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Exit Interview: Ken Kaitin On 35 Years At Tufts Center For Study Of Drug Development

by Ben Comer

At the end of December 2020, Kenneth Kaitin retired as director of the Tufts Center for the Study of Drug Development after 23 years in the role, and 35 years working with the CSDD. Kenneth Getz, previously professor and deputy director of the CSDD, succeeds Kaitin as director in 2021.

In late 2020, *In Vivo* spoke with Kenneth Kaitin about his tenure as director at the Tufts Center for the Study of Drug Development (CSDD), and the state of pharmaceutical and regulatory science. Kaitin was instrumental in expanding the CSDD's focus beyond the US market, enhancing the CSDD's professional development courses in pharmacology, drug development and regulation, and in building a multidisciplinary team of researchers, including health economists and attorneys.

Kaitin created the Tufts CSDD "Impact Reports" series, a bi-monthly subscription newsletter aimed at distilling the center's research findings into actionable and accessible information for executives and other interested parties. The Tufts CSDD is also well-known for its study – repeated every 10 years – on the average cost to develop and receive approval for a new pharmaceutical drug. Controversy over the cost figure – the most recent study, in 2014, put the average cost to develop and receive marketing authorization of a new drug at $2.6bn – is due in part to "unclear industry messaging," said Kaitin.

Q **In Vivo: You have worked at the CSDD for 35 years. What were your goals when you became director, and what accomplishments are you most proud of?**

A Kenneth Kaitin: When I came to the Center it was very US-based. We didn't have a lot of stakeholder engagement, we didn't work closely with industry on a lot of topics, for

a variety of reasons. But the environment has changed, which enabled us to change as well. We operated more as an academic-style group, our publications were focused primarily on peer reviewed journals, and one of my goals when I came in was to give us more of a global reach, to become a global organization that is focused on global drug development issues because it was becoming more and more clear that drug development was a global enterprise. There's no such thing as a US-developed and approved drug anymore, everything is global in nature.

KENNETH KAITIN

I also wanted the staff to be multi-disciplinary. When I started, everyone in the group was in the health sciences, and I thought that to really get an understanding of the area of pharmaceutical development, you need economists on the staff, a lawyer to focus on some of the legal issues, perhaps an MBA who can look at some of the industry management issues. I set out to do that and created what I think is the only multi-disciplinary academic group that focuses on pharmaceutical sciences. At one point we had two economists; one of them is still with the Center. We've had two lawyers over my tenure, we have an MBA now, we have a medical consultant, a pharmacologist and a pharmacist. I wanted a multi-disciplinary approach to start looking at some of these complex issues. I also wanted more stakeholder engagement. When I first came on board, there was clearly an adversarial relationship between industry and the FDA and regulatory authorities. The Tufts Center at the time when it was set up, which was at the University of Rochester in New York, it was set up as a group to really explore the dynamics between industry and the FDA, as well as to understand the intersection of regulation and innovation. That's something that nobody had really looked at, in fact the first study that the Center did focused on the lag in drug availability in the US relative to the UK, and the

impact of regulation on that lag. And the bottom line was that the FDA's slow approval process was contributing to delays in drug availability in the US, which became known as the "drug lag." The [CSDD] founder Louis Lasagna and the first director, Bill Wardell, testified in congressional hearings on the drug lag, and there was an FDA Commissioner at the time, Donald Kennedy, who said there is no drug lag, and published an editorial in the Journal of the American Medical Association claiming there was no drug lag. Lasagna and Wardell provided actual data to show that there was a drug lag, and Congress fired Donald Kennedy as FDA Commissioner; he ended up becoming the president of Stanford University, and I actually met up with him later on when I was doing a post-doc out there. But it was a revolution in thought, that what the FDA did could actually affect therapeutics and patient care. It was important for the Center and the group that was going to serve as an arbiter of these issues to not appear as if it was too close to one sector or the other. So there was a wall between us and industry. It became clear over time, and especially over the last 20 years that I've been at the Center, that the wall has either vaporized or has been removed. I don't think that there is an adversarial relationship at all between regulators and the regulated industry anymore. In fact, there's a sense of common purpose, to work together to ensure the best medicines reach patients who need them. That's happened over a long period of time, but what that has meant for the Center is that we can now start working more closely with industry, because the FDA would not look at that as a betrayal. Or it wouldn't make us look as if we were biased.

So, the working groups that we started running 15 or 20 years ago often included FDA people. FDA employees would come contribute to the conversation because it was clear that if it was the industry's problem, then it was patients' problem, and if its patients' problem, it's FDA's problem. It all became part of one big community. That's something that I really wanted to accomplish with the Center, I wanted it to become more engaged with stakeholders that were involved in bringing new products to the market.

The other part is communication. I mentioned that we were sort of an academic-style group, all of our publications went to peer-reviewed journals. When we started

working more closely with some of the groups like FDA, but also industry groups, there was a demand for more rapid availability of our findings, but also findings presented in a more accessible format. I wanted to create other means of communicating our research results. I created the Tufts CSDD Impact Report, which is now about 25 years old, and other publications that we put out, white papers and other things, that distill our findings, make them easily accessible to all of the folks that are interested in these topics. And they gained tremendous recognition and acceptance.

And there were a few other things I wanted to do. I wanted to expand our professional development programming. Louis Lasagna, the founder of our group, was a visionary, an MD clinical pharmacologist, and he had a strong conviction that people who go into industry and are involved in clinical drug development have to learn on the job. There's no training that they were getting in medical school or anywhere else that would prepare them for what they had to do. So, he created something called the CSDD Post-Graduate Course in Clinical Pharmacology Drug Development and Regulation, which actually predates the Center by two years. It was first created in 1974. I actually took the course as a graduate student in 1978, and then again in 1979, but the idea was to provide structured training in clinical drug development to help people who are involved in the process do a better job and be more efficient. At the time, and I know this because I was there very close to its founding years, it was all industry people, all men, they were all white, and there were about 25 people who would attend each year. They would meet in Rochester, NY, where I was a graduate student, and they would do their course and their learning.

It was clear that as the enterprise for drug development expanded, the course had to reflect that. One of things that I really worked on was to expand the scope of our course so that it would include pre-clinical topics, regulation was already in there, but it would include everything from biopharmaceutical development to sales and marketing, CMC, pharmacoeconomics, lots of topics that were not covered in the original courses, because there were people out there that even if they weren't

directly involved in CMC, I thought that they should know something about that area. They should understand what's involved in quality control, quality assurance and those areas, they should understand something about the biopharmaceutical industry. We've also recently included courses on financing, which even though very few people involved in financing take the course, it gets one of the highest reviews of any of the topics that we cover, because they're all so interested in how this industry is financed. That was my goal and I think we achieved that over my time period. I've been running the course as the director for about 25 years now, and I think we've achieved a program that is unlike any other program that's out there. It's a one-week intensive course, and it's always well-received, we get a lot of folks from industry, as well as from regulatory authorities, the Department of Defense always sends a large contingent. We were up to our 48th annual course this coming February, and it's the first time we've had to cancel it. We're disappointed to not get to 50 before we had to stop, but we will pick it up again in the following year.

One of my goals as a senior fellow at the Tufts Center is that I will continue managing and running that course, so I'm pretty happy about that. But I also wanted to offer other programming, so I expanded our professional development to courses on R&D management, as well as a very popular course that we've done for 19 years on leading drug development teams. We just held our first version of that course remotely, and it was wildly well-received. We had over 50 people who took the course, and I'm very pleased with how that course runs as well.

The last thing I wanted to do – and I'm ending on a down note – but I wanted to create within my institution more recognition and awareness of the importance of the field of pharmaceutical science. What I ran into was a wall in the medical side – not in the biomedical graduate side, where more and more graduate students are going into careers in industry, so they wanted someone to expose the graduate students to these topics, and I was happy to do that through course work and everything else. But there is still this wall of resistance in the medical school side, an idea that medical students should be kept at a distance from issues related to the drug industry. If you just look at Tufts in general, the building that the medical

school sits in is the Sackler building, and the graduate school of biomedical sciences, up until recently, was the Sackler School of Biomedical Sciences. They've struggled with this issue of looking as if they are too closely aligned with the industry and in particular, with the Sackler family. Despite my 35 years of trying, I've never been allowed to give a lecture to the medical students on these topics, even though I've tried to reassure them over and over again that I'm not in the industry, that I'm not talking for the industry, I'm not supporting the industry, all I'm doing is explaining how the drugs they are going to prescribe get into the pharmacy. And that just did not cut it. So that's kind of disappointing. Not all medical schools are like that. I've actually spoken a lot at other medical schools. I have a faculty appointment at the Shanghai Medical College in Fudan University in China, and they are very interested. I've spoken more to their medical students than I have to the Tufts medical students, whom I haven't spoken to at all. That's disappointing. And I report to the dean of the medical school, so it's not as if I'm not connected to them, and yet I was never able to make any headway there. All of that said, I'm very proud of what the Center has accomplished, through its research, through its professional development programs, through its communications and outreach and how it's run. I think that we are unlike any other group, I think we're the only multi-disciplinary group that focuses on these topics, and I have been extremely privileged and proud to have served on the staff and as director of the group for so many years.

Q **Under your leadership, the Tufts Center became well-known for its product development and approval cost estimate, which has been praised by the industry and criticized by detractors who think certain costs are inflated. What is the legacy, or impact, of the Tufts cost estimate?**

A It's an interesting topic.

We've always been known for our benchmarking studies, including our studies on drug development times and clinical success rates. Those are all used extensively in industry and by regulatory authorities, but they don't attract nearly as much attention as the cost studies. And the view is that the cost of drug development is used by industry as an excuse to charge high prices. My view on all of this is that we do a very detailed, complex analysis and economic evaluation of drug development

costs. We collect enormous amounts of actual data from the folks who develop the drugs. The notion that we shouldn't get this information from the industry is kind of silly in my mind, because where else would you get it, they are the ones developing the products. We've been in existence for 45 years, and we do these studies once every 10 years, so we have four studies that use very similar methodology. I think back to a study in the early 1990s, when the figure was $231m to bring a new drug to market. And Congress was outraged that this figure was being used. Rep. Henry Waxman (D-CA) commissioned the Office of Technology Assessment (OTA) to do their own analysis of drug development costs, because this figure could not be right. So, the OTA actually started working on a project, and they came up, independently, with exactly the same methodology that we used, however they used a higher opportunity cost discount rate. Their figure, instead of $231m, came out to $353m. And this immediately was buried. We actually take a very conservative approach to calculating these costs.

Now there are assumptions made in the study, and if you understand the study, then you understand what those assumptions are, but I think a large part of the hostility that this creates in the groups of folks that are hostile to the industry is created by the fact that the industry's messaging has not been clear. When we put out our most recent study at $2.6bn to bring a new drug to market, the industry immediately started using that in their promotional materials to say that they have to charge a lot of money because the Tufts Center says it costs $2.6bn to develop a new drug. And then if our state legislature says we're developing a pharma transparency bill – which many of them have been working on, some have actually passed – and we want to know exactly what you spend to develop the drug so we can assess whether the price makes sense, the industry's response is, the cost of development has nothing to do with the price. Any reasonable person would scratch their head and go, you've got to be kidding me, you're being two-faced on this. On the one hand, you say you have to charge a lot because it costs a lot, and on the other hand, the cost has nothing to do with the price. Which one is it? And here the industry has never figured out how to convey that message. I speak on this all the time, I'm always asked to go out and talk on this issue, and the bottom line is, both of those comments are correct. The

industry has to earn enough to cover the average cost to develop a new drug, but the price of an individual product is based on the value that the product provides, it's not on the cost of development. The cost of development is a sunk cost, as any economist would say, and so it has no bearing.

Nonetheless, we're an easy target for those that are attacking the industry. The culmination of this was a on 1 April, 2016. There was something called Pharma Greed Day, and activists, including Act Up, all around the world devoted that day to arguing that the prices of pharmaceuticals are too high, and that the pharmaceutical industry is greedy. They demonstrated in front of Pfizer in New York City, in front of PhRMA in Washington DC, in front of pharma companies all around the world ...and where did they choose to demonstrate in Boston? They demonstrated in front of our office. Our office! Why did they do that? Because the messaging by industry makes it easy for them to say that the industry is using our inflated figures to justify their prices. If the industry on day one stopped doing that, nobody would claim that we were inflating the figures, because if you really get down to it, it's almost impossible to forge or inflate those figures. We get those from so many different groups within the industry, the likelihood that not only within a company but across an industry, they are all working together, they are all colluding to give us inflated figures ... it's almost impossible to imagine. Any other group that does a study independently comes up with a figure that's equal or similar to ours. In fact, when we did our previous study, Deloitte did a study on the cost of drug development, and they came up with twice our figure, but they included marketing costs. And if you consider that marketing costs are about the same as development costs, then it makes sense, our figures would be the same. At the end of the day, we stand by the figures.

Q **How would you describe the state of regulatory science at the FDA? Are there changes at the FDA that you would like to see?**

A Let me start by just quickly saying what I think have been the changes in the landscape in the years that I've been with the Center. I mentioned earlier that the adversarial relationship has changed. That doesn't exist anymore, and a large part of what we've seen that has changed has been the result of HIV/AIDS.

AIDS was absolutely transformative. It was in the very early days of my first few years with the Center, and it was really coming to a head, it upended that relationship between industry and the FDA, regulators and patients, and at the end of the day, it required a whole change in the dynamics among all the stakeholders. And the result was the Prescription Drug User Fee Act, which I don't think would have happened without AIDS. Even though there were calls to pay for user fees in the past, in fact [former President] Reagan proposed it when he was president, way before this. But it never really happened until AIDS, which sort of paved the way. The most significant thing with the user fee legislation really was the speeding up of the overall approval time, and also, equally important, the fact that the FDA could do regulatory reform, every five years, without having to wait for a calamity of some sort, or a crisis, which is what existed in the past.

Jumping to today, I think the relationship today between the FDA and the industry is solid, they are very responsive to the changing environment. I know that the FDA is working hard on issues that are prevalent and important going forward, like the use real-world evidence, patient engagement, finding ways to incorporate artificial intelligence and machine learning into the drug development paradigm. It is also continually looking for ways to speed up not just the approval of products, but the development of products, with mechanisms like the Breakthrough Therapy Designation and other mechanisms for speeding the development or using the push/pull mechanism to increase not only the incentives to invest in early-stage development, but also the rewards of bringing a successful product to the marketplace. The FDA has shown that it is capable of playing an active role there, and it's been very successful.

Going forward, the changes that I'd like to see – we have some major disparities I think in the focus of developers. You can look at how many drugs are approved every year, and right away you'll notice that oncology products lead the list. In fact, in an analysis that we just did of the last 10 years of drug approvals, there were 102 oncology products that were approved, but only 48 or so in the next therapeutic area,

which were anti-infectives. There are very significant medical needs in the area of cardiovascular disease, where heart disease and heart failure still represent the number one killer in the US and in many industrialized countries increasingly around the world. Areas like Alzheimer's disease and diseases of aging, neurodegenerative diseases like Parkinson's, companies are starting to shy away from those areas because they can't make the big bucks like they can make in oncology, they can't do narrow indications the way they can in oncology, genetic diseases and immunologic diseases, and also overall, you're not getting those kinds of scientific rewards that you would in oncology. For example, our understanding of the genetic mechanisms of cancer have far exceeded those of any other disease area, so that provides all sorts of new leverage for companies. I'd like to see the FDA, and the NIH as well, commit themselves to increasing incentives to invest in and develop products for these other indications where the morbidity and mortality are high, human suffering is extensive, economic impact is great, and yet, companies are steering clear of it.

I was on a call yesterday talking about infectious diseases, and the fact that a lot of companies have moved out of the infectious disease area. Most of the questions I got after a talk were, "Will the pandemic change that environment? Will people finally see how important it is to address some of these infectious disease issues?" My thought is, yes, initially. I've never seen a time where the average person is so knowledgeable about what it takes to get new drugs into the market. A lot of people can now talk about Phase II and Phase III trials, as if they've been doing drug development their entire lives. It's very impressive. But I don't think this will last. Because at the end of the day, we had a pandemic, companies got involved, they found a vaccine, and the vaccine was approved in less than a year, and so why don't we wait for a catastrophe in infectious diseases and then we'll worry about finding a treatment. And that's just not the way to do it. We have to plan in advance for these things to prevent human suffering.

I think the FDA has a role to play in finding ways to encourage investment and development in some of these underserved therapeutic areas. And the reason why I bring NIH into this too is because I think the NIH also has been overly focused on

oncology and some of these genetic, narrow indication disease areas. I think they need to refocus on basic research as opposed to translational research. My fear is that within academic institutions, it's become clear that if you're a basic researcher, you're not going to get a grant from the NIH, or it's going to be very difficult. You have to focus on translational research, but translational research depends on basic research. If there's nobody doing basic research anymore, translational research is just going to dry up

Q **Do you have any thoughts about the types of incentives that could be used?**

A It's different depending on the therapeutic area. In infectious diseases, it's a market issue. You can come up with a breakthrough infectious disease agent, and bring it all the way to the market, but the Medicare system in the US underpays for infectious disease agents. There was an act called the Disarm Act, that was proposed in 2019, and now there's the [proposed] Pasteur Act, all of this attempting to address the issue, but it’s not getting much traction in Congress, it's not going anywhere. Until infectious diseases are addressed from the market approach, I don't think we're going to see much progress there.

In cardiovascular disease, it's remarkable. Think about the number of people who die from cancer every year. It’s important and it's notable, but so many more people die from heart disease, and yet that doesn't get nearly the emotional draw that cancer does. I'm not saying cancer isn't emotionally draining, but heart diseases are also important. In heart disease and in CNS indications like Alzheimer's, there needs to be more of a rallying cry, an Operation Warp Speed for Alzheimer's disease. Or an Operation Warp Speed for cardiovascular disease, or stroke. These are the areas where you need more public buy-in and more basic research. The idea that companies developing Alzheimer's drugs are still for the most part using beta amyloid plaque or the tau protein approach to try and treat the disease, and yet we've shown over and over again that you can reduce the tangles, and reduce the plagues, but people still have the symptoms. How many times are we going to keep doing this? We need new science and we need a new understanding.

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Q **In addition to the COVID-19 pandemic, this year also brought social justice and inequality back into the spotlight. The Tufts Center published a disturbing study examining the disparities among clinical trial participation rates, among racial, ethnic and gender groups, earlier in 2020. How has the industry benefited from this national conversation we've had on race over the last year?**

A I think this is a 100-car freight train that's just starting up. The first few cars are moving, and the last few cars, even though they're part of the moving train, their movement is imperceptible. I think that there is a change, and it's happening. Look at number of studies that were done on COVID that really emphasized the need for diverse patient populations, to make sure that the enrollees in the clinical trials represent a broad swath of the people who are suffering from COVID. I think all of that was positive. I think part of what the Center has done is to highlight some of the causes. Part of it is the fact that the principle investigators at a lot of these sites are not diverse. The investigative site landscape lacks diversity. You have to address this from multiple angles, but the awareness of the issue I think is more than I've ever seen in the past. It's growing and is definitely moving in the right direction.

A This movement goes way beyond just the clinical trials and who's being tested, even looking at company boards, and the data on diversity in senior management, there is a much greater awareness of the importance of these issues going forward. There has been a focus on diversity in clinical trials for quite a while. We've been doing our studies in this area and have gotten a lot of positive feedback that those in

Expanding The Tent: Improving Trial Participation Among Under-Represented Patient Populations

By Ben Comer

08 Apr 2020

The biopharma industry has struggled to recruit patients into clinical trials that adequately reflect the diverse patient populations they hope to reach with new products. Failure to improve minority subgroup participation now will cost trial sponsors later.

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the sites and those in the companies recognize that this is an important issue. Now whatever the objectives, whatever the rationale, if industry is saying we want to include a diverse population, not because it's the right thing to do but because we want to be able to include that patient population in our label, then so be it. It doesn't make any difference to me why they are doing it, as long as they do it. I think at the end of the day, we're moving in the right direction, it's just that it's moving slowly.

Q **You mentioned staying on as a senior fellow at Tufts, and you'll continue your professorship at the Shanghai Medical College at Fudan University, and you're also editor-in-chief of *Expert Review of Clinical Pharmacology*. What are your priorities going forward?**

A I wrote to *Expert Review* that I would like to step down as editor-in-chief, so I won't be doing that. But I think it's such an exciting and dynamic area. It's hard to just walk away from it, I mean I'm not that old. I have a lot that I think I can continue to offer, but I did it at one place for 35 years. One of the things I'd like to do is be free of some of the administrative responsibilities that I've had as director. This gives me the opportunity to do a lot of the stuff that I really enjoy, which is advisory boards and working on boards of directors where I actually can see how some of the work of the Center is incorporated into R&D strategy. I also want to continue to write and consult and do those kinds of things, I just want to do it at a rate that's more relaxing for me, and keeps my intellectual stimulation high.

Q **Any final thoughts you'd like to share?**

A I'm incredibly thankful for all of the folks I've met and interacted with over the years. I've had a great opportunity to travel the world and interact with regulatory authorities in different regions. I think the dynamic nature of this sector is just extraordinary. Part of what is so interesting about being in China and going there regularly now, and having the appointment at Fudan is that I get to work a lot with

> the local industry and see how the provinces in China are investing heavily in creating an infrastructure for pharmaceutical R&D. It's sort of like the Western pharma sector on steroids. Incredible amounts of money, energy and activity in this space, and it is so exciting. I love going there, I love working with the companies and seeing how much progress they've made, and the changes within the regulatory environment, and how it's done there. Nothing has to go to a Federal Register, if the government feels this is the way to go, it goes, it happens. I am so thankful and feel so privileged to have had the opportunity to experience these things and work with all these people, and many of them have become friends as well as long-time colleagues. I've really hit the jackpot in terms of careers.