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Congressional Hearing on the Impact of Medical Device Regulation on Jobs and Patients

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Mr. Chairman, Ranking Member DeGette and Members of the Subcommittee, I am Dr. Sean Ianchulev, and I would like to thank you for the opportunity to share my experience with the FDA and the regulatory process and its impact on patient care, innovation and the development of new technologies. The opinions I share are solely mine and not of the entities I am associated with and they reflect my experience as a physician, innovator and developer of new therapeutics and devices.

I will support the following statement with additional information.

I believe we have an overly burdensome CDRH regulatory process which negatively impacts all stakeholders in the medical device field - innovators, physicians, patients and investors. It probably negatively impacts the agency itself which devotes enormous diligence to maintain integrity, expertise and vigilance – all good causes which deserve better return on the effort invested. Much value can be obtained from process improvements that would increase efficiency, transparency, communication and streamline the regulatory process to achieve operational excellence and meet the needs of the new decade.

As a clinician and eye surgeon, I use medical devices and therapeutic intervention to treat serious medical problems and prevent blinding conditions such as glaucoma, cataract and macular degeneration. In fact, the most frequently implanted medical device (more than 3 million implantations per year) is the intraocular lens implant for cataract surgery - a product of groundbreaking innovation which transformed clinical care and patient wellbeing and is considered one of the best examples of a safe and effective clinical intervention today.

As an innovator I have considerable experience with both divisions of the FDA - the CDER and CDRH. As a drug developer who headed the clinical research and development of one of the most successful approved biologic therapies for eye disease (Lucentis® for macular degeneration) I have the added comparative experience with the CDER whose input and oversight were critical in the execution on this highly complex, rigorous therapeutic program and resulted in the commercialization of a groundbreaking therapeutic with more than \$2Bn annual sales and great impact for patients, physicians, industry and jobs. Simultaneously, as a physician executive and chief medical officer for a medical device company which has raised more than \$50 million to finance the development of an eye implant - a Class III device and one of the few medical devices in an ongoing PMA process, I have direct experience with the

CDRH in today's environment which gives me a perspective into some of the manifest challenges at the division.

Lastly, as a health care professional who is licensed both in the US and the EU and who frequently participates in clinical, academic and professional exchanges/collaborations in Europe, and spends significant amount of time with fellow European clinicians, I am acutely aware of parallels and contrasts in the changing paradigms of clinical practice and access to new technology across the Atlantic.

Physicians such as myself feel privileged to be educated, to practice and advance medicine in the US where access to cutting-edge innovation and latest technology has been the marquee of American health care. Medical devices represent a significant part of this innovation particularly for a surgeon like myself and in a field such as ophthalmology which boasts a high level of device innovation. As a leader in the medical device field over the past several decades, the US has been able to deliver enormous benefits to patients while cultivating an environment of innovation and expertise with simultaneous economic benefit in terms of highly qualified jobs. In my field, there are many examples but most salient is the fact that we can now successfully treat cataracts (one of the few chronic degenerative diseases to be cured) with a safe and effective implant technology which was developed mainly in the US in the 1980s and 1990s and perfected more recently.

Since regulatory approval is the gateway for allowing physicians to use pioneering technologies, there is no doubt in my mind that the US regulatory leadership in the past with a streamlined and responsive best-in-class regulatory process was in part responsible for these advances as it encouraged innovators, physicians and industry to deliver new safe and effective therapies. Similarly, there is no doubt that if we lack the necessary leadership and regulatory innovation today, it will be particularly detrimental in a global world where knowledge and expertise have no boundaries.

Since 2007, the review process for devices appears to have changed with a momentous swing towards a state of hyper-vigilance and conservatism which has significantly increased the burden, cost and timelines for the introduction of new devices. The sharp decline in the productivity of the regulatory pipeline (with a decrease in PMA filings- only 15 in 2009) is concerning at this very juncture when few diseases have been cured and there is great unmet need for new and better therapies to address the aging population.

Today, the overburdened regulatory process poses several dilemmas with real impact on all stakeholders, including the FDA.

The Patient Dilemma:

The direct patient experience is always the best indicator for whether we fail in our job in the health care field. As an eye surgeon I treat patients who are losing their sight either due to advancing cataracts or glaucoma or macular degeneration. As a physician who

not only delivers the standard of care, but also innovates in the ophthalmic field, I have failed on a number of times to treat patients with what I would have thought is the best therapeutic approach. On several occasions, I have had to refer patients to other countries (Europe and Canada) to receive the necessary treatment because the medical devices were not available in the US and were years away from being commercialized. I appreciate the counterpoint on fully characterized product efficacy and safety for FDA approval, but the already available worldwide clinical experience from colleagues and the peer-review literature well ahead of FDA registration in the US can inform physician clinical judgment and allow educated patient decision on the best therapeutic approach. In reality, even with approved FDA treatments, the product label rarely predicts the individual patient response and clinical experience.

In the ophthalmic field, virtually most technologies that were PMA approved in the US in the last 5 years, as well as many new technologies currently captive in a convoluted approval process (such as new Intraocular lenses, minimally invasive glaucoma stents, other intraocular implants), have been available in the rest of the world for many years, allowing foreign clinicians to practice advanced medicine and participate in new improvements and future innovation. In the US, the slow approval process limits physician access to such technologies even if there is ample data and experience from abroad. This leads to another dilemma: FDA or physician control on prescribed treatment choice at the point of care. Replacing physician judgment, experience and decision-making with a product label is not a good idea and seems to represent a dangerous trend in the more recent regulatory philosophy and process in the US today. While Congress never gave the FDA a mandate to regulate physician practice, such is being effectively exercised by curtailing access to new technology and products. Obviously, the balance between prescriptive labeling and physicians' access and judgment on how to use these new technologies is very different in the US and other developed countries, such as EU, Japan and others.

The Innovation Dilemma:

The ophthalmic field could be a good example as it is one with traditionally high level of technological innovation with a multitude of surgical and diagnostic instruments such as intraocular implants and lasers. However, due to the systematic problems of increased cost and hurdles of the regulatory process, there are multiple classes of innovative technologies that are languishing in a state of uncertainty or prolonged validation. These include new and potentially superior intraocular lens implants for cataracts, stent technologies for minimally invasive treatment of glaucoma and iris reconstruction implants and others such as cross-linking technologies. These are not single products but often classes of products and multiple companies affected.

In my opinion, we should be doing a better job of cultivating these innovative approaches in a much more hospitable and expedient regulatory environment. In fact, most of these technologies are registered and available products in the European countries under the CE mark.

Avoiding a long discourse on the meaning of this symptomatic state, it is not hard to see that we have failed to deliver new and innovative device technology to patients and clinicians in the US.

The Developer's Dilemma:

One of the most palpable dilemmas that comes up among medical technology developers is the 510K vs. the IDE PMA pathway. The IDE PMA process for Class III devices has been the most affected with the highest degree of regulatory uncertainty and slow-down. This has alienated innovation in this important category which is evidenced by the very few PMAs granted more recently (only 15 in 2009). This is most concerning because the PMA is the "lifeblood" of true innovation and pioneering in medical devices - some of the most significant advances derive from the IDE/PMA process such as cardiovascular stents and other implants. The process of securing unconditional approval and initiation of an IDE in this class of devices has become so burdensome that I am aware of timelines exceeding a year and a half before the sponsor can secure full unconditional approval - that is just to start the study enrollment. *As someone who has worked with the CDER drug division on a complex biologic program before, this makes a device IDE a hard proposition even for a well funded biopharma.* In fact, a fresh example from the ophthalmic device field, where it is much easier to approve a drug for the treatment of glaucoma with primary efficacy endpoints between 3 to 6 months only, versus a minimally invasive stent with CDRH requirements of 12 months for the primary efficacy endpoint. In fact, I stand corrected - within the last year, the CDRH requirements for the primary efficacy endpoint in this indication increased further from 12 to 24 months without clear transparency, advanced notice, stated rationale or guidance documents.

Another developer's dilemma facing device innovation is operating in the US vs. the rest of world. Several reports provide informative data and statistics on this, and in my experience, there is an increasing trend where companies not only do early clinical feasibility testing abroad, but initiate their main validation studies, their registration programs and more recently their primary commercial activities. And since US doctors will not have experience with these technologies, it may not be long before patient care and referrals follow the offshore route. This does not mean to advocate that the European CE mark process is perfect for implementation here, but if the *FDA were to do a robust randomized comparative trial/assessment between the European and US registration systems, the regulatory performance outcomes may not only be statistically significant but clinically and socially meaningful.* And there are examples (probably not just a few outliers) where the delay in approval timelines between CE mark and PMA exceeds half a decade.

The Academic Dilemma:

As a physician who is also a clinical faculty and teaches resident clinicians, in my professional path, I have been associated with two leading medical research

institutions- Harvard Medical School, Boston, MA and UCSF, San Francisco, CA. Research and innovation is critical to their missions. The only way to innovate is to move technology from the labs to patients, and the vehicle for this is industry, enabled by the technology transfer process. A bottleneck in the regulatory process will invariably affect our ability to conceive and initiate technological innovation in academia, hurting education, universities and researchers.

In summary, my experience is consistent with some of the recent data suggesting an overburdened regulatory process which impacts negatively on all stakeholders in the medical technology field - patients, physicians, innovators and investors. Significant improvement can be realized by increasing efficiency, transparency, communication and streamlining the regulatory process to meet the needs of the new decade.