# The Toolbox of 2025

**Previously, in our series – "Connecting the Dots in Drug Delivery" – we examined the current status of drug delivery. We saw how today's new therapeutics pose tough challenges for formulation scientists, and how companies are tackling those challenges with a range of tools, from micronization to hot melt extrusion. But what techniques will be in the toolbox 10 years from now? We speak to academic and industry experts to find out.**

## On Target

*With Hamid Ghandehari, Professor at University of Utah, Director of Utah Center for Nanomedicine and member of Catalent Applied Drug Delivery Institute Advisory Board*

What do you think will be the most important future trends in drug delivery?
For one thing, we are going to continue to see the approval of targeted drug delivery systems, including polymeric systems. There are several micellar polymer structures that are in various stages of clinical trials, and I expect to see those in the clinic in the next few years.

In the next decade, we are going to see local triggered-release drug delivery. Here, the drug delivery system is delivered to the target site and activated by local or external triggers to enhance the delivery of the active agent.

What is needed to drive continued innovation?
Two decades ago this was a very specialty field, but now a lot more research is going on. It is very satisfying to work with a younger generation of scientists and see their enthusiasm. I think the field needs more innovation and new minds to take it to the next level. In particular, we need more clinician–scientists in our ranks to help translate technologies for the clinic.

Broad support from the pharma industry is essential to bridge the gap between academia and industry, and speed up commercialization. To that end, the Catalent Applied Drug Delivery Institute is reaching out to the broader scientific community, as well as the younger generation with workshops and academic prizes.

How did you get into the field?
I was really in the right place at the right time. I completed my undergraduate degree at the University of Utah in the late 1980s and stayed on for my PhD in the early 1990s. At that time, the university had some of the pioneers in drug delivery, including my PhD mentor Jindrich Kopecek – one of the world leaders in polymer therapeutics. I was inspired to continue this great work.

To deliver the drug to the right site at the right time is so important – it really impacts on patient's lives by reducing side effects and improving efficacy.

What are you working on right now?
A lot of drugs, such as cancer chemotherapies, are fabulous at what they do, but have devastating off-target side effects, so can only be used in small doses – or not at all. We aim to confine the delivery of those drugs to the target tissue, for example cancer cells, by using novel drug delivery systems.

In our lab, we tailor-make recombinant polymers for gene delivery applications. These polymers are made using genetic engineering, which gives us a high degree of control over the sequence and length. In particular, we use them to deliver genes to accessible head and neck solid tumors. The particular polymers we use are made of silk and elastin blocks. They are liquid at room temperature and when mixed with viral gene carriers and injected they solidify at body temperature and improve localization and duration of gene transfer.

In another project, we use local hyperthermia to target delivery of polymer–drug conjugates to prostate tumors. We use plasmonic photothermal therapy or other means of hyperthermia, such as ultrasound, to maximize the delivery of the polymeric systems to the site of action. This improves blood flow in the tumor and enhances cellular uptake of the cytotoxic agents.

Where have you seen the most promising results?
There are a couple of areas where I think we have had particular impact. By using recombinant techniques we have been able to sustain the expression of adenoviral systems locally in head and neck tumors. More recently, we have developed recombinant polymer systems that are responsive to local enzymes, such as matrix metalloproteinases, that are overexpressed in tumors. This allows gene therapy to be delivered primarily in the tumor.

In the area of targeted delivery using hyperthermia, we have shown that by carefully controlling local temperature we can magnify the so-called enhanced permeability and retention (EPR) effect, whereby certain sizes of molecules tend to accumulate in tumor cells.





## Dissolving Delivery Challenges

*With Rosie McLaughlin, Director, Scientific Affairs at Catalent Pharma Solutions*

What's the focus of your work?
Right now, I'm looking at innovative ways to expand on the Zydis® drug delivery platform – a freeze-dried, orally dispersible tablet. We start with a dispersion of active pharmaceutical ingredient (API) in the formulation matrix, and freeze-dry it to create a very porous, lightweight product, which dissolves in the mouth in around three seconds and without the need for water. The drug can enter the body either by standard gastrointestinal absorption or through the oral mucosa, depending on the API. The sublingual area (under the tongue) is highly vascularized so certain APIs can be quickly transported through the oral mucosa and into the bloodstream, bypassing first-pass metabolism and potentially improving bioavailability.

What are your most exciting projects at the moment?
There's always something new and exciting! The best thing is when we push the boundaries. At the moment I'm working on two new developments – one is a new API coating process developed exclusively for Catalent by the New Jersey Institute of Technology. The process involves a Resonance Acoustic Mixer, which uses sound energy to generate vibrations for dry-coating very fine particles, increasing drug loading and improving taste masking. Previously, we haven't been able to use coated APIs in Zydis, so this expands the number of drugs we can develop in the platform. We've also been doing proof-of-concept work on oral delivery of vaccines, starting with influenza.

An oral flu vaccine could be quite a breakthrough…
We're using influenza in our proof-of-concept preclinical trials because it is so well characterized, but we hope the technology may be applicable to a whole range of vaccines. The availability of a noninjectable, room temperature-stable vaccine delivery system could certainly transform the whole field. This is particularly true of the developing world, where the logistics of cold chain storage are a big challenge, causing significant wastage, and where trained healthcare workers may not always be available to administer injections.

What approach are you taking?
Vaccines, except for some live attenuated viruses like polio, are generally destroyed in the gastrointestinal tract if swallowed. Using Zydis Bio, we're administering the vaccine sublingually, to bypass the acidic environment of the stomach and enzymes of the digestive system and go directly into the bloodstream via the oral mucosa.

Proteins, being large molecules, have less tendency to cross the oral mucosa. But we know it is possible because we have already used Zydis Bio to deliver an allergy vaccine. The active ingredient is a protein extract, which is delivered sublingually and induces tolerance in hay fever sufferers. Our work on oral vaccines is a natural continuation – the difference is that we're now trying to trigger an immune response, rather than immune tolerance. The results so far have been encouraging, although it may be several years before we see clinical trials.

What challenges will tomorrow's drug development scientists face?
Bioavailability challenges will continue to be a problem for drug manufacturers. As more and more biologics become available, the Holy Grail is to find new routes of administration to improve the patient experience – whether that's oral, inhalation or microneedle delivery.

## Innovation Events

*Get the inside track on the future of drug delivery at these Catalent Applied Drug Delivery Institute events.*

**Addressing the Challenges of Drug Delivery**

April 30, 2015 - *3M Customer Innovation Center, Bracknell, UK*

- Dr. Ralph Lipp on using patient insights to design drugs
- Dr. Mark Tomai on increasing the effectiveness of vaccines
- Professor Claus-Michael Lehr on innovative drug delivery methods

**Advanced Drug Delivery Applications**

September 17, 2015 - *University Of Tokyo, Japan*

- Bioavailability challenges
- Patient-centric drug design
- Innovative technologies

*Find out more at www.drugdeliveryinstitute.com/events*