Perspectives on Combination Products, Part 1

The marriage of a medical device with a drug or biologic has been increasing significantly within healthcare. The combinations have resulted in numerous benefits that could not have been realized with just one of the elements being indicated on its own. For this month's Perspectives, we asked what the future holds for these types of devices and what technologies would provide aid in their success.

What types of devices will see the marriage of drug/biologic and device in the future that aren't currently commonplace in medicine and what technologies will aid in the success of these devices?

Michael F. Adams
President & CEO, AdvanSource Biomaterials

Some of the most exciting areas for convergence lie in technologies such as the combining of a polymer with a drug or biologic.

Over recent years, the combination of a polymer with a therapeutic agent has been predominantly focused on drug eluting stents, primarily for coronary purposes, as well as secondary operations coatings. Recognizing the need to broaden this range, we have developed a family of proprietary polymers incorporating antimicrobial additives in the pre-polymerization stage, thus allowing for homogenous dispersion, beneficial and increasingly sought after for use in in-dwelling catheters, ports, and other access devices, as well as a multitude of other polymer-based medical substrates.

Coatings, in the meantime, remain a primary and expanding focus for both us and

the industry at large. Lesser redesign requirements have allowed this segment of the market to be broadened into a wide array of short-term implantable devices from cannulae and urological devices to sutures and guidewires.

Throughout each of these products, it has become increasingly important to maximize the mechanical characteristics of the polymer and target these specifically to the application use, without diminishing the antimicrobial properties of the material.

Polymers offer a unique platform in that they can easily be impregnated with a therapeutic agent and, based on the polymer, can be released very quickly or very slowly based on the indication. What is paramount, is that the drug/biologic and biomaterials companies form alliances that bring the two technologies together.

Keith Checca
Director of Business Development, Texcel Medical

An area in which we see integration of biologics into medical devices is with the tissue interface on many emerging electrical stimulation therapies. In some areas of device implant, the goal is for the encapsulation or absorption of the device. There are a couple alternate approaches emerging recently. The body naturally reacts to the placement of a lead with a slow encapsulation by scar tissue. One clinical effect is that the electrical properties change over this time, sometimes causing an ongoing adjustment of the therapy to continue managing the symptoms, and at times isolating the lead from the nerve. Additionally, reversal of these therapies rarely involves removal of the leads, since the potential exists for damage to the surrounding tissue. We see certain combinations of biologics and drugs being integrated into or onto the lead materials, altering the progression of the tissue interface. The goals are more consistent efficacy from the device therapies and longer term stability. Separately, the appropriate materials could allow for an increase in their safe removal in cases where the therapy term is shorter and

removal is preferred. Overall, we are beginning to see a transition from the basic research on biologics into their integration into the materials used for electrical stimulation therapies.

Barry S. Sall, RAC
Principal Consultant, PAREXEL Consulting

Over the past 50 years, medical devices have provided physicians with vital tools to diagnose and treat disease. Many factors including the aging population, reimbursement pressures, and comparative effectiveness research are providing powerful incentives for device developers to enhance the performance of their products and use new technology to design products. Combining drugs and biologics with devices is one powerful approach to create new clinical benefits.

With the advent of companion diagnostics, *in vitro* diagnostic products have recently begun to play a greater role in the pharmaceutical world as drug developers rely on laboratory tests to define the appropriate treatment population. As biomarkers are refined, this technology will increase both drug safety and effectiveness. Another diagnostic technology driven by combination products involves imaging agents that interact with the patient's metabolism, enabling clinicians to utilize various imaging modalities to identify abnormal tissues. At present, most imaging techniques generate data describing anatomical structures, but do not provide detailed data on metabolic activity in those structures. Imaging agents that interact and detect metabolic abnormalities in a highly specific manner would provide powerful new tools for oncologists, cardiologists, and other specialties.

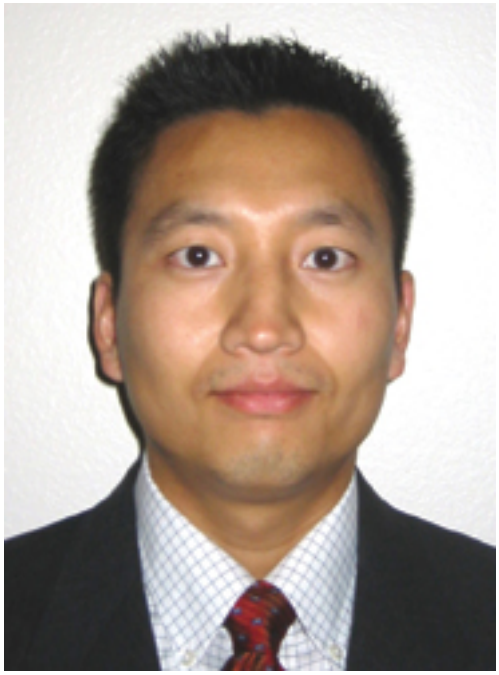
Therapeutic devices will also continue to benefit from combinations with drugs and biologics. For the past decade, drug-coated stents have been the most prominent example of this technology. Orthopedic implants will also benefit from increasing use of pharmaceutical and biologic agents to enhance their performance. Biologic-

Device products, in some cases in combination with nanotechnology materials, have the potential to provide breakthrough technologies. Devices can be used to harvest specific cell types from a patient, manipulate them *ex vivo*, and reintroduce them to the patient to treat a variety of diseases from cancer, heart disease, and diabetes to sports injuries.

Emma A. Durand
President & Chief Technology Officer, Isis Biopolymer Inc.

Physicians, patients, and managed care providers are seeking a more integrated, personalized approach to self-care that will enhance compliance and provide better medical outcomes. Innovation combined with integration will support development of delivery devices that enhance the pharmacoeconomics of drug therapy.

Isis Biopolymer has developed one such device that marries innovation with integration. IsisIQ is a polymer thick film iontophoretic transdermal drug delivery patch that features a proprietary selective barrier membrane that facilitates the transport or complete cessation of drug molecules through the skin. Transport can be modulated for up to three drugs per patch for discrete personalized delivery, programming, and monitoring via an integrated wireless communication platform. The single electrode design provides additional safety by eliminating variability in drug delivery that can occur with changes in the skin (temperature, moisture, movement), preventing inadvertent or over delivery. This technology is also a biosensor that can detect skin emanations that may be indications of cardiovascular or diabetic events. Breakthroughs in materials such as pliable, ultra thin polyester substrate and hydrogels will aid in the development of this technology to support flexibility, lower cost of manufacturing, and a more diverse range of delivery of drugs and biologics than are currently available.



Jin Xu
Principal Product Marketing Engineer, Medical Products Group, Microchip Technology Inc.

The recent SARS and bird and swine flu epidemics that have caused deaths and wreaked havoc around the world reminded us yet again of the serious impact infectious diseases can have. The epidemics also clearly demonstrated the inadequacy of the existing approaches to disease detection and control. The lack of efficient, effective means of diagnosing these types of illnesses hampered efforts to contain the outbreaks. Conventional methods, such as monitoring changes in body temperatures and lab tests that take days to yield results, are sometimes inaccurate and cumbersome, with too many delays. Often, the patient is diagnosed only after the sickness is in full bloom, when many others may have already been infected.

Medical devices that can perform *in-vitro* early diagnostics of contagious illnesses at any location will play a critical role in disease prevention and containment, moving forward. Disposable test kits with smart sensors capable of detecting multiple diseases in the early stages of infection using saliva or other non-invasive means could save valuable time, facilitating the containment of an incipient epidemic.

Neoteric advanced biochemical formulations that could detect the diseases, as well as electronic components, such as microcontrollers and analog peripherals that are needed to process, interpret, and display the results, are all critical components required for these one-step-does-it-all smart medical diagnostic devices. As new discoveries are made in both the biochemical and electronic worlds, the challenge is to produce these new medical test kits affordably and easily for mass consumption.

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