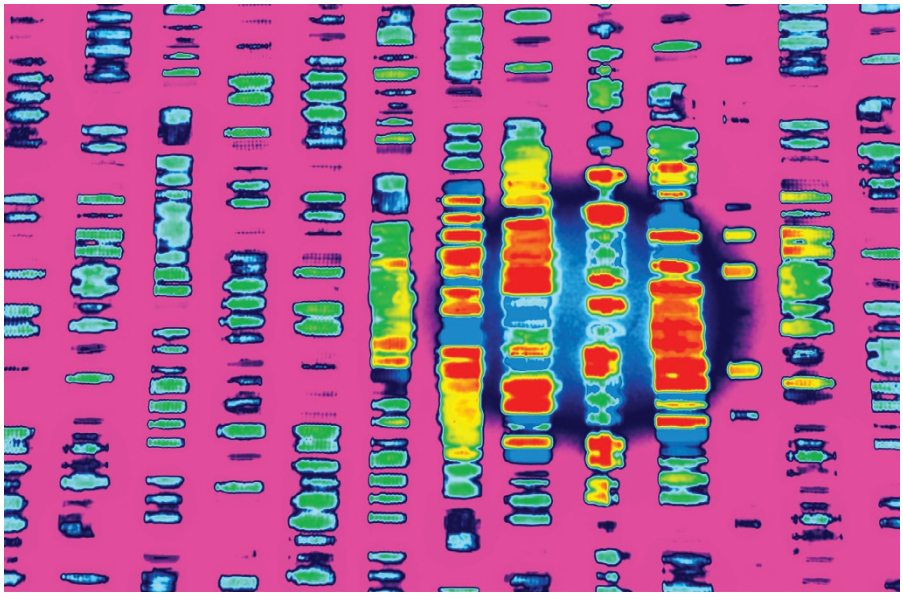
FDA wades into sequencing-based diagnostics regulation

The US Food and Drug Administration (FDA) has proposed a series of practical steps aimed at answering key issues surrounding next-generation sequencing (NGS) diagnostic tests and their use in precision medicine. The agency in collaboration with a number of stakeholders published a Perspective in *Science Translational Medicine* (**8**, 335, 2016) that outlines nine research challenge areas that must be explored to inform the regulation of NGS tests. The 'roadmap' published on April 20 lays out research plans to gain a better understanding of NGS products, how they are developed and the degrees of certainty that each method provides. The publication has drawn a mixed reaction from firms and laboratories that offer NGS-based diagnostics. Some welcome the roadmap but others remain wary of the agency's involvement and the potential hurdles that may result from tightening regulations.

Thus far, the FDA has approved only two NGS-based diagnostics for use in the clinic: Illumina's MiSeqDx Cystic Fibrosis 139-Variant Assay and its MiSeqDx Cystic Fibrosis Clinical Sequencing Assay (*Nat. Biotechnol.* **32**, 111–112, 2014). Other NGS-based tests are developed in-house and offered by laboratories accredited under the Clinical Laboratory Improvement Amendments (CLIA) program. NGS-based diagnostic tests used to identify or predict disease differ from traditional genetic tests in their ability to assess large segments of the genome and to detect variants in an untargeted way. The variants that can be detected include single-nucleotide polymorphisms, insertions or deletions, and copy number changes. The methods used are diverse, from short-read and long-read to nanopore sequencing, a broad spectrum of genetic information that makes it difficult to find a single set of evaluation metrics applicable to all tests.

For now, the FDA aims to answer practical regulatory science questions. These are set out in the Perspective co-authored by agency researchers; representatives from the Center of Excellence in Regulatory Science and Innovation (CERSI) at Stanford University in California, and the University of California San Francisco (UCSF); the National Institute of Standards and Technology (NIST); and the bioinformatics company DNAnexus, a Mountain View, California–based bioinformatics company. The next step will be to set up a regulatory framework for NGS diagnostics. Plans to release a draft guideline for NGS diagnostics approval are slated for the end of the year.

The roadmap's publication is largely the result of a series of meetings convened in September 2015 at CERSI Stanford, which included academics and FDA scientists. Kathy Giacomini, a professor of bioengineering at UCSF recalls: "We decided we should draft a paper that identified the key scientific issues that needed to be addressed to facilitate a path forward for evidence-based regulation" of NGS-based tests.



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Some players are concerned that FDA oversight of NGS-based tests will petrify innovation, but others welcome the agency's plan.

Biogen's once-monthly MS injection gets FDA nod

The US Food and Drug Administration (FDA) approved a long-acting multiple sclerosis drug from Biogen, of Cambridge, Massachusetts, and AbbVie, of North Chicago, Illinois, to treat relapsing forms of the disease. The agency gave the self-administered under-the-skin injection Zinbryta (daclizumab) the go-ahead in May, basing its decision on data from two trials, including one showing fewer relapses compared with placebo. Zinbryta is an antibody that binds the interleukin-2 receptor CD25 on T cells, inhibiting the proliferation of activated T cells and their involvement in autoimmunity and the immune responses that can follow organ transplantation. The drug originated from Protein Design Lab (now PDL BioPharma), which had pursued a collaboration with Roche resulting in the 1997 approval of the antibody for kidney transplant rejection. In 2005,PDL and Biogen Idec partnered to develop the antibody for use in multiple sclerosis, and in 2008, PDL spun off its biotech operations into Facet Biotech, of Redwood City, California. Then in 2010, Abbott outbid Biogen to acquire Facet for approximately $450 million (*Nat. Biotechnol.* **28**, 387–389, 2010). Although the once-a-month injection offers another option to patients who have failed multiple treatments, Zinbryta's safety and tolerability issues resulted a boxed warning. Some analysts predict that this label could hamper its market potential by relegating use to a smaller patient population. Biogen's MS pipeline took a knock in June when anti-Lingo-1 monoclonal antibody opicinumab missed its primary and secondary endpoints in phase 2 studies.

"The really critical question for NASA is whether these devices can detect signatures of life in the universe." Kate Rubins, a Whitehead Institute virologist, is training for her first tour on the International Space Station, where she will run more than 250 experiments, including DNA sequencing. (*Scientific American*, 1 June 2016)

"The simple fact is that after 24 years of research and breeding, Golden Rice is still years away from being ready for release." Glenn Stone, an expert on the human responses to agricultural trends, says researchers continue to have difficulty growing the beta-carotene-enriched strains with as good a yield as non-GM strains. (*Science Daily*, 2 June 2016)