutical products, in a form that is easily included in the manufacturing process. SICPA is able to provide needs assessment, a proven means to actively track tagged devices from factory to end-use, as well as data-gathering and ongoing performance monitoring. Data gathered from instantaneous authentication using a handheld detector can be uploaded and aggregated on a secure inspection platform from SICPA that facilitates real-time monitoring at global, regional or local levels.

MINIMISING RISK

As noted, device designers and developers have a host of new options to add colour and performance to components made of plastics, so long as they understand the regulatory complexities involved. There is almost always a risk associated with a simple and otherwise routine change in the supplier of a pigment or additive, even if the chemical type did not change. The key is in understanding where risk comes from and dealing with this in the early stages of design.

Approximately 10 years ago, Clariant Masterbatches recognised the issues facing the supply chain to the healthcare industry and reorganised its approach to the medical device and pharmaceutical packaging markets to help its customers rationalise their approach to risk. This involved creating a network of three global manufacturing plants (one each in the US, Europe, and Asia) and managing them under the ISO13485 quality system with change control protocols. This is important because, firstly, production of a medical device may be required in different regions or be transferred and, secondly, back-up supply is normally a requirement.

Then came standardisation of raw materials in terms of chemistry and supplier. This process involved the technical, product stewardship and supply chain functions that assess each raw material not only on performance characteristics, but on regulatory criteria such as RoHS, Reach, BSE/TSE and so on, and whether the supply was available in each of the three sites. Each plant uses the same defined raw material ingredients, the same formula, and the same key product quality parameters. The measurements not only include typical tests such as colour and physical properties, but also ISO10993 part 18 extraction, biological evaluation (ISO10993 and USP parts 87, 88) and comparison with a chemical "fingerprint"' of a reference product.

CONCLUSION

Whether the issue is regulatory compliance, change control, UDI, counterfeiting prevention, patient acceptance or marketing; or whether the material involved is polyethylene, polycarbonate or polyetheretherketone, there are solutions readily available to help manufacturers get a better product to market more quickly. Once some of the uncertainty that is part of the global material sourcing process has been eliminated, manufacturers can concentrate on making devices that are more functional, more attractive and, thus, more effective at giving patients around the world greater access to better and safer treatment.

Figure 4: A simple handheld device recognises covert taggants incorporated into plastic materials as anti-counterfeiting and brand-protection measures.