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For a Hearing Entitled "The Next Frontier: Translating Biomedical Research into Personalized Health Care"

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Chairwoman Eshoo, Ranking Member Guthrie, and members of the Health Subcommittee, thank you for inviting me to testify on a very important topic: Translating Biomedical Research into Personalized Health Care.

By way of background, my name is Dr. Amy Abernethy and I am the President of Clinical Studies Platforms at Verily. Launched in 2015, Verily's mission is to make the world's health data useful so that people enjoy healthier lives. Verily develops tools and devices to collect, organize and activate health data, and creates interventions to prevent and manage disease. My area of focus is clinical evidence generation, including prospective clinical trials, real-world data, and real-world evidence.

I am relatively new to Verily, having joined in July of this year. I had the pleasure of working with many members of this subcommittee when I was Principal Deputy Commissioner of Food and Drugs at the Food and Drug Administration (FDA) and the agency's acting Chief Information Officer. I appreciated the Committee's commitment to ensuring that FDA had the authorities and resources it needed to perform its critical public health mission and regulate effectively in a field that is defined by constant change and innovation.

I look forward to continuing that strong collaboration. There is no question that research institutions, the private sector, federal agencies, and Congress must work together to advance biomedical progress in a rigorous, responsible, and transparent way. My views in this area are informed by my experience as a leading researcher and expert in clinical evidence generation and healthcare data—and by my time as a practicing oncologist, caring for patients with melanoma and other cancers.

We are living in a time of unparalleled advances in science, technology, and capabilities to improve health. What is more, the constant learning and evolution of science, technology, and policy are a moral imperative—and an expectation held by the vast majority of Americans. However, there are significant challenges that need to be addressed before we realize our goal of translating biomedical research into something that benefits all patients. Clinical research and data gathering needs to be fully inclusive and equitable, and the information generated and used must represent the needs and values of all citizens. Safety and privacy must continue to be top priorities. Wide accessibility of new interventions is critical—we must achieve healthcare

personalization in a way that benefits all patients, and public health more broadly. We must be prepared to scale and deploy in times of healthcare crises, including but not limited to global pandemics on the scale of COVID-19.

Personalization in healthcare is a core goal for improving the health of all people.

This hearing focuses on a goal we share: personalized health care. This goal has been described in different ways and with different terminologies over the past several years, but I want to highlight a few of its core components: (1) the imperative to improve the health of all people; (2) the recognition that each patient is a unique individual and that, to be maximally effective, healthcare must be appropriately tailored to each individual; (3) the rapidly expanding ability to develop, test, and deploy interventions that are optimized for individual patients; and, crucially, (4) the need to evaluate and monitor health interventions continuously to make sure they are working well, under real world conditions, for *all* patients.

Among the many important lessons of COVID-19, perhaps none is as compelling as the reminder that public health depends on reaching all people in our society: making sure that appropriate care is accessible to patients when and where they need it. This will be no less true after the pandemic, when we in the health ecosystem will, appropriately, continue to be judged on our ability to address the health needs of individuals regardless of their location or circumstances.

The good news is that we have an expanding set of biomedical tools that are increasingly capable of being tailored to specific diseases and contexts of individual patients. Cell and gene-based therapies targeted against highly specific underlying causes of disease, mRNA-based vaccines against novel pathogens, digital therapeutics that promise to provide targeted mental health interventions—each of these are real-world examples of the tools that can help deliver personalized health.

Of course, personalized healthcare does not depend solely on biomedicine and technology. Healthcare is also about human relationships—between healthcare practitioner and patient—and human decisions. Increasingly, the relationship between patient and healthcare provider is enabled through technology, such televisits, instant messages, and mobile apps. And the decisions made by healthcare professionals are aided by advancing technologies that make better, more precise diagnoses and provide markedly better information to the provider to support decisions about when and how to intervene in the context of a specific patient.

As we move closer to achieving the vision of truly personalized healthcare, the process of matching a specific patient with the right intervention will get significantly more complex than in the past. It won't just be a matter of matching a certain cancer mutation with the appropriate drug for that cancer mutation. Rather, the selection of the appropriate intervention will depend upon a blend of many features, including a person’s symptom experience (and what symptoms are bothering them the most), the genetic basis for the disease (e.g., the specific mutation), and lots of additional details such as the likelihood for the intervention to work based on a person's background genetics or environmental exposures. Finally, the selection of intervention should account for the personal values of the patient. Personalization in healthcare means far more than

just matching a treatment to specific biological markers—it is the ability to consider many features and circumstances together to support ultra-tailored matching of an intervention at the individual patient level.

To translate biomedical research into personalized healthcare, we need new tools to generate the data and evidence needed to understand both *whether a promising therapeutic or diagnostic tool works* and *which patients will benefit from it.*

The focus of this hearing—*translating* biomedical advances—is a core challenge for personalized healthcare. Translating from research to healthcare is about using data and evidence generation tools that can evaluate whether a diagnosis or intervention *actually works for,* and *provides value to,* the patient. To achieve personalized healthcare, we need evidence about how treatments and other healthcare interventions perform in specific situations, taking into account all of the relevant circumstances of a particular patient. We also need to make sure that evidence generation is inclusive—that it generates the information needed to achieve personalized healthcare across the diversity of patients and healthcare settings.

To enable clinicians to play their part in achieving personalized healthcare, they need a way to quickly sort a large amount of information about a patient and about a possible treatment and then find the right match, in real time, at the point of care.

In addition, we will need evidence generation tools and methods that give us the ability to evaluate the performance of interventions or diagnostics *continuously, over time*. This is especially true in the case of artificial intelligence (AI)-based medical tools. Many of these tools promise to revolutionize certain aspects of healthcare because they learn and evolve continuously. We therefore must have the corresponding capability to monitor the performance of AI tools continuously to ensure they are producing reliable, unbiased results for all patients.[1] Without this capability, there are two options for these new tools: they will either be deployed without the safeguards in place to detect and avoid bias and improper decision making, or else the tools will not be deployed because of uncertainty about their performance, resulting in substantial lost opportunities to patients and society. Both of these outcomes can be avoided if we develop adequate means to monitor the performance of AI-based medical tools after they are deployed to the clinic.

Of course, evidence generation in medicine is an age-old challenge. A great amount of thought and energy have been dedicated, over many decades, to ensure that different components of our healthcare system are based on good evidence. We have requirements that drugs, biologics, and devices be shown to be effective before they may be marketed. We have developed the science and infrastructure needed to deploy large-scale, randomized controlled trials to test a new intervention against a placebo or the current standard of care. And, in limited circumstances, we

[1] Critically, FDA has expressed the expectation for transparency and monitoring of AI-based medical software to "enable FDA and manufacturers to evaluate and monitor a software product from its premarket development through postmarket performance." FDA, *Artificial Intelligence/Machine LEarning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan* (January 2021), *available online at* https://www.fda.gov/media/145022/download.

have deployed payment structures that are designed to incentivize and hold providers accountable for patient outcomes.

However, our existing evidence generation tools are, on their own, simply not up to the challenge of translating promising biomedical advances into personalized healthcare.

The complex, tailored treatments and other interventions that will make it possible to provide personalized healthcare illuminate significant gaps in our capabilities to generate and use evidence to inform healthcare decisions. Personalized healthcare will require substantial progress in our ability to generate the evidence needed to assess whether an intervention actually works for individual patients. This requirement is rooted in the medical and moral imperative to ensure that an intervention is safe and effective for the patient, and the practical necessity to ensure that limited resources are not wasted on interventions that do not provide value to the patient.

While randomized clinical trials are the most powerful tool we have to generate useful evidence, they also come with significant limitations. Many rare diseases affect such a small number of patients that a sizable clinical study is not possible.[2] A traditional clinical trial, however well designed, only captures data during a certain time period in the health journey of a patient, and is therefore unable to follow the long-term safety and effectiveness of a treatment. Even a relatively large clinical trial may not be able to represent the diversity of patients and their circumstances.

Moreover, traditional clinical trials consume substantial resources and, as a result, we only have so much bandwidth to use for evaluating potential new treatments. The solution to this problem is multifold. We need to improve the way we conduct prospectively designed, randomized clinical trials, including with decentralized or virtual technologies, where appropriate. We need to think about evidence generation differently, to ensure we are applying all available, relevant data to a given task. To achieve personalization in health care, we need to make sure we are generating evidence that goes beyond objective, disease-specific concepts and that also includes more human-centric concepts like patient experience, quality of life, values, and accessibility.

Below, I provide a few recommendations on (1) the scientific and technical tools needed to translate biomedical advances into personalized healthcare and (2) the policies that are needed to ensure that personalized healthcare is built on a strong, evidence-based foundation.

What expertise, methods, and tools do we need to translate biomedical advances into personalized healthcare?

Before I provide some ideas on how policies can helps achieve our shared goal of personalized health, I want to emphasize an equally important theme: even with the best policies in place, unless we make meaningful progress in the technologies, scientific methods, and expertise needed to generate evidence, we will not have the information needed to fully understand, quickly and on a continuous basis, whether a product or intervention is truly working for patients. If we underestimate the magnitude of the scientific and technical challenges associated

[2] *See* Janet Woodcock and Peter Marks, "Drug Regulation in the Era Individualized Therapies," *New England Journal of Medicine* Vol. 381, 1678-1680 (October 24, 2019), *available online at* https://www.nejm.org/doi/full/10.1056/NEJMe1911295.

with the use of RWD and other novel tools, we will fail to build the robust evidence generation capabilities needed to translate biomedical progress into personalized healthcare.

Fortunately, we are advancing rapidly in understanding how to use new data and technology solutions responsibly to generate the evidence needed to support personalized healthcare. Here are a few examples of ongoing work in these areas and the important tasks to address:

- **We need continued innovation in prospectively designed clinical trials, including formal traditional clinical trials, more pragmatic trials that generate randomized real-world evidence, and trial approaches using decentralized approaches.** The most powerful tool in evidence generation is randomization and we should leverage it whenever possible. In the pandemic, we've learned both the value of comparing multiple interventions simultaneously and prospective data collection leads to higher quality, more reliable information regardless of specific study design. It is a scientific imperative that, w*herever possible*, we use studies that are designed up front—prospectively. We should continue to advance the use of pragmatic clinical studies and decentralized or virtual clinical trial technologies, to make studies more efficient and to reach patients in a wider variety of settings.
- **We must learn how to base decisions on the totality of the evidence.** We need both clinical trials evidence and real-world evidence to generate the breadth of evidence that is needed to achieve personalization in healthcare. Yet we are only beginning to learn how to use real-world data to fill in the gaps from traditional studies and make decisions based on the "totality of the evidence." While the availability of more information is obviously a good thing, more information sources can often make decision making more complex. COVID-19 has provided many examples to illustrate this problem, as public health recommendations—and everyday decisions like when to wear a mask—must be made in the midst of a cacophony of incoming data. To fully realize the promise of real-world data to inform personalized healthcare, we need to recognize this challenge and continue to develop solutions and frameworks for synthesizing the totality of the evidence into efficient decisions. Science-based decision making in the era of personalized healthcare means being able to take advantage of lots of small, incremental evidentiary steps forward, in addition to the larger leaps of understanding provided by traditional, large-scale clinical trials.
- **We need to build the scientific foundation for the use of all available data.** The clinical research community has, for many years now, been working to understand how health-related data from a variety of sources can be used to complement traditional clinical trial data. Examples of this variety of data sources include electronic health records, administrative claims data, information about environmental exposures, patient-reported information, time-series data from a sensor in a watch, biological data including genomics and microbiome, and information about the socioeconomic determinants of health. Doing this effectively and efficiently is no easy task. On the one hand, it can be fairly straightforward, though often expensive, to assemble various sources of real-world data. But, any dataset is only as useful as the analytical methods used to convert the data into useful information—information on which decisions by regulators, physicians, payors, and public health authorities can confidently base their decisions. FDA has worked hard to help push this field forward, culminating in several recent, significant

draft guidance documents on various scientific and technical aspects of using real-world data to inform regulatory submission. For example, FDA's draft guidance on the use of data from registries, issued last month, addresses certain questions about the analysis of registry data, which can include billing or claims data, data from electronic health records, or from medical device outputs.[3] This and other recent draft guidance from FDA represent an important step forward in the discussion of real-world data, but there is substantial work to be done to develop scientific consensus around the use of real-world data in regulatory decisions—and other decisions in healthcare.

- **We need to build the technical foundation for the use of real-world data.** As we develop a solid scientific consensus on the use of real-world data to inform healthcare decisions, we must also develop the technical tools to ensure that real-world data has sufficient reliability, quality, and validation to enable appropriate linkage between different data sources.[4] The health technology industry has a central role to play in making advances in this area, which require strong collaboration between clinicians, data scientists, privacy experts, and software engineers.
- **We need to develop tools to monitor the longitudinal performance of medical products.** As described above, it is essential to develop the tools to monitor the performance of medical products, such as AI-based medical tools, over time. To do this at the scale that will be needed necessarily involves the use of real-world data, collected and analyzed in a continuous manner, to supplement randomized clinical trial data. The continuous evaluation of data involves unique challenges, especially from the analytical and software design perspectives.
- **We must find new ways to apply data for multiple purposes, including through the use of enhanced data governance.** Many different tasks can be informed by the same data—tasks such as describing treatment patterns, defining safety, understanding value, and understanding performance in different populations. One of the challenges to using data for multiple purposes—and to do so efficiently—is to develop the technological architecture to keep track of data attributes related to privacy, patient consent, data ownership, provenance, and other features. This is an important but complicated task and we will need substantial improvements in software and data tools to realize the potential benefits of multi-purpose data.

What policies are needed to ensure that personalized healthcare is built on a strong, evidence-based foundation?

We will also need to make sure the laws, regulations, and policies that govern our health system are designed to incentivize and optimize the use of evidence. Fortunately, we've made great progress in recent years on this front, including in the enactment of the 21st Century Cures Act, a process that members of this subcommittee were instrumental in championing. And the recent introduction of the Cures 2.0 Act is a notable example of the work that has been done by this Congress and the broader community to develop proposals for advancing the way we develop

[3] FDA, Draft Guidance for Industry, "Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products" (November 2021).

[4] FDA has recently addressed several technical areas of RWD generation and analysis in draft guidance. FDA, Draft Guidance for Industry, "Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-making for Drug and Biological Products" (October 2021).

evidence in support of new treatments. The Cures 2.0 Act touches on many of the important policy and technical themes needed to advance personalized medicine, such as diversity in clinical trials, decentralized trials, use of real-world data in post-approval study requirements for drugs and biologics, among many other areas.

Below, I highlight a few themes that should be considered by Congress, FDA, the Centers for Medicare and Medicaid Services, and other agencies responsible for shaping the health policy environment:

- **Incorporating advanced evidence approaches into health policies:** Put simply, when considering a new policy—whether related to regulatory requirements, research, or coverage and payment—policymakers should consider whether the policy appropriately incorporates the novel evidence generation approaches such as the rigorous use of real-world data and investments in the underlying data resources needed to drive evidence generation. Agency decision makers should have the tools to apply the best available science and methodology in support of their decisions.
- **Data privacy and governance**: We must achieve personalized healthcare in a way that provides confidence to the public that health-related data is treated with the appropriate privacy, security, and respect. Policymakers should be aware of technological advances that can allow health data to be used effectively to generate evidence while still protecting patient privacy, to ensure that new policies account for these capabilities.
- **Longitudinal, post-market monitoring of medical products**: Much of the policy framework for medical regulation, coverage, and payment was established at a time when the tools available to monitor the performance of medical products in the post-market setting were, relative to modern techniques, crude and imprecise. As our ability to develop and use evidence to understand how medical products are performing across time, policymakers should look for ways to incentivize—and, where appropriate, require—the development and evaluation of this evidence. As we move toward more personalized healthcare, such policies can reduce the uncertainty about whether a product or other intervention is safe, effective, and providing good value to individual patients across time.
- **Coordination among federal health agencies on data-related issues:** Agencies across the Department of Health and Human Services (HHS) should continue to work together to evaluate how the agencies' own data resources can be coordinated to provide better information to public health decision makers and external researchers. Congress should continue to look for ways to appropriate resources to HHS to achieve this goal.

I will leave you with a note of optimism about, of all things, COVID-19. We have learned a great deal during the pandemic precisely because of robust biomedical research. These advancements have better prepared the country to respond to the ever-changing realities of the virus but also put us in a better position to effectively address future epidemics and pandemics. For instance, in a matter of months we have seen the successful transfer of COVID-related discoveries into safe and effective medical products. Access to rapidly analyzable data is supporting real-time decision-making. Researchers have harnessed real-world data to describe the natural history of

the pandemic, plan clinical trials of new therapeutics, evaluate the real-world performance of diagnostic tests, and support real-world surveillance of vaccines.

On the government side, the rapid and complex decision making in the emergency use authorization context contributed to the science and familiarity needed to use the "totality of the evidence" for the regulatory review of drugs, biologics, diagnostics, and vaccines. Government agencies are working together in trans-government and whole-of-community coalitions to quickly advance the science, build capabilities and promote trust, such as in the COVID-19 Evidence Accelerator.

It is easy to lose sight of these positive developments amid a sea of negative headlines about novel variants, hospital overload and vaccination hesitancy, but there are some real success stories in our response to an unprecedented challenge. The key to leveraging these lessons fully will be taking what we have learned before, during, and after the pandemic and applying these lessons to biomedical research to continually improve care—even when we do not find ourselves in the middle of a global health emergency.