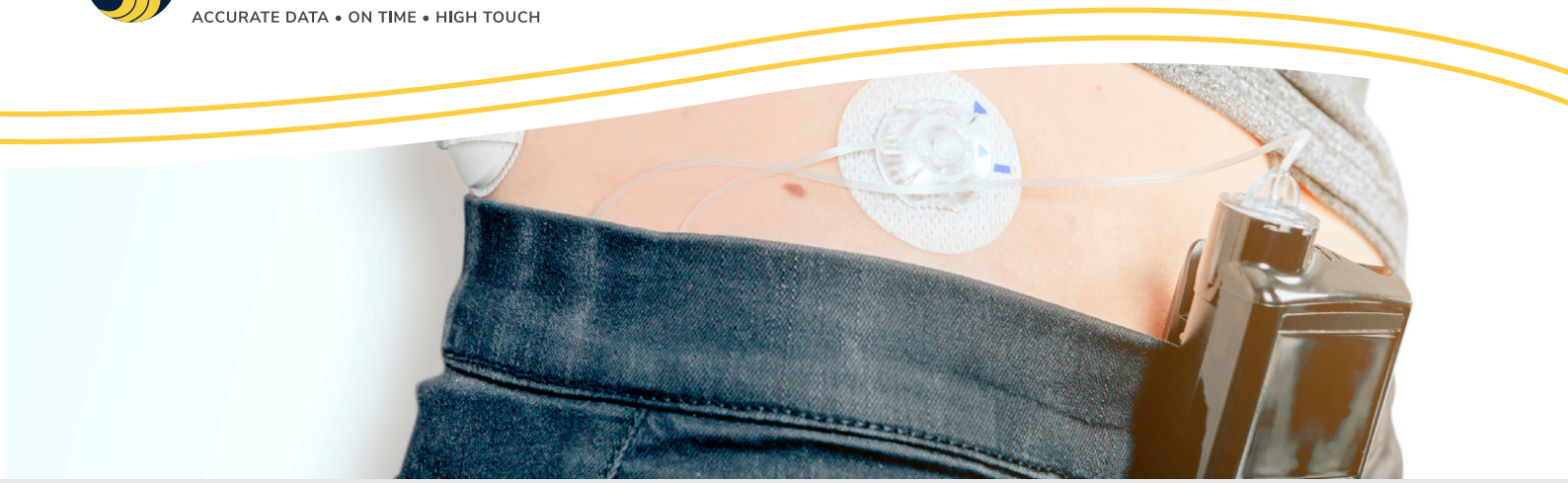
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The Future of On-Body Delivery Systems

Smithers experts Chris Berry and Gareth Wynne recently discussed wearable On-Body Delivery Systems with Medical Plastics News (MPN), including some of the key challenges for laboratory testing and future trends in the physical and functional evaluation of these devices

MPN: As a company with expertise in testing these devices, can you define On-Body Delivery Systems?

On-Body Delivery Systems are medical devices intended to be worn directly or indirectly on the body for the purpose of delivering medication to the patient. On-Body Delivery Systems include devices, such as patch pumps, which are directly affixed to the body of the user, or patient worn systems, which are attached over or under the patient's clothes but not directly to the skin and intended to provide a sustained or timed delivery of medication.

The medications can include small molecule pharmaceutical drugs, such as insulin, or large molecule products (biologics). In general, medical professionals are looking to accomplish one of three goals. They can be looking to deliver a large volume medication over a long period of time, specific doses of medication on a set timeline, or they can be seeking to combine the two, delivering a steady flow rate with defined dose injections, or boluses within existing flow.



MPN: Why are we seeing a higher prevalence of On-Body Delivery Systems in recent years?

The goal of On-Body Delivery Systems is to lessen the burden of treatment on the patient. These devices decrease the amount of time that patients must spend in clinical settings. This allows complex treatments to be brought directly into the user's home.

From the human element, they improve patient comfort. Due to the nature of bolus doses or medication with longer deliver times, patients previously were required to spend hours or days at a treatment facility. Now, On-Body Delivery Systems are attached to the patient, and they can go about their business in their own homes while staying on their medication schedule.

One specific example that demonstrates the value is a device in-development that delivers an immune system boosting drug post-chemotherapy. This drug must be injected 27 hours after the last chemotherapy event. Previously, this meant that patients had to return to the facility, often during the period where the side effects from chemotherapy were at their worst. Now, a clinician can set up this device and send the patient home where they can recuperate, confident that they will automatically receive the necessary injection 27 hours later.

From a healthcare standpoint, On-Body Delivery Systems also help to relieve overcrowding in medical facilities, allowing more appointment rooms and hospital beds to be available. During

the recent pandemic, this also meant that On-Body Delivery Systems could be used to better isolate at-risk patients away from potential sources of infection.

MPN: What types of materials are you seeing in On-Body Delivery Systems?

On-Body Delivery Systems are generally constructed with plastic bodies or plastic housings. The primary container is most often plastic, as well. Delivery is usually through a polyurethane cannula, though there are some devices that deliver through traditional metal needles. In addition to the plastic and metal components, these devices regularly have an adhesive that is used for adhesion to the skin.

Due to the flexibility of these systems, delivery can be performed sub-cutaneous, intradermal, intramuscular, or any type of delivery depth. The power source can be gas or battery powered, with most of these devices having an electromechanical element to them.

Other various technologies can also be inserted into that small profile. Many devices now feature Bluetooth, allowing them to connect with device readers, phone apps, and systems that allow clinicians to see the delivery profiles have been performed.

MPN: Do these devices use cartridges for medication?

While we are seeing many devices that have cartridges that can be reloaded, there are also devices where the full device is replaced after use. Some devices also permit delivery of a larger volume of drug through a separate, external pack that is connected to the delivery device, which can utilize glass, plastics, and/or metals in their construction.

MPN: What are the current testing standards for On-Body Delivery Systems?

These devices follow a brand-new standard, ISO 11608 Part 6. Released in 2022, this new standard references previous guidance from the 11608 series, including Parts 1-5. Part 1 covers dose accuracy, general requirements, and defines sample size. Part 2 covers needles and Part 3 addresses containers. Part 4 covers the device's electronics, and Part 5 covers the automated function of the device. By design, there is a requirement for On-Body Delivery Systems to fulfill needs from all the parts of the 11608 standard.

Non-standard tests must also be considered. For example, if you are using LED lights to indicate different stages of use for your device, you will have to test that those function correctly across various environments and use scenarios.



MPN: Do you test for weather and waterproofing?

The intended use of these devices will often be a user's home environment, but laboratories should also be testing scenarios that mimic the most extreme or challenging environments that the device is likely to encounter. This can include testing under cold, dry, hot, and humid conditions. Testing should clearly show at what point these devices failed, and Smithers can assist in determining the likely cause of failure. These environmental conditions can impact the dose accuracy standard mentioned earlier. In addition, we can also conduct testing and simulated

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Subject Matter Expert: Chris Berry

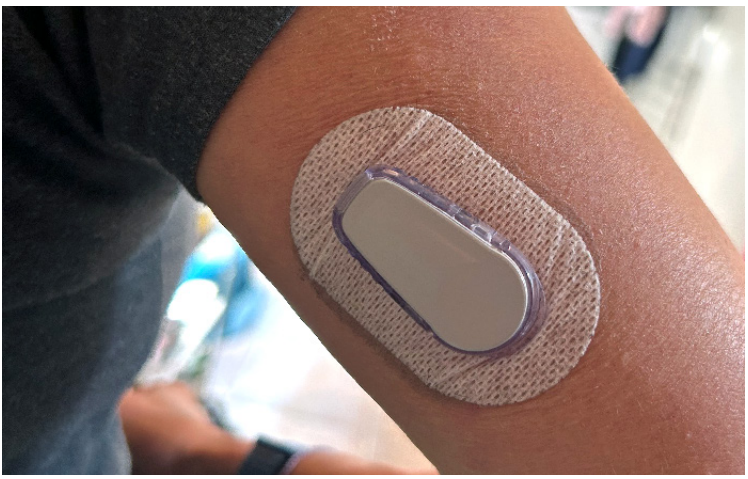
With more than 15 years' experience in materials testing, Chris Berry manages the Smithers Medical Device Physical Testing laboratory in Shawbury, UK.

Chris Berry has a PhD in Mechanical Engineering from the University of Bath, which he gained whilst working on a Smithers led research project investigating the behaviour of packaging materials. He is also an executive committee member of the Confederation of European Paper Industries (CEPI) Comparative Testing Service (CTS).

use in those environments in real time, combine this with exposure to free fall drops, and vibration conditioning and transport simulation.

MPN: What are some risks that people might not think to test for?

We have recently been specializing is occlusion testing, back pressure testing, and the evaluation of dose delivery profiles. These are complicated and time-consuming tests that many in-house laboratories find more convenient to test through independent laboratories like Smithers.



Occlusion is particularly important for pump devices, in which there is a separate cartridge and the product is delivered through a line to the patient. There is potential for the line to become blocked or occluded if the line becomes kinked or pinched, allowing the pump to create pressure within the line. Once that line is unblocked, the line could then deliver an unintended bolus.

Orientation is also an element people do not always consider. It may impact the functionality of the device if you put it on upside down. This may sound silly, but these devices are intended to become part of a patient's daily routine. If that person is getting ready in the early morning or it is dark, it needs to be expected that these devices may be applied in unpredictable orientations. This can include orientation during filling.

Orientation during filling is important. Many of these devices must be filled by the clinician or the patient before use. Experienced laboratories, like Smithers, should have the ability to test a device in a range of orientations to ensure correct function during intended use and conceivable unintended use.

The more technology and functionality a device contains, the higher the number of potential risks. If you have a pause function, for example, how does it interact with the dose accuracy? If the user pauses it for a second, (which should give a zero dose) when you restart, does the device continue and give an exact dose, as per the acceptance criteria, or does it give a little bit more, or a little bit less? You must design your experiments to test for these scenarios.

Some of the critical aspects of functionality that we are assessing include the potential for product leakage within the device during filling or delivery, the dead space volume, and delivery efficiency. Also of importance is the adhesion of the device, as well as the depth of the injection.

MPN: What unique challenges do miniaturization pose for device testing?

The device's physical design, especially if it included ergonomics, certainly can complicate testing, as it can impact the mounting or fixture of these devices. You want a skilled laboratory testing provider to ensure that they have the expertise and approaches necessary to customize the testing to meet that design. At Smithers, we use tactics like 3D printing to rapidly produce purpose-built fixtures to work with unique sizes and dimensions of devices. Custom fixturing and bespoke tailoring of our test methods have become standard to our design of experiments.

Particles are also of noteworthy concern, as there are more



Subject Matter Expert: Gareth Wynne

With more than 15 years of leadership experience in the Medical Device industry, Gareth Wynne is the Director of Medical Device Physical Testing Operationsat Smithers Medical Device Physical Testing laboratory in Shawbury, UK.

Gareth Wynne holds a Mechanical Engineering degree from the University of Central England and has completed formal training programs in design and development for medical devices such as AMMI Design Control - 21 CFR 820.30, ISO 13485 & ISO14971, Medical Device Risk Management, and Human Factors Engineering courses.

septums involved in these delivery systems, which can lead to particles entering the drug product.

These complex devices also require more than just physical and functional testing. Like autoinjectors and prefilled syringes, we are seeing interest in the biocompatibility of these devices, which includes the suitability of these materials for use, ensuring that chemicals do not migrate between the materials and drug products, and the biocompatibility of the adhesives used. These must be tested for extractables and leachables (E&L) to ensure their safety for patient use. We are, fortunately, in a unique position that we also have a chemistry department on site where we can perform the dose accuracy orientation testing, and then pass it on to our chemistry team for E&L testing.

MPN: What does the future of testing On-Body Delivery Systems look like?

Integration with more sensors is coming rapidly. You see this with the recent release of diabetes systems that feature blood glucose monitoring systems working in tandem with insulin pumps. Now, you can have a pump communicating with a separate sensor, measuring the blood glucose level, and automatically delivering the appropriate dose of insulin. We are confident that more of these devices will continue to enter the market to the benefit of patients.



The truth is that the industry has consistently increased the complexity of these devices over the years, so expertise in testing these devices is more important than ever. We are seeing an increase of in-house testing operations default to independent laboratories like ours because it is becoming harder to secure the expertise necessary to perform adequate testing of these devices.

Smithers Laboratories

Smithers helps medical device and pharmaceutical product manufacturers bring innovative, safe and highly effective products to market with world-class expertise and extensive, independent testing capabilities at accredited facilities in the UK and USA.

Our experienced team will provide advice, guidance and recommendations as well as delivering test data to help you demonstrate compliance to regulatory guidance or specifications set out by the FDA, EMA, MHRA, USP, ASTM and ISO.

Smithers is happy to share the experience and knowledge gained through years of medical device and pharmaceutical product testing projects. The information outlined in this document is to be used for general guidance and not to be used as a reference for standards. Please refer to the appropriate competent standards agency in your country for full details.

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