Volume 101 April 2021

OSCARTEK

The Journal

Keeping COVID VACCINE Cold and Effective (read below)

Famed Chef Wolfgang Puck views on Pandemic and Industry's Future

Dallas TX, April1, 2021. — A global pandemic certainly hasn't slowed the business drive of renowned Chef Wolfgang Puck, but that doesn't mean his journey over the last year has been a cakewalk.

Chef Wolfgang Puck

While some of his establishments are currently closed due to COVID-19, Puck remains proud of his teams' contributions in the last year and anticipates not only expanding internationally in 2021 but also opening two new restaurants inside The Pendry West Hollywood by March. Renowned Chef Wolfgang Puck was born in Austria and came to Los Angeles in 1975

Puck opened his first flagship restaurant, Spago, in 1982, which was originally located on the Sunset Strip in West Hollywood.

Since 2001, Puck and his Fine Dining Group have opened restaurants across the U.S. and abroad for the last 26 years, Puck and his team have catered each Oscars ceremony, but plans have changed this year due to COVID-19. Puck described one of these eateries, Ospero, as "a mixture of a French bakery, in the morning especially, with an Italian osteria," plus a pizza oven to offer a variety of options. Merois, located on the hotel's rooftop, will be Asian-influenced and may even include dishes from such classic Puck restaurants as Ma Maison, where he first garnered Hollywood's attention.

New style display combination, The Italian Kitchen By Wolfgang Puck (TX)

Speaking of Hollywood, every year for the last 26 ceremonies, Puck and his team of executive chefs have provided catering for Hollywood's biggest night: the Oscars. This year, however, they have no plans in place due to the pandemic.

"[Our catering company] is really suffering the most because there's no parties, no movie premieres," he said. "We do small parties sometimes at home for 10 people, 15 people, but that's it."

Today's challenging climate is not lost on Puck, and he knows the anticipated March 1 opening date for his two L.A. restaurants hinges on the city and county's regulations.

He said his well-known Spago Beverly Hills establishment has thrived during those months when the county permitted al fresco dining.

"We adapted," he said. "We only opened five days a week for dinner, and Spago did really, really well. I was surprised. We were sold out every day, because the people really want to go out. They want to be in an environment where they see other people and everything."

Steve Scott Springer, general manager of Spago Beverly Hills, echoed the same sentiment, adding that never before had he heard the word "pivot" more.

"We've certainly had to be creative, and I think that is a testament to Wolfgang," said Springer. "We decided that the rules that came out, the 20 pages of rules from the health department, were not oppressive. They were our ticket out of this. And so we embraced them."

This July 1, 2020 photo shows Spago Beverly Hills' outdoor seating arrangement. (Courtesy Wolfgang Puck)
When L.A. County shut down restaurants again recently, Puck and his team were frustrated because, as Puck and Springer explained, Spago was able to provide a safe environment for its staff. Puck requires all employees to get tested every Friday, for example, and now feels the lockdown is working against the well-being of his workers. "Don't forget, the restaurant industry is the largest employer in the country after the government," said Puck. "So all our people who don't go to work, they have to hang out at home. They have families. They have friends. They have relatives. What do they do? They get together."

"I think there was still a way to provide a safe environment and really be part of the solution," said Springer. "That's what we wanted to do, we were doing. We were part of the solution. The numbers were going down for six months while we were dining outside. So we think that we made a really important contribution to maintaining the health and safety of the public, so I feel proud of that."

While his Southern California restaurants remain closed for dine-in, Puck's Maui and Las Vegas locations have stayed open part-time for dine-in, but that is always subject to change due to surging COVID case numbers. Fortunately, his Fine Dining Group has business overseas as well.

"In 2008, when the economy was really bad here in L.A. and Las Vegas, I decided to expand internationally," said Puck.

While his London and Istanbul restaurants are currently closed, Puck still continues to extend his reach, looking to open restaurants in Budapest and Hungary this year — and possibly even expand into Saudi Arabia. Puck is already established in neighboring Bahrain, which he said is currently doing well. In the meantime, places like Spago Beverly Hills that are currently restricted to take-out and delivery need to keep their creative juices flowing in order to maintain a steady stream of business.

"We need to be able to react to this and be creative about how we respond and what kinds of experiences we're presenting to the public," said Springer. "We started what we call the 'Spago Explores' series, so we are kind of taking our guests on, what I would say, is a mutual exploration to different places." The limited-time take-out offerings deliver authentic cuisines originating from places like Austria (Puck's native country) and Thailand straight to customers' doorsteps.

Puck said he hopes things will start to turn around by the fall but remains skeptical due to current events.

"Look how bad the government effort is to get vaccinations," he said. "They said by the first of January, we're going to have 20 million."
Until the turnaround, Puck hopes that fellow restaurant owners can withstand the hardships with help from the Paycheck Protection Program, and that landlords won't act unruly towards the smaller establishments during the lockdown.

"You cannot ask a small restaurant to pay rent while they are closed," said Puck. "People aren't going to dip into their life savings to give it to somebody who owns a shopping mall." Meanwhile, Springer revealed a bit about the future of Spago once outdoor seating is permitted again.

"We have in plans, really since April, to build this giant pavilion outside [Spago] and close the street down," he said. "We think that that is a way for us to kind of COVID-proof our business, whatever happens."

Springer added that the sprawling outdoor tent has already been constructed inside a warehouse. They're just waiting on approval from the powers-that-be once al fresco dining reopens. "We are optimistic," said Puck. "It's only going to get better. We're sure 2021 is going to see a big rebound, but I think it's going to take longer than we think because of the way they are doing the vaccinations. Maybe in six months, they're going to get a better way, but right now, it's just very disappointing."

Keeping covid vaccines cold isn't easy.

From MIT Technology review

New formulas and off-grid approaches could help mRNA vaccines get to more places around the world.
by Wudan Yanarchive page
March 29, 2021

In order to truly end the pandemic, it will be essential to get vaccines to all parts of the world. The first part of that challenge involves boosting the supply and securing doses for all, but even if enough vaccines become ready, the next hurdles are storage and distribution. For some covid vaccines, that means shuttling through what's known as the "cold chain," a series of very well chilled environments—planes, boats, trucks, even boxes cooled with liquid nitrogen—to ensure that shots don't perish before they get to the people who need them. Currently, Pfizer's vaccine needs to be kept at -80 °C for long-term storage, and Moderna's at -20 °C. For reference, home refrigerators maintain temperatures of about 2 to 4 °C.

"These requirements are difficult," says Darrick Carter, the chief scientific officer of HDT Bio, a biotechnology company based in Seattle that's developing immuno-therapies for underserved regions of the world.

Some vaccines are already able to handle more typical refrigerator temperatures: Johnson & Johnson's and AstraZeneca's, for example. But messenger RNA (mRNA) vaccines such as those by Pfizer and Moderna, which have proved more effective and will be far easier to modify to fight new variants, have a shelf life of just a few hours once they're out of very cold temperatures.

Those temperature needs are an issue in places where access to ultra-cold freezers or even electricity is scarce, but keeping vaccines cold can be a struggle even in rich countries like the US.

To get around these problems, scientists and engineers are taking two different routes: changing parts of the cold chain, or changing the vaccines themselves.

How cold temperatures protect fragile vaccines

MRNAs are strings of nucleic acids that give cells instructions on what proteins to make—and with the right tweaks, they can give the body directions on how to fight diseases, including covid-19. They're essential components of vaccines like Pfizer's and Moderna's. But they're fragile: without some sort of protective coating, the mRNAs in a vaccine degrade quickly. To prevent that

damage, vaccine makers keep these mRNAs protected, essentially putting them in safe bubbles.

Currently, that bubble is a lipid nanoparticle—which, on a basic level, is a very tiny fat droplet. For Drew Weissman, one of the pioneers of mRNA vaccine technology, it took more than 10 years and about 40 different formulas to discover that lipid nanoparticles worked the best. Not only did they keep particles from being degraded, but they also boosted the response of the immune system.

I jumped the queue to get an expiring vaccine. Did I do the right thing?
When I got a call saying there was one available, I had to do some ethical gymnastics and decide whether to take it.
By the time Weissman and his colleagues began testing mRNA vaccines, about six years ago, it was evident that the lipid nanoparticles required ultra-cold storage, he says. That's because it takes more energy to freeze fats than, say, water. "The idea for storage was that you wanted to freeze the fat droplets so they wouldn't degrade, aggregate, or fuse together," Weissman says. "That's how -80 °C started."

Pharmaceutical companies have been testing various storage temperatures, hoping to bring them up a bit. Moderna tested how its vaccine would fare at -20 °C for long-term storage and found it to remain stable until the dose's expiration date. Pfizer and BioNTech didn't look at -20 °C storage until recently, but in late February, the US Food and Drug Administration approved the vaccine for storage at that temperature for up to two weeks.

Stronger bubbles could add stability
Scientists are now experimenting with other ways to make mRNA vaccines even more temperature stable.

"The more thermostable [a vaccine or pharmaceutical product], the better," says Pat Lennon, who leads the cold chain team at PATH, a global health organization that's working to improve health equity. "You can take the pressure off the cold chain."
For example, Weissman says, some vaccine developers are altering the concentration of sugars in the formulas they use. Sugars can coat fat droplets—the way flour can coat bread dough—and prevent the lipid nanoparticles from sticking together, allowing doses to stay stable and usable for longer.

HDT Bio, the biotechnology company in Seattle, has an alternative solution. Working with Deborah Fuller, a microbiologist at the University of Washington, it's pioneering a different kind of protective bubble for the mRNAs. If it works, it would mean that an mRNA vaccine for covid-19 could be stable in a regular fridge for at least a month, or at room temperature for up to three weeks.

Their method: instead of encasing the mRNA in a lipid nanoparticle, they've engineered molecules called lipid inorganic nanoparticles, or LIONs. The inorganic portion of the LION is a positively charged metal particle—so far they've been using iron oxide. The positively charged metal would bind to the negatively charged mRNA, which wraps around the LION. The resulting particle is solid, which creates more stability and reduces the reliance on refrigeration.

"The cold chain has always been an issue for [the] distribution of vaccines, and it's only magnified in a pandemic." Deborah Fuller

HDT Bio initially developed LIONs to treat liver cancer and tumors in the head and neck, but when the pandemic hit, they pivoted to trying the particles with mRNA vaccines. Early preclinical trials in nonhuman primates showed that the LION, combined with an mRNA vaccine for covid-19, worked as they'd hoped.

Carter of HDT Bio says that in an ideal situation, LIONs could be sent to clinics worldwide in advance, to be stored at room temperature or in a regular refrigerator, before being mixed into vaccine vials at clinics. Alternatively, the two could be premixed at a manufacturing facility. Either way, this method would make doses stable for at least a month in a regular refrigerator.

Fuller says that some scientists have criticized the need for two vials—one for the LION and another for mRNA before they're mixed together. "But I think the advantages of having an effective product more amenable to worldwide distribution outweighs those negatives," she says.

HDT Bio is applying for permission to start human clinical trials in the US and is looking to start clinical trials in India this spring. In the US, it faces some unique challenges in FDA regulation, since the LION particles would be considered a drug separate from the vaccine. Regulators in Brazil, China, South Africa, and India—where HDT Bio is hoping to launch its product—don't consider the LION a drug because it isn't the active component, says Carter, meaning that there would be one less layer of regulation than in the US.

For now, it's still very much an early-stage technology, says Michael Mitchell, a bioengineer at the University of Pennsylvania who works on drug delivery systems. He stresses that more research should reveal whether the iron oxide causes any side effects.

Keeping the cold chain properly chilled

While changing vaccines themselves may take time, other ways of managing the cold chain are already happening, especially in low- and middle-income countries where electricity and refrigeration are harder to come by.

PATH, the global health organization, developed temperature-tracking methods for vaccine distribution a generation ago by designing stickers that change color with increased heat, taking into account a vial's cumulative exposure to temperatures outside its required refrigeration range. This information helps reduce spoilage and wasted doses—if, say, a freezer goes out, medical staff don't have to assume vaccines are spoiled.

More than 9 billion of these stickers have helped in the successful distribution of various vaccines worldwide, and as covid-19 vaccines finally roll out to more countries, they'll be another way of ensuring proper temperatures.

Then there are the refrigerators themselves.

In 2009, engineers at the Bill and Melinda Gates Foundation in Seattle started designing an off-grid refrigerator for use in places

with little to no infrastructure for the cold chain.

The result was the Arktek—a barrel-size super Thermos intended to refrigerate vaccines or other biological samples. Different substances can prime it to store materials at different temperatures: dry ice can keep samples at -80 °C, while a mixture of water and ethanol can set the temperature at around -20 °C. If it holds 450 vials, they will stay chilled for three to four weeks, while 750 vials can remain cold for at most two weeks, says Daniel Lieberman, Arktek's inventor at GHLabs, a nonprofit created by the Gates Foundation. Because the device has no electrical parts, it's extremely hard to break: it will be rendered useless only if someone manages to puncture the vacuum seal.

The device was first put to the test in 2014, when Ebola ravaged villages in West Africa. The vaccine available at the time, developed by Merck, required refrigeration at -80 °C. When Arktek was deployed in the field in 2015, it played a role in vaccinating 8,000 individuals and helped stop the Ebola outbreak.

Since then, the 3,000 or so units have remained in countries throughout Africa, says Lieberman, and are used to store routine vaccines for diseases such as measles, polio, chicken pox, and hepatitis. Various international organizations, such as UNICEF and Doctors Without Borders, purchase Arkteks for countries that need them. Around 1,000 new units have been manufactured specifically to handle distribution of covid-19 vaccines, says Shouda Li, the general manager of the device's manufacturer, Aucma, which is based in China. Those new units will be sent to South and Southeast Asia, the Middle East, and some countries in Latin America, Li says.

There is one more experimental approach in development—one that would avoid the cold chain altogether, says Weissman. Some developers have dehydrated the current covid vaccines. Dehydration would make the dose stable at room temperature indefinitely, says Weissman, until it is reconstituted right before use. The drawback is that it would make the vaccine harder to produce: dehydration adds extra processing, which would significantly increase the manufacturing costs. Still, Pfizer says it may have this ready by 2022.

For mRNA vaccines, reliable room-temperature storage would be a game changer, eliminating one long-standing obstacle to vaccines for all.

This story is part of the Pandemic Technology Project, supported by The Rockefeller Foundation.