WRITING DEFINITIONS IN *REWRITING NATURE*: LESSONS FROM FDA LAW[†]

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Paul Enríquez' book *Rewriting Nature*[1] fits neatly within what has become a cottage industry of legal takes on genome editing. It is also something that many books in this area are not: fun; an entertaining tromp through a wide variety of legal doctrines and how they relate to this new, powerful technology. Used judiciously and well, Enríquez' book serves as a resource to those getting rapidly acquainted with genome editing and its attendant legal issues.

In his book, Enríquez strives to align a variety of legal conclusions with scientific ones in many fields, from agronomy to zoology, joyfully detailed in its chapters. But as Enríquez notes, this alignment is an aspiration often unmet. The primary prescriptive thrust, in response, is that legal decision makers should learn from this failed ambition. Judges, lawyers, and legislators need to better understand the science of genome technology if they are going to regulate it. And to do so, one needs clear definitions of what genome editing *is*.

To that end, Enríquez advocates for "the adoption of a (more) uniform definition of genome editing primarily aimed at building a science-based, legal and policy framework to address current and future predicaments within the ambit of genome-editing technologies."[2] Unclear definitions, in Enríquez' estimation, promulgate "misunderstandings or worse, inadequate laws, regulations, and bad policies, when there is a failure to convey the meaning of that which is the subject of discussion."[3] "A definition of genome editing, therefore, should be as descriptive and as precise as reasonably possible, to facilitate uniformity and predictability in statutory and regulatory interpretation

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[1] PAUL ENRÍQUEZ, REWRITING NATURE: THE FUTURE OF GENOME EDITING AND HOW TO BRIDGE THE GAP BETWEEN LAW AND SCIENCE (2021).

[2] *Id.* at 73.

[3] *Id.*

and construction."[4] Absent such a definition, poor policymaking "may hinder technological progress and innovation"—or let the technology run wild without an appreciation for its consequences.[5] "*Congruity* and *uniformity* on genome-editing terminology," Enriquez argues, "is sorely needed at this point in time."[6]

I want to push back on this principal claim with a few lessons from another scientifically complex and highly technical area of law: FDA Law. And I want to begin from Enríquez' premise that what the law needs at this juncture—or, perhaps, any juncture—is definitional *congruity* and *uniformity*. Sometimes definitional uniformity is helpful. The tax code does not uniformly define the word "family" across its provisions, and this produces, as scholars have noted, significant confusion and some particularly odd results.[7] But sometimes the absence of uniformity is benign. The word "sale" means one thing in the tax context, another in the real estate context, and yet another in the commercial goods context.[8] Despite this, no one seems to be particularly confused. It very well may be the case that the law is quite able to muddle along without a clear definition of a particular thing. Indeed, the law—taking the expansive view presented in Enríquez's book—is replete with "nose[s] of wax," to use Justice Bradley's famous quip about patent claims.[9]

Legal definitions are consequently not, to borrow a phrase from *Rewriting Nature*, "scientific facts."[10] Whether COVID-19 is caused by a virus, for example, is beyond rational debate.[11] But how to define the word "virus"? Breaking down the word into a discrete set of Platonic elements is bound—in the "contingently true" world of biology—to produce exceptions.[12] As but one example, some viruses infect through DNA; others through RNA; and every

[4] *Id.* at 90.

[5] *Id.* at 82.

[6] *Id.* at 73 (emphasis added).

[7] *E.g.*, Bridget J. Crawford, *The Profits and Penalties of Kinship: Conflicting Meanings of Family in Estate Tax Law*, 3 PITT. TAX REV. 1, 42-47 (2005).

[8] Richard A. Leavitt, Comment, *The "Selling" of Patented Goods: In Search of a Definition*, 66 TUL. L. REV. 1903, 1913-18 (1992).

[9] White v. Dunbar, 119 U.S. 47, 51 (1886) (referring to how patent claims may be "turned and twisted in any direction" to change the scope of the claims).

[10] *See* ENRÍQUEZ, *supra* note 1, at 195 ("Before we embark on a discussion of law and policy, however, it is imperative to frame that discussion within the bounds of scientific facts, so that the discussion will be productive."). It is unclear whether Enríquez considers "scientific facts" to be different from other types of facts, or—to channel Nancy Cartwright—whether "scientific facts" are "facts" at all. *See generally* NANCY CARTWRIGHT, THE DAPPLED WORLD: A STUDY OF THE BOUNDARIES OF SCIENCE (1999) (examining the nature of scientific facts).

[11] Note: *rational* debate.

[12] *See* John Beatty, *The Evolutionary Contingency Thesis*, *in* CONCEPTS, THEORIES, AND RATIONALITY IN THE BIOLOGICAL SCIENCES 45, 46 (Gereon Wolters & James G. Lennox eds., 1995) ("[T]here are no laws of biology. For, whatever 'laws' are, they are supposed to be more than just contingently true.")

possible permutation of the two under the sun that constitutes virology's famous Baltimore classification system.[13] Perhaps the best we can say is that a virus is an "obligate intracellular parasite."[14] But even that's overly inclusive and ropes in some very non-virus-like things such as bacteria, like *Rickettsia*, and protozoans, like *Toxoplasma gondii*.[15] Even coming up with a workable, robust definition of the word "virus" doesn't necessarily answer deep questions about them, such as whether they are *alive*. That depends, of course, on what one means by "alive," a long, simmering debate in biology and philosophy.[16] Ascribing universal definitions to such concepts gets us no closer to scientific facts—no better understanding of what viruses do or what we should do about them. Perhaps that's just language. In the words of Dan L. Burk and Mark A. Lemley, in a completely different context, "it may simply be impossible to cleanly map words to things."[17] But we make do.

Instead, definitions may be malleable across different areas of law because they have *functional* purposes; they frequently serve instrumental ends.[18] As everyday tools, definitions can be used to describe the constitutive essence of things, to identify them, to approximate their common usage, to coin new words, to stipulate to things' characteristics, to describe, to explicate.[19] Differential definitions can even serve as shibboleths.[20] In the law, definitions similarly have

[13] *See* David Baltimore, *Expression of Animal Virus Genomes*, 35 BACTERIOLOGICAL REVS. 235, 235-37 (1971).

[14] John Goulding, *Viruses: Introduction*, BRIT. SOC'Y IMMUNOLOGY, https://www.immunology.org/public-information/bitesized-immunology/pathogens-and-disease/viruses-introduction [https://perma.cc/9783-7UGZ] (defining virus).

[15] Hiroyuki Ogata, Patricia Renesto, Stéphane Audic, Catherine Robert, Guillaume Blanc, Pierre-Edouard Fournier, Hugues Parinello, Jean-Michel Claverie & Didier Raoult, *The Genome Sequence of* Rickettsia felis *Identifies the First Putative Conjugative Plasmid in an Obligate Intracellular Parasite*, 3 PLOS BIOLOGY 1391, 1391 (2005), https://doi.org/10.1371/journal.pbio.0030248; Dominique Soldati & John C. Boothroyd, *Transient Transfection and Expression in the Obligate Intracellular Parasite* Toxoplasma gondii, 260 SCIENCE 349, 349 (1993), https://doi.org/10.1126/science.8469986.

[16] Patrick Forterre, *To Be or Not to Be Alive: How Recent Discoveries Challenge the Traditional Definitions of Viruses and Life*, 59 STUD. HIST. & PHIL. BIOLOGICAL & BIOMEDICAL SCIS. 100, 106-07 (2016).

[17] Dan L. Burk & Mark A. Lemley, *Fence Posts or Sign Posts? Rethinking Patent Claim Construction*, 157 U. PA. L. REV. 1743, 1745 (2009).

[18] *Definitions*, STAN. ENCYCL. OF PHILO. (May 7, 2021), https://plato.stanford.edu/entries/definitions/ [https://perma.cc/6CAS-BQ56] ("[D]ifferent definitions do not all have the same goal: the boundary commission may aim to achieve precision; the Supreme Court, fairness; the chemist and the lexicographer, accuracy; the debater, clarity; and the mathematician, fecundity.").

[19] *Id.*

[20] As but one example: a "schooner," aside from being a type of sailing ship, is also a type of beer glass—the sizes of which dramatically differ throughout the world. A schooner in the Texas panhandle can be as large as 32 oz.; in Seattle, as small as 8 oz. Schooners in the British Commonwealth have similarly varied sizes. *Schooner (glass)*, WIKIPEDIA,

a suite of functional purposes: they can be used to enumerate,[21] to claim or disclaim authority over,[22] to put others on notice,[23] to claim as property,[24] to use as mere shorthand,[25] to incorporate an outside understanding,[26] or to outsource an understanding to others.[27] There may be no universal definition of something in the law, because different areas of the law seek to do different things with the same term. Definitions, in some cases, are purely functional.

This is, indeed, the conceit of much of FDA law. In a chapter of their casebook titled, "FDA Jurisdiction: A Matter of Definitions," Peter Barton Hutt, Richard A. Merrill, and Lewis Grossman synoptically describe FDA's power this way:

The scope of FDA's power is defined almost entirely by the list of product categories over which it has jurisdiction. The statutory definitions of these categories thus delineate the outer boundaries of the arena within which the agency operates. The definitions are also important for another reason. FDA has different degrees of power over different categories of products. . . . [T]he product definitions are strikingly broad and thus confer jurisdiction over a vast range of goods. Furthermore, the definitions, which are often not mutually

https://en.wikipedia.org/wiki/Schooner_(glass) [https://perma.cc/32WK-LY3G]. Size definitions for the word "schooner" can be used to identify someone as belonging (or not) to a particular area of the world.

[21] For example: the definition of *X* consists of the following elements. *See, e.g.*, RESTATEMENT (SECOND) OF TORTS § 13 (AM. L. INST. 1965) (defining "battery" as consisting of two elements, "(a) [one] acts intending to cause a harmful or offensive contact with the person of the other or a third person, or an imminent apprehension of such a contact, and (b) a harmful contact with the person of the other directly or indirectly results").

[22] For example: the definition of *X* includes regulable things *Y*. *See, e.g.*, Burwell v. Hobby Lobby Stores, Inc., 573 U.S. 682, 708 (2014) (defining "person" under the Religious Freedom Restoration Act of 1993 as including "for-profit corporations").

[23] For example: "You are hereby informed *X* activity is a form of *Y*." *See, e.g.*, McConnell v. FEC, 540 U.S. 93, 222-23 (2003) (defining "coordination" as "in cooperation, consultation, or concer[t] with, or at the request or suggestion of [another]"—enough to give "fair notice to those to whom [it] is directed").

[24] For example: the definition of *X* includes all that is owned by *Y*. *See, e.g.*, 11 U.S.C. § 541 (defining bankruptcy "estate" to include "all the following property, wherever located and by whomever held").

[25] For example: the definition of *X* includes both *Y* and *Z*. *See, e.g.*, Gater Assets Ltd. v. Moldovagaz, 2 F.4th 42, 49 (2d Cir. 2021) (defining "foreign state," under the Foreign Sovereign Immunities Act, to include "both the sovereign itself and its agencies and instrumentalities, which are separate legal persons from the sovereign").

[26] For example: the definition of *X* is the same as *Y* in this other area. *See, e.g.*, Global-Tech Appliances, Inc. v. SEB S.A., 563 U.S. 754, 766-68 (2011) (defining "knowledge," for patent infringement purposes under 35 U.S.C. § 271(b), to be the same as that in criminal law and include "willful blindness").

[27] For example: the definition of *X* is whatever *Y* defines it be. *See, e.g.*, 21 U.S.C. § 321(h)(1)(A) (defining "device" for purposes of FDA law as including anything recognized as such in the *United States Pharmacopeia*, a treatise updated by the United States Pharmacopeial Convention, a nonprofit organization).

exclusive, are remarkably plastic, providing the agency with great flexibility to decide whether and how to regulate products. Sometimes FDA has interpreted definitions expansively, so as to expand its power. On other occasions, the agency has construed the definitions narrowly, so as to avoid taking responsibility for products it does not want to regulate or to minimize the burdensomeness of the requirements it does impose.[28]

What the Drug Enforcement Agency calls a "drug" may be quite different from what FDA calls a "drug," not because FDA (and its lawyers) don't understand the science of drugs, but because defining the term has a particular and different legal function, important for each agency.[29]

Besides these difficulties with definitional uniformity *across* different areas of law, definitional *congruity* between law and science may still raise several problems. Definitions of this sort can fail, temporally, because they don't incorporate an unforeseeable, after-arising technology. They can unduly limit jurisdictional scope in suboptimal ways. Or the mere act of defining a term can itself become a stumbling block for regulatory authority. FDA law has examples of each of these as well.

FDA's definition of "gene therapy"—dating back to 1993—does a poor job of envisioning much of the genetic modification technology we have today.[30] While this definition is expansive, it primarily focuses on the insertion of new genetic material into a patient for therapeutic purposes.[31] But newer technologies—genome editing as detailed in Enríquez' book among them—do not necessarily use *new* genetic material, while yet other "gene therapies" seem to use genetic material even though that is not their primary mechanism of action.[32] In this sense, FDA's definition of "gene therapy" is overly inclusive in some areas and under inclusive in others—and stands to miss out on capturing a number of more recent technologies.[33] This has been made all the more important during the COVID-19 pandemic because of claims, by anti-vaccine

[28] PETER BARTON HUTT, RICHARD A. MERRILL & LEWIS A. GROSSMAN, FOOD AND DRUG LAW: CASES AND MATERIALS 77-78 (4th ed. 2014).

[29] *See* Rebecca S. Eisenberg & Deborah B. Leiderman, *Cannabis for Medical Use: FDA and DEA Regulation in the Hall of Mirrors*, 74 FOOD & DRUG L.J. 246, 246-48 (2019) (examining these cross-purposes while criticizing broader policies).

[30] Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products, 58 Fed. Reg. 53248-51 (Oct. 14, 1993) ("Gene therapy products are defined for the purpose of this statement as products containing genetic material administered to modify or manipulate the expression of genetic material or to alter the biological properties of living cells."); *see also* Jacob S. Sherkow, Patricia J. Zettler & Henry T. Greely, *Is It "Gene Therapy"?*, 5 J.L. & BIOSCIENCES 786, 786-87 (2018).

[31] Sherkow, Zettler & Greely, *supra* note 30, at 788-89.

[32] *Id.* at 789.

[33] *Id.*

advocates, that COVID vaccines are experimental "gene therapy."[34] To the extent such claims seek to fit the pegs of scientific advances into FDA law's round holes, they're more consequential than just being a poor fit.

In FDA law, congruity in scientific and legal definitions may also improperly limit the agencies' jurisdictional scope. A "drug," according to a scientific, or even a lay, interpretation of the word, would likely not include fecal microbiota transplants ("FMT")—yes, the transplantation of feces from one patient into another for purposes of reengineering the gut microbiome.[35] But in a 2016 guidance, FDA determined FMTs to be so.[36] And they did so in order to preserve regulatory authority over a new practice that brought with it serious concerns related to patient safety and efficacy.[37] Indeed, relying on technical definitions of "drugs," "medical devices," or even "human tissue" would not have clearly brought the practice under FDA's authority—a potentially dangerous proposition.[38]

Lastly, definitions themselves can become a stumbling block—a sole determinant even where things other than technical accuracy seem to matter more. Since 1987—and for decades since—FDA rested on a definition of "software" in medical devices that did not include a wide variety of significant applications.[39] After promulgating guidance that included such definitions—and constrained, perhaps, by an ever expanding target of what "software" truly meant in the medical device context—FDA withdrew its guidance without a replacement.[40] Or, to put it another way, "during a revolution in computerized

[34] Bill McCarthy, *Joe Rogan Falsely Says mRNA Vaccines Are 'Gene Therapy*,' POLITIFACT (Aug. 31, 2021), https://www.politifact.com/factchecks/2021/aug/31/joe-rogan/joe-rogan-falsely-says-mrna-vaccines-are-gene-ther/ [https://perma.cc/66CU-VL4T].

[35] *See* Jotham Suez, Niv Zmora, Gili Zilberman-Schapira, Uria Mor, Mally Dori-Bachash, Stavros Bashiardes, Maya Zur, Dana Regev-Lehavi, Rotem Ben-Zeev Brik, Sara Federici, et al., *Post-Antibiotic Gut Mucosal Microbiome Reconstitution Is Impaired by Probiotics and Improved by Autologous FMT*, 174 CELL 1406, 1407, 1411 (2018) (describing the process), https://doi.org/10.1016/j.cell.2018.08.047.

[36] FDA, ENFORCEMENT POLICY REGARDING INVESTIGATIONAL NEW DRUG REQUIREMENTS FOR USE OF FECAL MICROBIOTA FOR TRANSPLANTATION TO TREAT *CLOSTRIDIUM DIFFICILE* INFECTION NOT RESPONSIVE TO STANDARD THERAPIES: DRAFT GUIDANCE FOR INDUSTRY 1 n.1 (2016), https://www.fda.gov/media/96562/download [https://perma.cc/G599-LLT8].

[37] Rachel E. Sachs & Carolyn A. Edelstein, *Ensuring the Safe and Effective FDA Regulation of Fecal Microbiota Transplantation*, 2 J.L. & BIOSCIENCES 396, 398 (2016), https://doi.org/10.1093/jlb/lsv032.

[38] *Id.*

[39] Draft Policy Guidance for Regulation of Computer Products, 52 Fed. Reg. 36,104 (Sept. 25, 1987); Nathan Cortez, *Regulating Disruptive Innovation*, 29 BERKELEY TECH. L.J. 175, 191-96 (2014).

[40] Annual Comprehensive List of Guidance Documents at the Food and Drug Administration, 70 Fed. Reg. 824, 890 (Jan. 5, 2005) (listing guidance documents once issued by Center for Devices and Radiological Health but withdrawn in preceding year).

medicine, when software became critical to patient care, FDA offered only tentative guidance, and then—nothing."[41]

What does all this mean for genome editing—and for *Rewriting Nature*? At a minimum, it should pour cold water on being overly enamored with scientific definitions for the law. Perhaps what we want is something other than "[c]ongruity and uniformity on genome-editing terminology."[42] Instead, perhaps we should recognize that we may, in fact, *want* different definitions of genome editing for different areas of law. We may instead *prefer* that "genome editing," whatever it may be, is defined differently under FDA law from patent law or from tort law. FDA law seeks to regulate a new technology's safety and efficacy; patent law is often after what terms mean to persons having ordinary skill in the art; and tort law is designed, for one reason, to deter against and insure for harms resulting from negligence. A definition of genome editing may very well be different in these different contexts, and making a definition broad enough to encompass all of them—like our attempt to define what a "virus" is—is likely to be remiss in potentially significant respects. Ironically, Enríquez tacitly recognizes that the scientific community—the same from which we derive sturdy "scientific facts" for policymaking—"has not called, or expressed an appetite, for a uniform definition either."[43] Genome editing is a tool. And so are definitions.

Wanting simplicity in an age of seemingly maximum complexity is admirable. Enríquez goes out of his way to explain the importance of educating the public and lawmakers alike and, well, simpler is better on that score. But a uniform definition may fall prey to one of the very things Enríquez counsels against: "deceptive simplicity."[44] Enríquez paints a compelling picture of striving to get the science right on genome editing. But maybe, for the law, universal definitions are too blunt of a cut.

[41] Nathan Cortez & Jacob S. Sherkow, *Presidential Administration and FDA Guidance: A New Hope*, 2021 U. ILL. L. REV. ONLINE 179, 182, https://www.illinoislawreview.org/wp-content/uploads/2021/04/Cortez-Sherkow.pdf.

[42] ENRÍQUEZ, *supra* note 1, at 73.

[43] *Id.* at 91.

[44] *Id.* at 272.