BOOK REVIEW

Biotechnology and the Law, Second Edition. Hugh B. Wellons & Robert F. Copple. Editors-in-Chief & Authors. William N. Wofford. Editor & Author. (American Bar Association Publishing, Chicago, IL, 2019). (LCCN 2018055633 & ISBN 9781641053228). Primer on Biotechnology Law published by the American Bar Association Section ("ABA") of Science and Technology Law ("SciTech" or "ABASciTech") (Biotechnology Committee of the ABA) (hereinafter "Biotech ABA"). 1137 pages. Table of Contents. Contributing Authors. Preface. About the Editors. About the Authors. Text (Chapters 1-20 inclusive). Three Appendices. Detailed Index. Reviewed by Dr. Arthur Kyriazis.[1]

I. The Preface to the Second Edition

By way of background, the Preface to the Second Edition (hereinafter, the "Preface" and the "Second Edition, or the "Volume Under Review") states:

> The 20th century looked to physics, chemistry and the microchip to better the human condition. The 21st century looks to the life sciences with the same hope…these days, a major medical breakthrough often includes intellectual property developed in collaboration across a variety of technological specialties and industry sectors, in a number of countries on several continents. Winston Churchill once said, "The empires of the future will be empires of the mind." …. Companies developing

> biotechnology products have very broad legal needs…. as a result, lawyers (and the biotechnology clients they serve) need a resource that will enable them to spot legal issues critical to companies in this [biotechnology] industry—a tool that will, at the very least, tell them the right questions to ask in order to avert difficulties….
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> In 2005, the Biotechnology Committee of the ABA acknowledged the pressing need for such a resource…. Before a word of [the First Edition]…was written…a year and a half was invested in developing the [First Edition's] format and scope….
>
> The First Edition, published in 2007, was surprisingly successful. Totally unexpectedly, college and law school professors used the book to teach classes on this topic. In about 2014, we began discussing a new edition….[2]

The first edition of this book was very successful. (Hereinafter, the "First Edition").[3] The Second Edition is a revision (with substantial additions and new sections) of the First Edition.

II. Run, Don't Walk,[4] to Order the Second Edition

This Review concludes that the Second Edition is a great improvement over the First Edition, and thus well worth acquiring and/or adding to one's basic practice library, or adding it to one's business library. The Second Edition's use in academia is self-evident; professors and teachers who teach biotechnology should order this book. It would be a valuable addition to any classroom.

III. Differences and Changes in the Second Edition Discussed in the Preface

The Preface goes on to recite some of the substantive differences between the First Edition and the Second Edition:

> 1) The Second Edition has deleted the Technical Glossary of the First Edition, primarily because such words can now be found online.[5]
> 2) There is a new Chapter [Twenty] on Bioethics[6]
> 3) Appendix A contains a Case Study[7]
> 4) Appendix C contains an example of a detailed Patent and Technology License ("Tech Transfer") Agreement based upon the University of Texas ("UT") Model Agreement circa 2018.[8]

In addition to the two Editors-in-Chief and Authors, there are three (3) editors and authors, an Appendix author, and twenty (20) more authors and contributors to this volume, each of whom have and/or share primary responsible for individual chapters and areas of expertise.[9] In addition, as noted in the Preface by the Editors, the American Association for the Advancement of Science ("AAAS"), the University of Texas and a private law firm attorney were also consulted.[10] The Preface devotes considerable time to thanking individual authors and contributors to the Second Edition.

IV. Plan of the Second Edition

The Preface and Chapter 1[11] serve as an Introduction and Overview. Chapters 2,[12] 17[13] & 19[14] are devoted to patent & litigation issues related to

IP (and biotech generally), while Chapter 18 is a new Chapter entitled "The Impact of Bankruptcy,"[15] devoted to discussing matters of insolvency, creditor and debtors' rights, and thus belongs under the general rubric of litigation chapters (Hereinafter, collectively the "Patent Prosecution, Litigation and Bankruptcy Chapters").

Chapters 3,[16] 4,[17] 5,[18] 8[19] & 16[20] are devoted to Company Formation (including choice of entity and corporate matters), Tech Transfer & Licensing (acquisition of biotechnology & relevant technology), obtaining financing of the biotech venture, Research and Development Collaborations ("RDCs"), and Development and Commercialization Alliances ("DCAs"). Chapter 6 discusses Employment Issues (including the many applicable Federal State and Local statutes) which can arise and which should be anticipated in any biotech venture or entity. These Chapters can be grouped as bread and butter biotech corporate issues, including *inter alia,* (1) Tech Transfer/Licensing (2) Corporate Matters (3) Funding (4) Collaborations (5) Alliances and (6) Employment Issues (Hereinafter, collectively, the "Corporate Chapters").

Chapters 7,[21] 9,[22] 10[23] & 12[24] go to various regulatory issues surrounding the biotech company, including preclinical, clinical, privacy, environmental and federal and state regulation after approval of the drug (or

device). Chapter 11[25] deals with Medical Reimbursement, and is pertinent to potentially gaining health insurance reimbursement for pre-clinical and clinical trial patients. Chapters 13,[26] 14[27] & 15[28] also deal with approvals; Chapter 13 deals with "Approval of Biotechnology Products for Human Use," Chapter 14 deals with "Agricultural Biotechnology Approval Processes." and Chapter 15 deals with "Federal and State Regulation After Approval. Chapters 7, 9, 10, 11, 12, 13, 14 & 15 can collectively be grouped as dealing with Regulatory and Regulatory Approval Matters. (Hereinafter, collectively, the "Regulatory Chapters").

Finally, Chapter 20, also new to the Second Edition, discusses the mighty topic of Bioethics. The Bioethics Chapter 20 will be discussed separately. Finally, we have the new Appendices,[29] which carry over one section from the end of the First Edition, but add two new valuable Appendices, which collectively contain a Case Study, a list of Biotechnology Resources, and a valuable sample Patent & Technology [Transfer] License Agreement.[30]

Thus, the schema of the Second Edition covers a comprehensive introduction to issues that in house or outside counsel to a Biotechnology (and/or Medical Device) Company might need or require to serve in those roles: 1) Patent Prosecution, Litigation & Bankruptcy; 2) Corporate Matters,

including Tech Transfer, Funding & Employment Issues; 3) Regulatory Issues; 4) Bioethics Issues; and 5) Sample Agreements and Case Studies. Also, although the general Technical Glossary has been dropped from the First Edition, many of the Chapters contain, or have introduced, lists of "Key Acronyms Used," which serve in much the same role as the general Technical Glossary did. However, by focusing these lists Chapter-by-Chapter, they provide more specific, pertinent and relevant word/acronym definitions, and thus have the advantage of being contextual, as well as being shorter lists for the generalist to master. In summary, the schema of the Second Edition is much improved over that of the First Edition. The First Edition was terrific. But the Second Edition is better. The Second Edition is more organized, coherent, and focused, and reads more precisely, accurately and relevantly than its predecessor. In short, the Second Edition is a triumph, and well worth the purchase price.

V. The Second Edition is a Primer, Not a Comprehensive Treatise

The Preface and Chapter 1 to the Second Edition recite nearly *verbatim* the same disclaimers as the First Edition and thus bear quotation:

> And now, the disclaimer: this book is meant to be a primer. No chapter will educate you sufficiently to practice in that area. The information in the book should not be taken as legal advice. Given space and scope limitations, it does not seek to address all legal and regulatory concerns that

> companies or lawyers might have to consider in a specific situation. Each chapter could have been expanded into a book, but that was not our mission. We hope this primer will provide enough information for counsel and management to plan strategically, and enough guidance to know when you need a specialist's advice….
>
> This primer [the Second Edition] was never meant to be the last word on Biotech Law. Instead, it is intended to serve as a starting place for lawyers faced with the challenge of identifying the legal issues and processes that must be faces by their clients in building, marketing and protecting a biotech business. The authors of the individual chapters, all of whom are accomplished in their respective fields, have provided thorough, yet accessible, overviews of biotech subspecialties with an eye to practical application…. [The First Edition]…has also been used to teach law school classes on the subject [of Biotechnology Law]…. we hope you find this primer [the Second Edition] a useful and often-consulted resource in your biotech practice.[31]

This disclaimer is vitally important. Being an in-house counsel (or an outside counsel) to a biotech (or medical device) company is far more complex in many respects than the analogous roles for non-tech companies—although in today's global, tech-driven economy, it is increasingly rare that a company would be founded without advanced scientific technical knowledge and IP being at the forefront of the corporate endeavor. The Second Edition attempts to anticipate the multiple issues

facing the tech-related representation, not exhaustively research them all; in this, it succeeds magnificently.

VI. Additional Changes, Chapter Headings and the New Appendices

The Chapters in the Second Edition preserve much of the material as their counterparts in the First Edition, but with amendments, changes and new Sections, as well as an influx of new authors and co-authors, all of which substantially enhance the Second Edition. The Chapter Headings in the First Edition were numbered by Roman Numerals, *e.g.* I, II, III, *et seq.*, while the Second Edition Chapters are numbered by more conventional Arabic Numerals, *e.g.* 1, 2, 3, *et seq.*

The Appendices to the Second Edition are new; amended and expanded Appendix B replaces First Edition, Chapter 21, while Appendices A & C are entirely new.[32] Appendix A provides a "Legal/Biotech Case Study."[33] The Case Study presents a complicated fact scenario which has many issues which a biotech attorney would normally see in real life—tech transfer issues, partnership issues, IP issues, differing technologies—and even a curveball issue (one of the prospective partners has a potential marital legal issue that may possibly end up clawing back assets of the enterprise unless dealt with legally or otherwise).[34] The Case Study concludes by stating "our challenge is to identify all the legal/business issues and to

establish a plan to solve them." [35] Thus the Case Study easily functions as potential classroom exercise, mid-term or final examination in a biotech law or business class. This is eminently useful.

Appendix B provides an extensive list of "Biotechnology Resources,"[36] which includes a lengthy bibliography of Treatises and Books, National Academies Press publications, Current Awareness (a list of biotech and patent relevant websites, periodicals, articles and web resources relevant to biotech and the law of biotech), Major Federal Acts, Federal Agency Resources, including without limitation a list of Centers for Medicare and Medicaid Services (CMS), lists of services and resources available from the Departments of Agriculture (USDA), Health and Human Services (HHS), Labor, State, EPA, FDA, Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH), Office of Regulatory Affairs, Center for Food Safety and Applied Nutrition (CFSAN), Center for Veterinary Medicine (CVM), Good Clinical Practice in FDA-Regulated Clinical Trials, a list of FDA forms, a list of Speeches and Articles, miscellaneous resources, NIH resources, USPTO resources, US Citizenship and Immigration Services (USCIS) services and resources and a list of "other" resources.[37] Appendix B continues with a list of Key Federal Cases,

a list of State Laws and a list of Additional Resources (including many websites and web links). [38]

Appendix C is also very useful, being a sample "tech transfer agreement" (aka "licensing agreement") for the conveyance and/or licensing of patent and technology rights from a university to a corporation.[39] All counsel looking to effect tech transfer from a University to a Corporation under the provisions of the Bayh-Dole Act of 1980[40] must be familiar with the provisions of both the Bayh-Dole Act and a Sample Licensing Agreement; there are boilerplate provisions in the Sample Licensing Agreement required by the Bayh-Dole Act,[41] as well as provisions which can be negotiated from deal to deal. A skilled licensing attorney needs to be familiar with each and every kind of term and clause in such tech transfer agreements. Thus, the Sample Licensing Agreement in Appendix C is most useful. The Appendices are followed by an Index, which is detailed, comprehensive and useful, particularly for a book of this length and breadth of subject matter.[42]

Some material from the First Edition has not been carried over to the Second Edition for reasons of relevance, editing and brevity. Chapters 7, 14 and 18 of the First Edition have no counterparts in the Second Edition.[43] The First Edition, Chapter 7 dealt with "Federal Regulation Through

Funding" and had a long discussion of SBIR/STTR grants as well as other kinds of grants with strings.[44] The First Edition, Chapter 14 concerned "The Regulation of Biomedical Products for Animal Use," and had discussions of the Animal Health Industry, FDA Regulation of Animal Drugs, the differences between FDA regulation of animal vs. human drugs, and a discussion of USDA regulation of animal biologics and veterinary drugs.[45] The First Edition, Chapter 18 was entitled "Expansion: European and International Considerations for Biotechnology Companies" and had a very long discussion of European approval, regulatory and marketing frameworks, together with many other topics.[46] Thus the First Edition may remain a valuable shelf reference for the retention of these three chapters, unless supplanted by more recent treatises or books on the subject matter.

After the Preface and Chapter 1, the Second Edition then breaks out as laid out in the plan of the Second Edition, discussed *supra*.

VII. Chapter 1 - Introduction

Chapter 1 of the Second Edition has added an additional author, and as noted, the glossary at the end of Chapter I of the First Edition has been deleted. Chapter 1 provides us with a working definition of "Biotech" ("Biotech Defined") and then provides what will be a roadmap for the remainder of the book—"The Biotech Company Life Cycle"[47] (which is

quite familiar to those of us in Biotech). The definition is very similar to what it was in the First Edition.[48]

Obviously there have many dramatic developments since the publication of the First Edition in 2007. As Chapter 1 notes, "we are in a very different place technologically"; the authors go one to provide examples of advances in gene therapy, personalized genetics & genomics, genetic testing, stem cell approaches, dendritic cells, bioinformatics utilized to power drug development & design, mobile technology, personalized medicine, medical devices, and the machine-human interface.[49] Changes in the domestic (USA) patenting laws are noted, as well as recent court decisions and FDA developments.

The further globalization of biotech and biotech sales internationally (not to mention filing internationally and under the PCT) are noted, as well as the increased role of the EU, Japan, Australia, China and the BRAC nations. The fact that clinical testing is now often done abroad is noted. The ACA's role is noted.

Finally, the Recession of 2007 *et seq.* and its effects on biotech funding are noted, with the positive note that investment in biotech is finally back to pre-recession levels.[50]

VIII. Chapters 2, 17, 18 & 19 – Patenting Basics; Patent Litigation and Dispute Proceedings Overview for the Non-Patent Attorney; The Impact of Bankruptcy; and Risky Business: Litigation, Risk Management, and Dispute Control

Here, we have four related Chapters, discussing the filing and prosecution of patents and the backend issues of protecting those patents post-issue in the litigation sphere. It is crucial at all stages of a patent prosecution, to avoid defects and/or mistakes, which may or might lead to a judicial finding of invalidity. Thus, these Chapters are vital reading.

1) Getting the Patent(s) and Claims – Chapter 2

Chapter Two[51] covers domestic and foreign patenting basics, as well as patent portfolio management, all in the space of sixty-one (61) pages.[52] As a prefatory note, it is critical to distinguish between a company's *intellectual property portfolio* and a company's *patent portfolio*; the latter is a subset of the former.[53] On average, approximately 60-70% of any given company's business value generally now consists of intangible assets, such as patents, trademarks, copyright, goodwill, rights to internet domains, and the like.[54]

Chapter 2 has been expanded and revised, appropriately reflecting important changes in patent law both in the United States and

internationally. Chapter 2 incorporates a detailed, running discussion of various recent changes in patent law, particularly changes since 2007. These are most useful for the non-specialist General Counsel ("GC") or for the non-lawyer charged with working in the biotech field.[55] These changes include, *inter alia*, the America Invents Act ("AIA") (2012); a string of Supreme Court and lower court decisions which have narrowed patentability generally, and particularly with respect to the biotech field; changes in the term of patent protection; changes in the PCT; the changeover from "first to invent" to "first to file"; and the rise of post-patent protection and maintenance issues in light of a rising tide of avenues for challenging the invalidity of a biotech patent.[56]

The sections of Chapter 2 on Patent Term, the AIA, and the new restrictions on patentability emanating from recent Supreme Court decisions expanding the doctrines of "Laws of Nature" and "Abstract Ideas", and expanding those doctrines expressly to biotechnology patents, are crucial to read and understand, as well as the underlying case law.[57]

Indeed, the United States Supreme Court has (in addition to undertaking more certiorari jurisdiction of patent cases since 2007) been at times openly hostile to patent holders and litigants seeking patent protection, occasionally even stating its opinion adversely and openly in oral arguments,

as Justice Breyer did during an oral argument before the Court in 2016: "There are these patent trolls [sic], and the Patent Office has been issuing billions [sic] of patents that shouldn't have been issued—I overstate—but only some."[58]

The *Vanda* decision and the recent United States Patent Office ("USPTO") internal memo to examiners in light of *Vanda* has had some positive effect on the allowance of biotechnological patents—but only some; we are not back to the golden days of 2007.[59] Chapter 2 in the Second Edition also expands out its discussion of the basic requirements for patentability under 35 U.S.C. 101 *et seq.* devoting separate sections to the requirements of novelty, non-obviousness, utility and adding a subsection on "other requirements" – obviously all required in light of the changed landscape in patent examination.[60]

However, it should be noted statistically that the absolute number of patents being filed and issued by the USPTO has sharply *increased* during the period 2010-2019; and that 2019 saw a record of more than 350,000 patents being issued; moreover, the overall number of patents filed and issues during the 2010s dwarfed any preceding decade by a staggering amount.[61] As to how many of those patents (and claims) will be sustained

post-issue and in the face of inevitable litigation claims, given the changed landscape, of course remains an open question.

Chapter 2 ramps up its exposition of the Patent Application Process in greater detail as well as adding a section on Post-Issue Patent Considerations (see *infra, below*), again, most useful in light of the changed landscape both in patent examination and allowance; and subsequently in post-issue challenges to issued patents and their potential disallowance on re-examination under certain new AIA procedures.[62] As discussed, *supra*, Chapter 2 adds a very important section on "Post-Issue Patent Challenges" which is vital reading, and which is yet another reason to purchase and peruse with purpose the Second Edition. As Chapter 2 states:

> The AIA created several new post-grant review procedures to challenge issued patents. Beginning September 16, 2012, these include: (1) post-grant review ("PGR"), (2) *inter partes* review ("IPR") and (3) covered business method patent review ("CBMR"). These post-grant proceedings are essentially mini-trials before the PTAB[63] as opposed to a district court judge.[64]

The remainder of this subsection of Chapter 2 discusses in vital detail the PGR, IPR and CMBR procedures. This is bookended *infra* in the litigation chapters 17, 18 & 19. While hardly exhaustive, this section is important,

especially since we are now in an environment where the mere granting of a patent does not guarantee that you are "home free."[65]

Chapter 2 has detailed discussions of filing and prosecution of U.S. patents, foreign filings and PCT filings. The Chapter 2 discussions are substantially larger and more detailed than their predecessors in the First Edition and further provides a detailed walkthrough of when to file, how to file, how to prosecute biotech patents, and ultimately, how to manage the biotech patent portfolio, or as Chapter 2 terms it, the "patent estate."[66] Thus, the revised and expanded Chapter 2 is a welcome revision, which warrants purchase of the Second Edition.

2) Litigating the Patent - Chapters 17 & 19

Chapter 17 begins with an introduction, followed by a "General Overview of Patent Litigation in Federal Court" including discussions of direct, indirect and literal infringement, as well as the technical requirements of proving infringement, followed by a discussion of pre-litigation considerations noting the pre-filing investigation and the cease and desist letter.[67]

The remainder of Chapter 17 is very useful. It discusses how to choose an appropriate forum and the appropriate parties for litigation, discusses pleadings, examines the under-discussed topic of remedies

(actually quite important with regards to intangible assets), and breaks down remedies into damages, equitable relief and attorneys' fees awards. Then Chapter 17 delves into a "general overview" of post-grant proceedings before the USPTO, which has become much more important since 2007 (see discussion, *supra*) and bookends the discussion in Chapter 2. Finally, Chapter 17 discusses Alternative Dispute Resolution ("ADR"), always a welcome alternative to the courts, and advantageous with regards to confidentiality and as an alternative to foreign litigation.[68] There is an important discussion in Chapter 17 on when, if and how to send a "cease and desist" letter that is short but exceedingly useful.

Chapter 19 has a nice Introduction, and then starts where all litigation discussions should start, by reviewing how to draft "Dispute Management Provisions in Commercial Agreements." There are pertinent discussions of this, most notably ADR provisions, along with a discussion of compliance counseling, how to maintain IP, trademarks and client trade secrets, a discussion of products liability and insider trading, all valuable. There is then a long and useful discussion of document and information retention, quite relevant in the age of electronic discovery and cyber security. Finally additional time is devoted to discussing ADR.

Chapter 19 is one of the best Chapters in the Second Edition—it is essentially a handbook on avoiding litigation by looking out for it from the outset. Nothing could be more valuable to any client, in house counsel or businessperson than advice like this.

3) The Impact of Bankruptcy – Chapter 18

Chapter 18 is essentially an Introduction—as it says at the start—to "Bankruptcy Basics."[69] The Laws and Rules of Bankruptcy Court are fundamentally different than their analogous counterparts in Federal or State Court; thus, filing for Bankruptcy by a Debtor (usually a Corporation) is often a litigation strategy utilized to gain a more advantageous forum, although that is not explicitly stated in Chapter 18. Chapter 18 assumes (as many of us do) that entities and individuals file for bankruptcy due to insolvency issues; however, it should never be forgotten that there are litigation advantages to shifting the forum to U.S. Bankruptcy Court, for the reasons to be discussed, *infra*, which are discussed explicitly in Chapter 18.[70] Chapter 18 notes "There is, in fact, no requirement than an entity be insolvent before it can seek protection under the [U.S.] Bankruptcy code through either chapter 7 or chapter 11."[71]

Essentially, Bankruptcy Court, through the power of the Automatic Stay and several other special powers granted the Debtor-in-Possession

("DIP"), grants an overwhelming advantage to the DIP in any litigation battle ongoing, especially in the short run. Thus, Bankruptcy Law is often also appellated as "Debtor-Creditor Rights," since it is essence a clash of the rights of Creditors and the rights of the DIP, arbitrated by the Laws, Rules and Procedures of the U.S. Bankruptcy Court.

Chapter 18 first covers Creditors rights, and then covers DIP rights. Creditors come in essentially two forms, "secured" and "unsecured", and also "priority" and "non-priority." Chapter 18 has an excellent discussion of how to achieve secured status and how to perfect liens, although there are many other technical points that should be covered with expert counsel.[72] The Right to Representation is covered. A Creditor should be represented by expert Bankruptcy Counsel.

We will leave out any discussion of personal bankruptcy to the text of Chapter 18, except to note that prior to the 2005 Amendments to the Bankruptcy Act, Individual Debtors could repeat file bankruptcy petitions and strip off 100% of unsecured debt; following the passage of said Amendments, Individual Debtors are now means-tested, can only file one Petition every 5-7 years except upon a showing of good cause or changed circumstances, and normally must pay approximately 25% of their unsecured debt together with 100% of their secured debts. Thus the

Amendments of 2005 have created a tilted playing field far more favorable to creditors than to individual debtors filing under Chapters 7 & 13.

Chapter 18 then turns to a discussion of DIP rights. Despite the 2005 Amendments, corporate debtors retain great and tremendous advantages filing under Chapters 11 & 7, even after the 2005 Amendments. Creditors want to be sure that their debts are "secured" and "prioritized" so that if a corporate entity debtor of theirs files for bankruptcy suddenly and without warning, they can have some say in the distribution of the "bankruptcy estate" assets.

As Chapter 18 explains in long detail, the DIP has certain advantages, which consist of 1) the Automatic Stay under 11 U.S.C. Section 362, which stays ALL litigation, claims, collection actions, whatever, AGAINST the Debtor, and is broadly construed 2) the power to marshal and claw back assets into the Bankruptcy Estate, sometimes as far back as several years 3) the power to assume assign or reject executory contracts 4) the power to modify certain obligations 5) the power to assume or reject leases within a 120 day period 6) the power to either reorganize or liquidate 7) the power to do 11 U.S.C. Section 363 "spin-offs" of property—literally an auction—held by the U.S.B.J.—of the most valuable assets, tangible or intangible—of the debtor, upon notice and motion, sometimes abbreviated notice.

A clever corporate DIP represented by good insolvency counsel will often come into court with a "pre-packaged" bankruptcy and will file motions quickly. The pace of Bankruptcy Court is rocket docket fast, lightning fast, faster than any other court.

Also, motions can be even further accelerated and short noticed, including Section 363 sales of major assets of the Debtor. Often such proceedings will be filed in certain *fora*, such as Delaware, that are favorable to corporate debtors. Biotech companies and their in house and outside counsel may be unfamiliar with the speed, rapidity and celerity of U.S. Bankruptcy Court proceedings. Motions, literally, fly by half a dozen a week.

In any event, it is critical that a Creditor be represented by VERY experienced outside Bankruptcy Counsel. The Creditor-Debtor bar is small, usually quite chummy, and the attorneys and Judges of the Bankruptcy Court know each other in a way that newcomers do not. Beware appearing in Bankruptcy Court without having an experienced hand (or six or seven) at your side.

As to the other basics, Chapter 18 explains much of this, including the development of the Bankruptcy Law of 1898, which was replaced by the Bankruptcy Reform Act of 1978, which in turn was amended by the

Bankruptcy Abuse Prevention and Consumer Protection Act of 2005. Chapter 18 discusses classes of creditors, how one obtains security and priority under the UCC by perfecting liens, discusses creditors' committees, and many other details of insolvency practice not covered here but very relevant. There is an excellent discussion of the eternal question of liquidation versus reorganization, and also Chapter 18 brings forth data (that we all know exists) which shows that many, many debtors attempt to reorganize, but in truth, few succeed.

A footnote explains a powerful weapon that Creditors should be aware of—the "Involuntary Bankruptcy Petition."[73] A group of three or more creditors may throw an entity or individual into involuntary bankruptcy by filing a petition for involuntary bankruptcy under 11 U.S.C. Section 303. This strategy is not without its risks, but at times, it may have advantages, such as when a Creditor is secured and wishes to select the Bankruptcy Court as a forum for litigation. In such situations, the roles are reversed and often the Movants will drive the litigation, making demands for payment in return for settling their claims so that the Involuntary Debtor may escape the Court.

One important point raised by Chapter 18 is that IP is an asset of the Debtor—including patents, trademarks, and the like. Licensing Agreements

may be executory contracts or assets or a hybrid depending on the language. If a company goes into insolvency and files for Chapter 11/7 protection, it is incumbent upon the Creditor or Party in Interest to retain Bankruptcy Counsel and immediately negotiate with the Debtor terms for re-affirming those executory agreements and spinning out that IP under a quickly filed, short-noticed Section 363 motion before anyone else has the chance to act. In Bankruptcy Court, speed, focus and experience are everything. That is why exceedingly skilled attorneys often concentrate in this area of law. In short, everything you spent all that time on negotiating in the Corporate Chapter of the Second Edition—be prepared to insert clauses therein to prioritize and perfect your liens on your property interests in other corporate entities in the event of insolvency. Those clauses will give life to your bankruptcy counsel's efforts to maneuver you into advantageous position.

There is an important discussion of 11 U.S.C. 365(n) and the case of *Lubrizol v. Metal Finishers, Inc.*[74] Under 365(n) "if a licensor of intellectual property rejects a non-exclusive license in bankruptcy, the licensee may elect to treat the license as terminated and get rejection damages, or, notwithstanding the rejection, the licensee may retain its non-exclusive intellectual property rights 'as such rights existed immediately before the bankruptcy case commenced'". [75]

Then there follows an important wrinkle in how 11 U.S.C. 365(n) interacts with licensees of rejected trademark licenses, because when Congress amended 365(n) it included IP, but excluded trademarks (go figure), so this is a big difficulty of sorts for the Creditors' attorney representing such a claimant.[76] Ideally one must seek a side deal (to be approved by the Court) for assumption of the executory contract/license; in the alternative, for purchase of the trademark itself in a Section 363 spin out sale on approval by the Court. The last and least preferable option would be rejection damages. The DIP has assignment and sale powers in Bankruptcy, and these can be used to achieve mutually satisfactory ends.

Bankruptcy is one of the most fascinating areas of law, and combined with biotechnology and tech licensing, a tremendous and growing field for those striving to get ahead. Also, it is intellectually fascinating, fast paced, and full of bright, clever and able attorneys. Finally, for those who persevere and gain a good reputation at the bankruptcy bar, there is the prospect of appointment to the Bankruptcy Bench—even though USBJs are not Article III Judges, they serve for fifteen (15) years, and can often use their sinecure as a stepping stone to higher Judgeships which are of an Article III character.

Thus, Chapter 18 is one of the most important in the Second Edition, and by itself, merits purchase of same.

IX. Chapters 3, 4, 5, 8 & 16 – the Corporate Chapters

1) Chapter 3 – Entity Formation & Choices

Chapter 3 covers "Company Formation," and offers key insights. Like the First Edition, it is bullet pointed with grey-shaded "practice points." The very first practice point is probably the most important: "Biotechnology companies are almost always either raising money or getting ready to raise money. The company's attorney is encouraged to view legal issues through the additional filter of 'will it help us raise money?'"[77] Many new features appear, including sections on the LLC, and various other funding methods.[78]

Chapter 3 has critical revisions and expansions. First, there are two new subsections under the introductory discussions devoted to the role of "Founders" and "Financing and Product Development Plan."[79] The role of the founders must be analyzed carefully as to 1) who are the founders 2) what discussions they have had with each other and/or with outsiders 3) what discussions they have had with each other and/or with outsiders regarding equity allocations and/or allocations of ownership 4) due diligence review that the founders are not contractually bound to current or former employers, invention rights agreements, former companies, *et seq.*[80] A

Financing and Product Development Plan refers to having a "comprehensive business plan" and "an outline of that comprehensive plan"[81] moving forward, in order to serve as a:

> Basis for licensing discussions with technology transfer offices, financing discussions with seed investors, recruiting discussions with prospective team members, discussions with interested partners, and discussions to focus prospective serve providers. The plan with change over time, of course, and there will be holes, but a strong initial plan provides a good starting point for building a company….
>
> Further, the plan should acknowledge exit opportunities along the way and provide some guidance for the potential valuations at those exits.[82]

The Plan must also discuss clinical and human studies, when generation of revenues might be anticipated, the regulatory pathway for the company's product or service, and so forth. This is critical to establishing a baseline of costs for each step or stage in the process, and from there, an estimation can be made of whether the "market will support the amount of funding needed, the valuations proposed at various stages, and the returns expected."[83] Thus Chapter 3 stresses the importance of visualizing and planning for an Exit Strategy at the *beginning* of the biotech company organization process.[84]

Another welcome addition to Chapter 3 is in the subsection on "Biotech Company Models" where a new section on "Holding Company and Series LLC" is introduced to the existing list.[85] This is a brand new section

discussing how the company may "establish a holding company or a series LLC structure." [86] Chapter 3 adds an entirely new section on "Building a Strong Team" which has subsections on the Founders, the Board of Directors, the Scientific Advisory Board, and then Management proper, including the Chief Executive Office ("CEO"), the Chief Financial Officer ("CFO"), the Chief Scientific Officer ("CSO") and Clinical/Regulatory Management. [87] Thus, the criticality of having a strong team and the correct management structure at the top of the biotech company (once you are fully funded) is emphasized in great detail. This entire discussion is very important because biotech companies operate in a highly regulated environment; in addition to the foregoing, biotech companies will also often need an in-house Legal Counsel/Legal Department as well as an in-house or independent Ethics Adviser or Ethics Advisory Board.[88] The section in Chapter 3 on building a strong team also discusses employees and confidentiality agreements.[89]

"Entity selection and formation" along with the concurrent discussions of tax issues and choosing a state to operate and/or incorporate in are discussed in detail; there are new and/or revised sections on "LLCs," "Name Selection" and "Capital Structure and Stock Grants."[90] The LLC Section is revised, and as one might imagine, discusses in greater detail the

advantages, disadvantages and problems of utilizing an LLC. Chapter 3 emphasizes the LLP, LLC and LLLP, all entities have come into more widespread use and existence since 2007. [91] Chapter 3 states as a key practice point is that normally, a biotech company should be "a(n) 1. C-corporation 2. S-Corporation or LLC." [92] So clearly Chapter 3 weighs in positively on the use of the LLC.[93]

Chapter 3 revises and expands the Name Selection section and breaks down the discussion of Name Selection into five discrete areas; (1) Trademark Search (2) Finding a Unique Name (3) Trademark Registration (4) Foreign Registration and (5) State Corporate Law considerations.[94]

Chapter 3's discussions of Capital Structure, Federal and Blue Sky Securities Law issues, Stock Grants, Warrants, an other complex issues pertaining to corporate equity, debt and options, as well as how to legally effect the preferred treatment of early participants, have relevant updates.[95] These changes and emendations in Chapter 3 consist, *inter alia*, of 1) a more detailed discussion of "Founders' Stock, Restricted Stock, and Stock Options" 2) addition of three new subsections on a) Convertible Debt b) Simple Agreement for Future Equity and c) Series Seed Preferred Stock.[96] These are welcome additions and make Chapter 3 one of the most useful Chapters in the Second Edition.

2) Chapter 4 – Tech Transfer and Biotech

Chapter 4 is substantially reworked and new sections are added.[97] Chapter 4 deals more comprehensively with the topic of technology transfer (hereinafter "Tech Transfer").[98] Chapter 4 does contain an express disclaimer:

> This is merely an overview of this practice area. This chapter does not seek to address all legal and regulatory issues that companies or lawyers would have to consider in this practice. Some specific omissions are local laws, regulations with respect to the use and transportation of hazardous or restricted materials (if applicable), environmental law, product liability law, and "generic" issues such as local contract, labor, real estate, corporate, taxation and antitrust law.[99]

Chapter 4 covers comprehensively the acquisition and protection of core technology by the biotech company and its founders, a process coined as "tech transfer;' Chapter 4 notes that "few biotech products are invented in 'whole cloth' by one person" and that "commonly universities and nonprofit companies own or control critical components" and further notes there is a complex web of federal and state laws (as well as institutional rules) governing the use and/or transfer of this biotech patent and/or intellectual technology.[100] Thus Chapter 4 terms biotech tech transfer a subset of "Technology Creation."[101] Chapter 4 has a detailed review of Company Records and the requisite review of Work for Hire (Copyright v Patent) and

U.S. v. Canada v. EU law is conducted.[102] Trade Secrets and the Uniform Trade Secrets Act[103] are reviewed; while not as useful for biotech as other forms of IP protection, they have a place, particularly as to enforcement of NDAs and Mutual Confidentiality Agreements ("MCAs").[104]

Chapter 4 contains important practice pointers on proprietary concerns, confidentiality, priority of invention, keeping records, the thorny issue of works for hire under both copyright and patent laws as to both independent contractors and employees, and the importance of a written work for hire agreement/employment agreement. There is a similar discussion of state laws, Canadian and European Laws, and a expanded discussion of trade secrets, as well as some additional review of the patent fundamentals discussed in Chapter 2, *supra*.[105]

Chapter 4 has important revisions, emendations and amendments. Notably, there is an entirely new subsection on "Typical Considerations of the Licensor" which carefully examines the viewpoint of the entity licensing the biotechnology patents and/or IP. [106] This is a very valuable section, as the interests of an IP licensor are often quite different than the interest of an IP licensee.[107] Next there is in a similar vein, an expansion of a subsection on "University Considerations" under the general section of "Transfer From Academia" wherein new sections on "Considerations of

Employee/Researcher" and "Considerations of Community/Society" have been added.[108] As an overview, Chapter 4 expands its discussion of the background and passage of the Bayh-Dole Act and the evolution of tech transfer at universities.[109] Chapter 4 also importantly discusses the role of the Association of University Technology Managers ("AUTM") and its development into a major driver for standards and practice of university technology transfer.[110] There are also some important additional minor edits to Chapter 4, First Edition, which are helpful and valuable in Chapter 4, Second Edition.[111]

There is an important expansion in Chapter 4 on "Applicability of the Bayh-Dole Act"[112] wherein eight (8) new subsections are added on "Written Employment Agreements," "Royalty Sharing," "Reporting," "U.S. Manufacturing," "United States Retains License," "License Only: No Assignment," "Termination of License If Commercialization is Inadequate," and "Other Considerations." [113] Crucially, all of these are *statutory* requirements of tech transfer licensing agreements drafted under the Bayh-Dole Act; Chapter 4 is careful to note that while some of these restrictions are rarely or never enforced:

> Despite the lack of enforcement of some restrictions under Bayh-Dole, it is still important to recognize the possible restrictions and address them in drafting the license agreement and any

> sublicense agreements. Bay-Dole does not specifically restrict sublicensing, but it requires that sub-licensees carry forward the restrictions imposed by Bayh-Dole on the university and the initial license.[114]

Chapter 4's subsection on the "Conflict Between Publication and Protection of IP" receives new subsection Headers, "Academicians Want to Publish" and "Licensee Due Diligence." [115] This section is generally and specifically discussing the novelty and publication bars to patentability under 35 U.S.C. §§102(a) & 102 (b) *as amended*.[116]

Without getting into great detail, Chapter 4 here is discussing the 102(a) and 102(b) bars on patentability flowing from the novelty requirement relating to publication, public use, offer for sale, and of course, prior art.[117] Likewise, in the next section, Chapter 4 urges due diligence be done by a prospective licensee "before executing a license with the university" to "ensure that no disclosure has been made of the licensed invention."[118]

Chapter 4 has a brief but useful review of how and when to file patents, including why to file a patent, the requirements of patentability, the patent claims and rights, the types and stages of patents and patent filing & patent prosecution, post-issue considerations, foreign patent filing and the PCT.[119]

The effects of outside funding upon ownership of IP are wisely discussed:

> Outside funding of IP comes at a price. Funding by commercial entities usually requires either (1) ownership or rights to future ownership in the company developing the product, or (2) ownership, license, or other rights in the technology being developed. The sources, cost and dilutive effect of outside capital must be factored into the inventor's business plan to insure that the full effect is well understood.
>
> Research funding from a nonprofit institution may also come at a price: many nonprofit corporations limit the extent to which researchers they sponsor may own an interest in companies that license the resulting technology. An example of this is the Howard Hughes Medical Institute ("HHMI"), which generally limits the percentage of equity a sponsored researcher can hold in a company benefitting from that research. That is not uncommon.[120]

A noteworthy observation; part of advising the aspiring biotech entrepreneur is to advise them that even the intellectual property may have to be shared in some respect, whether due to capital requirements or due to institutional requirements of the University (or non-profit) the inventor's laboratory is associated with.[121] Chapter 4 notes therefore:

> In general, the most financially favorable approach to acquiring rights in IP, at least in the short run, is to license the IP from an academic or research institution in return for a royalty stream back to the licensing entity. This avoids dilution of company

> stock and creates no payment obligation unless the product sells. This approach is most commonly acceptable to a university or other nonprofit research institution.[122]

This is followed by a discussion of "kickers" and sublicenses ("royalty sub-stacking").[123]

Thus, Chapter 4 with brevity succinctly covers a wide variety of topics—licensing, collaboration, tech transfer, protection of acquired technologies, acquisition of technologies from universities & private actors; while each of these topics deserve separate specialized volumes in the library of the specialized or serious biotech practitioner, as an introduction or primer to the area, Chapter 4 succeeds in raising all of the correct issues.[124]

The remainder of Chapter 4 delves into many of the same issues, but in much more detail; along with Chapters 2 & 3, the Sample Confidential Agreement at Appendix A to Chapter 3, the Sample Biological Materials Transfer Agreement at Appendix B to Chapter 3, and the Sample Patent & Technology License Agreement at Appendix C to the Second Edition, there is a wealth of material devoted to tech transfer and licensing of biotech, IP & patent rights which simply was not in the First Edition, or did not receive the same amount of emphasis in the First Edition.[125] This represents an important reason to purchase the Second Edition. No competent attorney

can practice in this field without a primer on tech transfer[126] and licensing. Clearly, more specialized books, seminars and websites are needed; most preferably, you should have a stint working in a tech transfer office of a major university. [127] As the Second Edition version of Chapter 4 summarizes:

> There are three lessons we all learned in kindergarten.
>
> First, look both ways before you cross the street. Look at all the IP and determine what the various components are. When you have done that, you can determine whether IP belongs to others and how best to negotiation with them for rights to use that I.
>
> Second, put yourself in the other's shoes. Understand what they need and why….
>
> Third, play well with others…. In southwest Virginia where I grew up, we say that pigs get fat and hogs get slaughtered. This is an important concept…. Fighting hard for the "best possible" deal is still fighting, and fighting often goes badly for both parties.[128]

This is wise advice, indeed.

3) Chapters 5 and 6 – Finance, Fundraising, Securities Law and Employment Law Issues for the Biotech Company

Chapter 5 covering Finance, Fundraising and Securities Law has added a new co-author; also, a new Appendix A to Chapter 5 has been added

which is a useful Glossary of basic equity, VC and securities laws terms.[129] Chapter 5 also covers some issues with crowd-funding and finding safe harbor in this new method of fundraising. Essentially, it should be noted, the Securities Laws still apply, even if you think they do not, unless there is explicit safe harbor and you have reviewed an offering with counsel.

Chapter 6 covering Employment Law is substantially reworked and new sections are added.[130] In light of recent developments in Title IX, the "me too" movement and the need to hire, retain and keep talented employees, as well as firewall valuable IP, trade secrets and trademarks, it is critical to not just monitor employees, but also sign them to legal and binding employment agreements as well as viable agreements which will protect the Company's IP.

Both Chapters are valuable to the in house counsel as well as the outside counsel of the biotech or medical device company.

4) Chapters 8 and 16 – Research and Development Collaborations; Development and Commercialization Alliances

Chapters 8 & 16 do a wonderful job of reviewing RDCs and DCAs. Obviously RDCs are a favored form of collaboration, and Chapter 8 covers this ground thoroughly as well as updating the section thoughtfully and with insight. This is a most valuable Chapter.

Chapter 16 likewise reviews DCAs, which are a favored form of Alliance. DCAs often form a method of "exit strategy" for the startup, mezzanine or even mature biotech/medical device company, and thus Chapter 16 is vital reading. Entering into a 3-5 year DCA which can result in upstream acquisition either of the targeted technology or of the Company itself by the larger Company with which you have allied, can be a utopian ideal in the difficult terrain of biotechnology business. As Chapter 16 summarizes:

> **Conclusion: the Importance of Getting It Right**
> Development Alliances are crucial to the viability of both the pharmaceutical and biotechnology industries. Spurred by weak pipelines and expiring patents, 82% of pharma companies were actively seeking biotech development alliances in 2014—the highest level in history. (citation omitted)….most…obstacles to these deals are, at bottom, business issues. Through careful drafting and through insightful counsel, we can assist our clients over many of the hurdles that might otherwise result in a failed alliance.[131]

Thus Chapters 8 & 16 are crucial for content and bottom line.

X. Chapters 7, 9, 10, 11, 12, 13, 14 & 15 – The Regulatory Chapters

1) Chapters 7 & 9 – Regulation of Preclinical Research and Clinical Research

Chapter 7 is the counterpart of First Edition, Chapter 8, dealing with "Regulation of Preclinical Research," retaining the same author with some

deletions, and some noteworthy additions, including an introduction and a list of key acronyms used.[132] One of the important takeaways from this Chapter 7 (as in its First Edition counterpart) is that bioterrorism laws, rules and regulations instituted since 9/11/2001 potentially apply to all commercial laboratories, including biotechnology laboratories, and compliance must therefore be monitored.[133]

Chapter 9 "Federal Regulation of Clinical Research" is partly the counterpart of First Edition, Chapter 10 "Federal Regulation of Biomedical Research," but just as the Titles of the Chapters are somewhat different, so is the authorship (Chapter 9 has three new co-authors), subject matters and coverage, even though some of the coverage obviously overlaps to some degree.[134] Chapter 9 now nicely bookends Chapter 7, and thus together they collectively introduce one to the subject matter of Federal Regulation of Preclinical and Clinical Research.

These are vital topics for anyone in the Biotech field to read and understand, and beyond this, to master and keep up with, as FDA approval matters are often subject to frequent legislative and regulatory changes, as well as trends emanating from individual FDA Commissioners and FDA regulators.[135] The FDA is constantly changing and emitting new regulations

and regulatory regimes; it is incumbent upon counsel, inside or outside, as well as those in industry, to keep abreast.

2) Chapter 10 – Privacy Issues for Biotechnology Companies

Chapter 10 has a different author and is very much reworked and revised from the First Edition counterpart.[136] Chapter 10 include pertinent discussions of the Privacy and Security Rules promulgated pursuant to the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"),[137] the EU's General Data Protection Regulation ("GDPR") [138] and the California Consumer Privacy Act of 2018 ("CCPA"),[139] and other relevant privacy laws.[140] A table of Key Acronyms Used is added at the end of Chapter 10, which is most useful.[141]

There are many more things that could be said about privacy issues, but the main points are made in Chapter 10—mainly the compliance issues which mostly apply to biotech and medical device companies. It should go without saying that the confidentiality of participants in clinical and pre-clinical trials must be respected in accordance with those guidelines as well, and that any biotech/medical device company must have a social media policy with respect to all principals and employees which is rigorous. The EU is even more strict than the US in regards to these matters, but Chapter 10 touches on them all the same.

3) Chapter 11 – Medical Reimbursement

Chapter 11 adds an Introduction, acronyms are substituted for some spelled out terms and a list of "Key Acronyms Used is provided."[142] Chapter 11 remains a useful, key component of the treatise as revised since it deals generally with the important topic of getting medical insurance reimbursement for qualifying clinical trials and new technologies. Ideally, the Federal reimbursement scheme would reimburse 100% of all patients enrolled in all stages of all clinical trials in pharmaceutical and clinical trials for their care. The U.S. Government's failure to do so could be a contributing cause to the perceived high prices of U.S. drug and biologics development; Chapter 11 denotes demarcations between eligibility and non-eligibility with definiteness and clarity. Certainly this Chapter is most pertinent.

4) Chapter 12 – Environmental Regulation of Biotechnology

Chapter 12 is entirely new and has no counterpart in the First Edition, and thus is a welcome addition.[143] As a prefatory note, the current administration has been actively rolling back a good deal of EPA oversight and regulation, so it is important to consult with counsel and monitor up to date developments in this field.[144] Generally speaking, Chapter 12 discusses how EPA regulates biotechnology under the Toxic Substances Control Act

("TSCA") and the Federal Insecticide, Fungicide and Rodenticide Act ("FIFRA").[145] Of course, there is much more to it than that, but for the interested reader, just pick up the Second Edition to learn more.

5) Chapters 13, 14 & 15 – Approval of Biotechnology Products for Human Use; Agricultural Biotechnology Approval Processes; and Federal and State Regulation After Approval

Chapter 13 is much revised, devoting more time to fast-track expedited regulatory pathways to market, biologics, medical devices, and drugs, as well as the conventional means via the New Drug Application ("NDA"), 505(b)2) Application ("505(b)(2)"), Biologics License Application ("BLA"), Pre-Market Approval Process ("PMA"), 510(k) Notification Process ("510(k)") and various fast-track approval processes which now exist, such as Orphan Drug Designation.[146] Chapter 13 also wisely adds a list of Key Acronyms Used.[147]

Chapter 14 has a slightly different title, a different author, and devotes time to agribiotech's newest and latest issue, genetically modified crops aka Genetically Modified Organisms ("GMOs").[148] The sections on the roles of the USDA, EPA and FDA are reworked and expanded, and there is new material on GMOs and the regulation of "genetic editing in agriculture."[149] Of course, prior to 2018, Monsanto was one of the biggest agribiotech

players in the USA, if not the world, but it was acquired in a complex deal by Bayer, which involved divestiture by both Bayer and Monsanto of certain assets, which went to BASF, in a $66 Billion acquisition, the net result of which was Bayer acquiring the Monsanto agribusiness, the extinction of the Monsanto name, and Bayer and BASF gaining these valuable rights.[150] Chapter 14 has incredibly useful discussions of the interactions of state, federal, international and regulatory regimes as to labeling and many other issues pertaining to agricultural biotechnology. It cannot be overstated how vital and pertinent this material is.

Chapter 15 has a somewhat modified title and reworked index and content.[151] It has an overall discussion of the Regulatory Authorities, including the FDA, OIG/HHS, DOJ/Civil Division, FTC & SEC; a long discussion of "post-approval responsibilities" covering CGMP, post-approval reporting, import-export requirements, and regulation of advertising/labeling.[152] Finally, there is a new and very useful listing of nearly two dozen cases from 2005 through 2017 brought under the False Claims Act[153] (so called "*qui tam* or "whistleblower" actions) all of which brought bio-pharmaceutical companies to heel in large settlements.[154] Chapter 15 should thus be read in conjunction with the litigation (and

prevention of litigation) Chapters 17, 18 & 19. Overall, this is yet another excellent exemplar of the Second Edition.

XI. Chapter 20 – Bioethics

Chapter 20 devotes a chapter to Bioethics; obviously, books could be devoted to this subject. Bioethics are relevant because:

> Since the development arc of a pharmaceutical product…usually is 10-15 years, ethical standards and the law can change critically during that time. Keeping apprised of these issues give you a head start on predicting future regulatory changes or concentrations. The reality is that in order to manage or advise a biotech company effectively, you must understand the basic concepts of bioethics. Ethical questions today may be hard law, regulation and liability tomorrow.[155]

Meta-ethically speaking,[156] this essentially furnishes a utilitarian[157] basis for keeping track of, and complying with, bioethics.[158] For most of us in the real word, that concludes the matter.

1) Hippocrates of Kos and the History of Bioethics

Chapter 20 states that "the concept of bioethics is ancient, dating back at least to Hippocrates [of Kos, Greece] and further notes that the first principle of the Hippocratic Oath is 'Do No Harm', the famed '*Primum non Nocere*."[159] As it turns out, Hippocrates may not even have come up with this famous phrase.[160]

Perhaps the most important thing about Hippocrates of Kos is the sheer amount of biology, biotechnology and medical conferences which convene at the Island of Kos (a luxury resort in Summer and well into Fall, located in the Cycladic islands).[161]

Foundational Sources and History of Bioethics, according to Chapter 20, include the Hippocratic Oath, Percival's Medical Ethics, the Nuremberg Code, the Belmont Report and the Helsinki Declaration, together with the works of Hippocrates, Maimonides, Aristotle, Kant, Mill, Percival, Hume, Rousseau and others.[162]

To this list, one might add the experiences we had with eugenics and irregularities with prison experimentation here in the United States both before and after World War II; as well as the horror of the concentration camps and the revelation of the ghastly experiments conducted upon human subjects by Nazi doctors in the name of "science."[163]

2) Core Principles of Bioethics

Chapter 20 takes us rapidly through the invention of the term "bioethics," the complexities of the issues involved, various approaches such as deontological, utilitarian, virtue ethics, the four principal approach (patient autonomy, patient benefit, no maleficence, and justice) with a fifth principle added of confidentiality. Chapter 20 also discusses casuistry. In

the end, Chapter 20 seems to rest on the "Core Principles of Bioethics" as being 1) Personal Autonomy 2) Beneficence/Nonmaleficence 3) Justice and 4) Confidentiality.

3) The Abortion and Euthanasia Debates

Chapter 20 then gets into a long discussion about Reproductive Rights as well as the issue of the so-called "right to die." This is a long and quite useful section.[164]

4) Metaethics – How are Ethics Possible, Let Alone Bioethics?

From the meta-ethical, philosophical point of view, there is substantial dispute as to whether an ethics of anything is even possible, notably the Philosopher J.L. Mackie, who introduces his famous book *Ethics: Inventing Right and Wrong* (1977) by declaring bluntly "[t]here are no objective values."[165] These types of arguments are grouped together as "moral anti-realism" and subsist of moral error theory (moral skepticism), championed by Mackie, moral non-objectivism, moral relativism and so forth, boiling down to the essentially morally nihilistic view that moral judgments are meaningless and lack any objective or subjective basis whatsoever.[166]

This trend only worsens with Thomas S. Kuhn,[167] W.V.O. Quine[168] and Richard Rorty,[169] all of whose works tried to disestablish epistemology itself from objectivity, and instead substitute relativity, or at best, in the case

of Kuhn, some kind of Kantian constructivist paradigm in lieu of scientific laws and facts.

5) The Antidote to Radical Skepticism

The antidote to radical skepticism of this kind is perhaps best considered in the wake of what we discussed, *supra*, and what was discussed in Chapter 20—the widespread horror at the bad outcome of the Penn gene therapy trials in 1999 in the Jesse Gelsinger case; the *Terry Schiavo* & *Abigail Alliance* cases; the Nuremberg Code (and the U.N. Declaration of Human Rights) passed in the wake of the horrors of the German camps, and the German medical experiments; and the dreadful unearthing of terrible secret U.S. experiments, unethical and barbaric, including the Tuskegee Syphilis Experiments of 1932, brought to light only in 1972.

Our visceral response must be to recoil in horror, and say, "well, this is all WRONG." And by emitting that one word, we have made a determination, based upon fact and reason, that wrong and evil exist. From there it is but a short step to agree to construct a system of ethics, for if we agree on what is wrong, that perhaps we can agree upon what is right.

For it is one thing to argue theoretically that there no ethics, or only relativistic ethics; but quite another to face an evil so absolute, so horrible, that nearly all of us can *intuit*, or as Kant famously said, using his

analytic/synthetic distinction, *know by pure mind* or "transcendental logic."[170] For without God, there can be no devil, and without Right, there can be no wrong. And thus we come to rules, regulations, and bio ethics. And it is good.[171]

This is not the hardest thinking in the world, but so simple even a child knows it. Every Court knows it---their test of sanity is, does the defendant know right from wrong? Philosophical exegeses will not assist one in defending such a proposition. Hence, we must have a *practical* ethics to govern our actions, lest evil overtake us.

6) <u>The Nazi Horrors and U.S. Horrors</u>

Chapter 20 drills in on the brutal, horrible experiments on patients conducted by the Nazis:

> …some of the first high-profile examples of abuse of human beings in research came to light in the aftermath of World War II, when 23 Nazi Doctors were tried at Nuremberg for using thousands of concentration camp prisoners as subjects in brutal experiments….[172]

Chapter 20 then discloses the 1963 Henry Beacher paper which disclosed 22 studies "in which adherence to ethical standards was questionable" including a study in Brooklyn in 1963. The Tuskegee syphilis study from 1932 was exposed in 1972. This all led to enactment of the 1974 National Research Act, and the creation of the National Commission for the Protection of

Human Subjects of Biomedical and Behavioral Research. As part of the act and report, it enunciated the bedrock principles of 1) respect for persons 2) beneficence and 3) justice, as well as issuing guidelines for human subject research.[173]

7) Kinds of Guidelines Issued

Chapter 20 then discusses HHS Human Subject Protection Regulations, FDA Human Subject Protection Regulations, and famously, rDNA regulation. Recombinant DNA ("rDNA") regulation is illustrated as a paradigm of how "many herald it as an example of creative management of risks and ethical conflicts raised by advances in science."[174]

Next Chapter 20 discusses a series of case studies, including the Dalkon Shield litigation, the Jesse Gelsinger gene therapy case at Penn (COI), the lead abatement study by Kennedy Krieger Institute/Johns Hopkins, an informed consent case involving ASU, and so forth.

Finally, Chapter 20 concludes:

> Sensitivity is the key to recognizing the potential pitfalls ahead of time….Do not harm the patient; be sure the patient understands the procedure and the risks; do not break the law; be sure that your motives are pure…essentially, common sense, or, "Everything I Need to Know I Learned in Kindergarten" will avoid problems most of the time."[175]

Indeed.

XII. CONCLUSION

Biotechnology has advanced greatly since 2007. Indeed, it is estimated that every five years in Molecular Biology represents a doubling of knowledge in the field. This reviewer was recently at a CAR-T gene therapy/oncology conference for several days at the University of Pennsylvania, where it can be envisioned that a cure to cancer is finally upon the horizon; efficacy studies passing the three rungs of the FDA showed amazing results for hopeless cases of acute leukemia patients facing nearly certain death sentences under the old approaches. Within the last 2-5 years, hundreds if not thousands of new companies have flooded into the CAR-T/gene therapy/oncology space. Meanwhile, other promising therapies, like RNAi, antisense, CRISPR and many others continue to flourish and advance, despite legal, regulatory and societal hurdles. The biotechnology enterprise has just begun.

Into this bright future enters the much-heralded Second Edition and its wonderful Editors-in-Chief, and its many marvelous contributors and authors, including author-editors. This is a substantive reference work, a well-thought out compendium, and a book that has a place on the shelf of everyone who works, teaches, counsels or otherwise endeavors in the beautiful, bounteous and boundless endeavor of Biotechnology.[176]

THE END

ENDNOTES

[1] J.D., MSc.E., Molecular Biologist, Consultant, Adjunct Professor, Scholar & Life Sciences Patent Attorney (retired from law practice); Consultant to the Pharmaceutical & Biotechnology Industries (Philadelphia Biotech & Pharma, Inc. ("PPBI")); Visiting Adjunct Lecturer, Penn, Princeton, Johns Hopkins, & others; Editorial Board Member, Biotech Law Reports & other peer-reviewed journals, 2005-present. © Arthur J. Kyriazis, 2019, all rights reserved. Independent Scholar Author & Editor.

[2] Second Edition. Hugh B. Wellons & Robert F. Copple. "Preface." *Id.* at pp. xxxvii-xxxix. (Hereinafter, "Preface").

[3] Hugh B. Wellons *et al.* Eds. *Biotechnology and the Law.* (2007). (Hereinafter, the "First Edition"). *C.f.* Arthur Kyriazis. "Book Review: Biotechnology and the Law." 29 *Biotech. L. Rep.* 187 (2010).

[4] *C.f.* The Ventures first LP, 1960, "Walk Don't Run." Original Vinyl Issue, Dolton BLP-2000 (mono). Also issued in stereo. *C.f.* Wikipedia & sources. https://en.wikipedia.org/wiki/Walk,_Don%27t_Run_(album). For a video of the Ventures performing Walk Don't Run on the Saturday Night Beech-Nut Show. August 27, 1960, introduced by the late, great Dick Clark, *see https://www.youtube.com/watch?v=owq7hgzna3*

[5] However, as is noted, *infra*, many of the Chapters in the Second Edition have added lists and/or appendices of "Key Acronyms Used." These serve much the same function as the General Glossary did in the First Edition, and are far more useful, *see discussion, infra.* The original glossary was in the First Edition, Chapter 1 at pp. 13-23 and can still be found online at http://ucbiotech.org/glossary/index.html. For a more complete glossary online, the FAO maintains one, as do many, many others. *See, e.g.*, *http://www.fao.org/3/X3910E/X3910E04.htm*

[6] Second Edition. Chapter Twenty. Gary E. Merchant, Robyn S. Shapiro & Hugh B. Wellons. "Bioethics." *Id.* at pp. 977-1016. (Hereinafter, "Chapter 20" or the "Bioethics Chapter"). This Chapter has no counterpart in the First Edition.

[7] Second Edition. Appendix A. "Goat-Tech Bioscience: A Legal/Biotech Case Study." *Id.* at pp. 1017-1020. (hereinafter, the "Case Study" or "Appendix A").

[8] Second Edition. Appendix C. "Patent & Technology License AGT. NO. _____." *Id.* at pp. 1053-1086. (Hereinafter, "Sample Licensing Agreement" or "Appendix C").

[9] *See* Preface *passim*: "About the Editors" & "About the Authors" at pp. xlii-lv, *passim.*

[10] Preface at pp. xl-xli.

[11] Second Edition. Chapter One. Robert F. Copple & Hugh B. Wellons. "Introduction to Biotechnology and the Law." (Hereinafter, "Chapter 1"). *Id.* at pp. 1-13. This Chapter had a Counterpart in Chapter I of the First Edition (Hereinafter, "First Edition, Chapter 1").

[12] Second Edition. Chapter Two. Margaret J. Sampson & Michelle M. LeCointe. "Managing Innovation: Patent Basics for Biotechnology Counsel." *Id.* at pp. 15-76. (Hereinafter, "Chapter 2"). Chapter 2 has its counterpart in the First Edition, Chapter II. (Hereinafter, "First Edition, Chapter 2). Note that Chapter 2 is revised, has different authors, and covers somewhat different ground than the First Edition, Chapter 2.

[13] Second Edition. Chapter Seventeen. Michelle G. Breit & Robert F. Copple. "Patent Litigation and Dispute Proceedings Overview for the Non-Patent Attorney." *Id.* at pp. 829-883. (Hereinafter, "Chapter 17'). Chapter 17 has its Counterpart of sorts in the First Edition, Chapter 19 (Hereinafter, "First Edition, Chapter 19"). Chapter 17 is broader and adds two new co-authors as well as being substantially re-written and being re-worked. Chapter 17 has been expanded to included dispute proceedings not resolved in the Courtroom (*e.g.* ADR, arbitration, mediation, and the like) and thus takes into account a substantive development since 2007: litigation has become expensive, especially in the federal courts. A corollary development is the explosion of electronic discovery, which requires prophylaxis at the earliest stages, lest a trade secret or patentable idea escape the parameters of a Protective Order by electronic means.

[14] Second Edition. Chapter Nineteen. Robert F. Copple. "Risky Business: Litigation, Risk Management, and Dispute Control." *Id.* at pp. 937-976. (Hereinafter, "Chapter 19"). Chapter 19 is the approximate counterpart to the First Edition, Chapter 20, but it is differently titled and substantially reworked. (Hereinafter, "First Edition, Chapter 20"). Note that Chapter 19 speaks of "Risk Management" and "Dispute Control," again recognizing the risks and costs of litigation in 2020 and future years, as opposed to the environment *circa* 2007.

[15] Second Edition. Chapter Eighteen. Craig B. Young. "The Impact of Bankruptcy." *Id.* at pp. 885-936. (Hereinafter, "Chapter 18").

[16] Second Edition. Chapter Three. Andrew T. Hoyne & Cortney E. Mendenhall. "Company Formation." *Id.* at pp. 77-169. (Hereinafter, "Chapter 3"). *Including* Appendices to A-B at pp. 144-169. (Hereinafter, "Appendices to Chapter 3"). Appendix A at pp. 144 *et seq.* is a "Mutual Confidentiality Agreement" while Appendix B at pp. 151-169 is a "Biological Materials Transfer Agreement." Chapter 3 had a Counterpart in the First Edition; one of the authors is the same, one is different, and there are changes in the material covered at relevant areas. First Edition. Chapter III. (Hereinafter, "First Edition, Chapter 3").

[17] Second Edition. Chapter Four. Hugh B. Wellons, "Acquisition of Biotechnology—Technology Transfer." *Id.* at pp. 171-240. (Hereinafter, "Chapter 4"). Chapter 4 has a Counterpart at First Edition, Chapter IV (Hereinafter, "First Edition, Chapter 4"), but Chapter 4 is reworked and expanded substantially.

[18] Second Edition. Chapter Five. Bill Wofford & Ken Maready. "Financing a Biotech Company." *Id.* at pp. 241-310. (Hereinafter, "Chapter 5"). *Including* Appendix A ("Glossary of Frequently Used Basic Equity, Venture Capital and Securities Law Terms"). (Hereinafter "Appendix A to Chapter 5"). Chapter 5 had a Counterpart in the First Edition, at Chapter V, but adds a new co-author and substantive revisions. (Hereinafter, First Edition, Chapter 5").

[19] Second Edition. Chapter Eight. Eileen Smith Ewing & Hugh B. Wellons. "Research and Development Collaborations." *Id.* at pp. 413-447.

(Hereinafter, "Chapter 8). Chapter 8 is the counterpart of First Edition, Chapter 9; it has the same title, adds a co-author and is seasonably amended and updated. (Hereinafter, "First Edition, Chapter 9").

[20] Second Edition. Chapter Sixteen. Eileen Smith Ewing & Hugh B. Wellons. "Development and Commercialization Alliances." *Id.* at pp. 799-828. (Hereinafter, "Chapter 16"). Chapter 16 has its Counterpart in First Edition, Chapter XVIII. (Hereinafter, "First Edition, Chapter 17").

[21] Second Edition, Chapter Seven. Daniel T. Pancamo. "Regulation of Preclinical Research." *Id.* at pp. 375-411. (Hereinafter, "Chapter 7"). There is also a new subsection on "NIH Policies Regarding the Use of Chimpanzees in Research," *id.* at p. 393 *et seq.* Chapter 7 has its Counterpart at First Edition, Chapter VIII (Hereinafter, "First Edition, Chapter 8").

[22] Second Edition. Chapter Nine. Erika Lietzan, Afia Asomoah & Linda McCarty. "Federal Regulation of Clinical Research." *Id.* at pp. 449-500. (Hereinafter, "Chapter 9"). Chapter 9 is the Counterpart of the First Edition, Chapter X. (Hereinafter, "First Edition, Chapter 10").

[23] Second Edition. Chapter Ten. Rebecca Frigy Romine. "Privacy Issues for Biotechnology Companies." *Id.* at pp. 501-573. (Hereinafter, "Chapter 10"). Chapter 10 is the Counterpart of the First Edition, Chapter XI. (Hereinafter, "First Edition, Chapter 11"). Chapter 10 has different authors and is much reworked from First Edition, Chapter 11.

[24] Second Edition. Chapter Twelve. Stephen A. Owens. "Environmental Regulation of Biotechnology." *Id.* at pp. 607-657. (Hereinafter, "Chapter 12"). Chapter 12 has no Counterpart in the First Edition; it is entirely new.

[25] Second Edition. Chapter Eleven. Paul W. Radensky & Amy Hooper Kearbey. "Medical Reimbursement." *Id.*at pp. 575-605. (Hereinafter, "Chapter 11"). Adds a list of "Key Acronyms Used" at pp. 604-605. Chapter 11 has a Counterpart at First Edition, Chapter XII (Hereinafter, First Edition, Chapter 12), but adds an author and revises the material covered.

[26] Second Edition. Chapter Thirteen. Areta Kupchyk & Snehal Trivedi. "Approval of Biotechnology Products for Human Use." *Id.* at pp. 659-708. A list of "Key Acronyms Used" is provided at pp. 707-708. Chapter 13 has an approximate Counterpart at First Edition, Chapter XIII (Hereinafter, "First Edition, Chapter 13), but Chapter 13 adds a new co-author, the title is different and the material covered is different to a large degree, reflecting the newer more expedited paths to market.

[27] Second Edition. Chapter Fourteen. Thomas P. Redick. "Agricultural Approval Processes." *Id.* at pp. 709-736. (Hereinafter, "Chapter 14"). Chapter 14 has its Counterpart of sorts at First Edition. Chapter XV. (Hereinafter, "First Edition, Chapter 15"). However, Chapter 14 has a different author, a different title, and covers somewhat different and updated subject matter, including the now current & vital subject of GMOs, which are discussed in Chapter 14, *passim* & at pp. 723-736.

[28] Second Edition. Chapter Fifteen. Areta Kupchyk. "Federal and State Regulation After Approval." *Id.*at pp. 737-798. (Hereinafter, "Chapter 15"). Chapter 15 has a list of "Key Acronyms Used" at pp. 979-798. Chapter 15 has its Counterpart at First Edition, Chapter XVI. (Hereinafter, "First Edition, Chapter 16").

[29] Appendix A, *cited supra;* Appendix C, *cited supra;* Second Edition. Appendix B. Jennifer Korpacz Pelaia. "Biotechnology Resources." *Id.* at pp. 1021-1052. This list is somewhat different than its Counterpart in the First Edition. (Hereinafter, "Appendix B"). (Collectively, the "Appendices").

[30] *Id.*

[31] Preface at p. xl; Chapter 1 at p. 5.

[32] Second Edition. Appendices A, B & C, at pp. 1017 *et seq.*

[33] Appendix A.

[34] *Id.*

[35] *Id.* at p. 1020.

[36] Appendix B, *passim.*

[37] *Id.* at pp. 1028-1042.

[38] *Id.*

[39] Second Edition. Appendix C. "Patent & Technology License AGT. NO. _____" *Id.* at pp. 1053-1086. (Hereinafter, "Sample Licensing Agreement" or "Appendix C").

[40] 35 U.S.C. §§200-212 *as amended.* (Hereinafter, the "Bayh-Dole Act"). For an explanation of the importance of the Bayh-Dole Act in the development of biotechnology, *see* Chapter 4 at pp. 202-205 & p*assim. See also* Arthur J. Kyriazis. "Thirty Years of Biotechnology: Another Observer's Perspective." 31 *Biotech. L. Rep.* 9 (2012). (arguing, *inter alia*, that three key drivers for the biotech industry from 1980-2010 were the *Chakrabarty* decision (*Diamond v. Chakrabarty,* 447 U.S. 303 (1980)) (holding that a bioengineered strain of *Pseudomonas putida* which digested petroleum oil byproducts more rapidly than the natural strain was patentable subject matter), the Bayh-Dole Act and the creation of the Federal Circuit Court of Appeals in 1982.). *Id.*

[41] *See id. and* the Federal Laws and Regulations pertaining to Cooperative Research and Development Agreements (Hereinafter, "CRADAs). *See* 35 U.S.C. §§200-212 & the regulations promulgated thereunder; 15 U.S.C. §3710a (governing CRADAs); 37 C.F.R. §§401 *et seq.* & 37 C.F.R. §401.3 (dealing with required provisions in tech transfer/licensing agreements under the Bayh-Dole Act).

[42] Second Edition. Index. *Id.* at pp. 1087-1137. (Hereinafter, the "Index").

[43] First Edition. Chapter VII. G. Melissa Ince & Jenny Kim. "Federal Regulation of Research Through Funding." *Id.* at pp. 325-405. (hereinafter, "First Edition, Chapter 7"). Chapter XIV. Robert B. Nicholas & Kent D. McClure. "The Regulation of Biomedical Products for Animal Use." *Id.* at pp. 623-660. (Hereinafter, "First Edition, Chapter 14"). Chapter XVIII. Daniel Pavin. "Expansion: European and International Considerations for

Biotechnology Companies." *Id.* at pp. 735-812. (Hereinafter, "First Edition, Chapter 18") (collectively, "First Edition, Chapters 7, 14 & 18").

[44] *Id* at pp. 325 *et seq.* & *passim.*

[45] *Id.* at pp. 623 *et seq.* & *passim.*

[46] *Id.* at pp. 735-812.

[47] *Id.* at p. 11 & pp. 6-13 *passim. See also "*Figure 1-1: "The Biotech Company Life Cycle, Biotech Business Life Cycle," *id.* at p. 7.

[48] First Edition, Contents at p. iii & First Edition, Chapter 1 at pp. 4-12, *passim.*

[49] Chapter 1 at p.3.

[50] *Id.* at pp. 3-4.

[51] Second Edition. Chapter Two. Margaret J. Sampson & Michelle M. LeCointe. "Managing Innovation: Patent Basics for Biotechnology Counsel." (Hereinafter, "Chapter 2").

[52] *Id.* at pp. 15-76, *passim.*

[53] The big picture is that modern companies in the 21st century manage ideas, not things:

> [W]e are increasingly operating in an economy that revolves around the production and management of information rather than physical production. The more than an organization is involved in managing information, the more likely it is to be operating in the realm of intellectual property, as opposed to physical property, in a variety of respects.

John Palfrey. *Intellectual Property Strategy.* (2012), Introduction at pp. 11-12. Biotech companies' IP Portfolios will be conformed and distributed

quite differently than other companies' IP Portfolios; the biotech company's patent portfolio/patent estate will occupy a much greater proportion or ration of the IP Portfolio. In short, the biotech patent estate is often the highest impact portion of the IP Portfolio of a startup, mezzanine or even a mature biotech company. This is well understood by biotech specialists, and thus Chapter 2 properly focuses upon the patent estate closely.

[54] David Bainbridge & Claire Howell. *Intellectual Property Asset Management: How to Identify, Protect, Manage and Exploit Intellectual Property within the Business Environment.* (2014). *Id.*, Preface at pp. i-ii;

> In the 19th & 20th centuries, land, labor and capital were the crucial factors in wealth creation. This has changed: today it is IP. Intellectual or intangible assets are now recognized by many organizations as their most important resource….
>
> In this digital age a company's IP Portfolio represents on average 60-70% of its business value. U.S. companies now invest more than $1.1 trillion annually in intangible assets. There is good evidence that those companies with large well-managed IP Portfolios are more profitable than those that are IP passive. *Id.*

[55] Biotech patent law (and patent law overall) has changed greatly since 2007; it is much more difficult to 1) obtain a patent and 2) maintain a patent against challenge in 2019 than it was in 2007, due to statutory changes, Supreme Court and lower court decisions, as well as numerous regulatory and examination guideline changes by the USPTO in light of said decisions.

Thus, as one empirical study has found in studying challenges to issued patents after *Alice Corp. v. CLS Bank International*, 573 U.S. 208 (2014);

> As of June 19, 2016, courts have examined 568 challenged patents brought under § 101 motions citing Alice, resulting in 190 valid patents and 378 patents invalidated with an average invalidation

> rate of 66.5%. Specifically, the Federal Circuit upheld 3 patents and invalidated 34 patents — an average invalidation rate of 91.9%. Also, courts have decided a total of 500 motions brought under § 101 citing Alice, resulting in 109 validation holdings and 391 invalidation holdings with an average invalidation rate of 78.2%. Specifically, the Federal Circuit has decided 26 motions, resulting in 2 validation holdings and 24 invalidation holdings with an average invalidation rate of 92.3%. The district courts have decided 251 motions, resulting in 84 validation holdings and 167 invalidation holdings with an average invalidation rate of 66.5%. The PTAB has decided 209 motions, resulting in 23 validation holdings and 186 invalidation holdings with an average invalidation rate of 89.7%.

Jasper L. Tran. "Two Years After Alice v. CLS Bank." 98 *J. Pat. & Trademark Soc'y* 354 (2016). *Id.* at p. 355. (Hereinafter, "Tran 2016"). However, in a more recent empirical study by the very same author which was published in 2019, the invalidation rate has fallen (somewhat) to 56.2% from the higher numbers cited in Tran 2016:

> **Abstract:** This paper updates the statistics on the five years after *Alice v. CLS Bank* and discusses 19 Federal Circuit cases (including their exemplary patent claims) that found eligibility upon *Alice* challenges. The *Alice* invalidation rate at the Federal Circuit and district courts has lowered over time, averaging cumulatively 56.2% at its near-five-year mark.

Jasper L. Tran & J. Sean Benevento. "Alice at Five". 2019 *Patently-O L.J.* 25 (2019). *Id.* Abstract at p. 25. (hereinafter "Tran 2019").

56 Chapter 2 at pp. 15-76, *passim*. Noteworthy U.S. Supreme Court cases discussed in the text include several landmark cases: 1) *Alice Corp. v CLS Bank International,* 573 U.S. 208 (2014) (narrowing the scope of

patentability of software patents under 35 U.S.C. §101 by expanding the doctrine of "abstract ideas" and instituting a two part test of patentability under Section 101**;** 2) *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013) (claims for patenting BRCA1 & BRCA2 genes rejected because merely isolating genes found in nature did not make them patentable, extending *Prometheus* to biotech claims); 3) *Mayo Collaborative Services v. Prometheus Laboratories Inc.* 566 U.S. 66 (2012) (invalidating biomedical claims under 35 U.S.C. §101 by expanding the doctrine of "unpatentable laws of nature"); and 4) *Bilski v. Kappos*, 561 U.S. 593 (2010) (narrowed "business method" patentability claims under 35 U.S.C. §101 by narrowing the test of "usefulness"). (hereinafter, these cases are cited as "*Alice", "Myriad Genetics", "Mayo" & "Bilski"*).

[57] *Id. (incorporation by reference all cases cited therein). See* Chapter 2 at pp. 20-28 for their analysis of the changes in patent terms, the AIA changes, their analysis of *Mayo*, *Myriad Genetics, Bilski & Alice. See also Vanda Pharma v. West-Ward,* 887 F.3d 1117 (Fed. Cir. 2018) (*request for en banc review denied).* (this time allowing patentability under the *Mayo* doctrine).

[58] Tran at p.355, quoting Breyer from an oral argument held before the Court in 2016. (original citation omitted). Justice Breyer once wrote a law review in which he considered at length the abolition of copyright protection altogether, and urged Congress strongly to 1) not extend copyright terms and 2) not strengthen copyright protections. not be strengthened by Congress, all upon policy grounds. S. Breyer "The Uneasy Case for Copyright: A Study of Copyright in Books, Photocopies and Computer Programs." 84 *Harv. L. Rev.* 281 (1970).

[59] *Vanda, cited supra.* On the USPTO Memo, *see* Donald Zuhn, "USPTO Issues Memorandum on Vanda Pharmaceuticals v. West-Ward Pharmaceuticals." Patent Docs Blog. (July 9, 2018). https://www.patentdocs.org/2018/07/uspto-issues-memorandum-on-vanda-pharmaceuticals-v-west-ward-pharmaceuticals.html. The empirical research by Tran, *cited supra*, Tran 2016 & Tran 2019, would suggest that it is possible to hypothesize that some of the reason for increased sustainability of patents upon challenge between 2016 and 2019 could be the *Vanda* decision, although Tran himself did not test, hypothesize or control for that

variable or thesis. It certainly is worth studying in a future paper using basic quantitative and statistical tools.

[60] Chapter 2 at pp. 28-30 & *passim.*

[61] Dennis Crouch. "How Many Patents Issued in 2019?" *PatentlyO Blog.* "New Record – 354,507 Utility Patents issued by the USPTO in 2019. The decade (2010s) also outstripped any other decade by leaps and bounds." *Id.* *https://patentlyo.com/patent/2019/12/many-patents-issued.html* *See also* graphs and tables therein. *Id.*

[62] *Id.* at pp. 30-50 & *passim.* The patent filing, examination and post-grant processes have changed substantially since the publication of the First Edition; not just as to form but as to rigor and challenge of having a biotech patent's claims granted and surviving post-issue challenge and ultimately litigation challenge. The need for skilled patent prosecution counsel and skilled patent litigation counsel has thus never been more acute than at the present time. This is a substantial change one should note together with the Second Edition. *Id.*

[63] The Patent Trial and Appeal Board (Hereinafter, "PTAB"). https://www.uspto.gov/patents-application-process/patent-trial-and-appeal-board/about-ptab

[64] Chapter 2 at p. 50 & n 27 (citation omitted in quotation).

[65] *See* Tran 2016 & Tran 2019, *supra*.

[66] Chapter 2, *passim.*

[67] Chapter 17 at pp. 829-839.

[68] *Id.* at pp. 840-883 & *passim*.

[69] *See* Chapter 18 *passim.*

[70] *Id* at pp. 914 *et seq.* (discussing the rights of the Debtor-in-Possession "DIP").

[71] Chapter 18 at p. 912 & n.75.

[72] For example, for maximum security, it is not unheard of to require personal mortgages and notes of each individual that is party to a transaction, securing their primary residences as collateral to secure transactions, in addition to taking first lien interest and anti-subordination anti-dilution language, *et al.* It is fundamentally incumbent on any Creditor holding a lien interest to constantly do due diligence to maintain their secured, priority lien status. Also, if any of the parties have a boat, take a first lien status on the boat—it can be arrested to settle a debt pursuant to the *in rem* rules of the Admiralty court upon notice and motion to the Bankruptcy Court. Or seized prior to the Bankruptcy Filing, even better.

[73] Chapter 18 at p.914 & n.81, *citing* 11 U.S.C. § 303, *as amended.*

[74] 756 F.2d 1043 (4th Cir. 1985) (holding when DIP rejected the license agreement containing a right to use a coating process being used by Creditor-Licensor, the only remedy was a claim for rejection damages). *Cited in* Chapter 18 at p. 924. This case resulted in the enactment of 11 *U.S.C. 365(n). Id.*

[75] Chapter 18 at pp. 924-25.

[76] Chapter 18 at pp 926-926.

[77] *Chapter* 5 at p. 77.

[78] *Id.* at pp. 83-90.

[79] *Id.* at pp. 81-82.

[80] *Id.*

[81] *Id.* at p. 82.

[82] *Id.*

[83] *Id.*

[84] *Id.* at pp. 130 *et seq.*

[85] *Id.* at p. 86-87. The discussion of Biotechnology Company Models is at pp. 83-90, *id.*, and included *inter alia*, the "Company Formed before In-Licensing While R & D Continues at University", the "Technology Flip", the "Revenue Funded Company", the "Corporate Deal Funded Company," the "Holding Company and Series LLC," the "Venture Fund Launched Company," the "Angel Investor Funded Company," the "Significant Self-Funded Company," the "Shoestring Self-Funded Company," the "Charitable Corporation or Foundation," and the "Debt-Funded Company." *Id.*

[86] *Id.* at p. 86.

[87] *Id.* at pp. 90-99. As Chapter 3 explains, the ideal Biotech Company generally requires not just a Board of Directors and a Management Team, but also a Scientific Advisory Board, a Founder or Board of Founders, a CEO who normally is NOT a scientist, a CFO, a Regulatory team to handle clinical and other regulatory issues such as ANDA, FDA and the like; and of course ideally, an in house legal team. Thus this type of company may need a CEO, a CFO, a CSO, a Chief Regulatory Officer, and so on. Looking downwards to ethics, many biotech and pharmaceutical companies have a Bioethics Advisory Board ("BAB") (aka Ethics Advisor Board) ("EAB) or an outside Bioethics Adviser. *Id.* & Second Edition *passim.* The Merck Corporation famously had a "Mission Statement" for decades which defined its ethical course of conduct—it was not purely a for profit corporation. Of course, capital concerns, the "burn rate", and many other factors will dictate the speed at which all these parts come together smoothly. *Id.*

[88] *Id.*

[89] *Id.* at pp. 97-98. Second Edition, Chapter 6. Jeffrey A. Van Doren. "Employment Issues for Biotechnology Companies." *Id.* at pp. 311-373. (Hereinafter "Chapter 6"), is devoted to discussion of employees of biotech companies (*see discussion infra*).

[90] Chapter 3 at pp. 108-115 & 119-130. On LLCs refer to Limited Liability Corporations (Hereinafter "LLCs"); Chapter 3 at pp. 108-115. On Name Selection, *see id.* at pp. 119-120. Finally, on Capital Structure and Stock Grants, *see id.* at pp. 120-130.

[91] *Id.* at pp. 99-117.

[92] *Id.* at p. 99.

[93] *Id.* However, this should be reviewed carefully with corporate counsel in light of year to year changes in the federal and state corporate tax provisions, rather obviously, which can be a rather complex matter requiring both skilled counsel and experienced CPAs or both.

[94] *Id.* This is a useful general survey as to name selection issues, but 1) trademark counsel should be consulted 2) it is important that trademark counsel advise the client about the need to use the federal trademark, pay regular federal trademark fees or face abandonment of the registered federal trademark and 3) it behooves the wise attorney businessperson or consultant to also register ALL the domain names on the internet which may or might be similar to the selected name for the foreseeable future, in order to avoid any possible cybersquatting issues. IP, trademark or specialized cyber/internet counsel can resolve this. The bottom line is, in the digital world, it is critical to protect a corporate name in all directions and dimensions. The flip side of this, of course, is cyber security. Increasingly, corporate entities do not list their physical locations online, and with ever increasing good reason.

[95] *Id.* at pp. 120 *et seq.*

[96] *Id.* at pp. 122-130.

[97] Second Edition. Chapter 4. Hugh B. Wellons. "Acquisition of Biotechnology—Technology Transfer." *Id.* at pp. 174-240. (Hereinafter, "Chapter 4").

[98] Chapter 4.

[99] *Id.* at p.171, note 1. Special thanks are accorded to Mark Coburn, senior associate director, Georgia Tech Research Corporation. *Id.*

[100] *Id.* at p. 171. *See also Id.* at pp. 172 *et seq.*

[101] *Id.* at p.172 *et seq.* Chapter 4 caries over from the First Edition discussions of Confidentiality Agreements, Lab Notebooks and Workbooks, NDAs, Employment Agreements and Outside Funding; all are reviewed with at least one eye to eventual filing of one or more valid utility patents with one or more allowable claims. *Id.* Of course, with tech transfer, you can *acquire* existing patents and existing allowed claims, which considerably shortens the time to eventual sale of product and eventual exit strategy and return on investment for all. *Id.*

[102] *Id.* at p. 175 *et seq.*

[103] *Id.* at p. 181. "The Uniform Trade Secrets Act ("UTSA") is a piece of legislation created by the Uniform Law Commission ("ULC"), a nonprofit organization. The USTA defines trade secrets and describes claims related to trade secrets." https://www.law.cornell.edu/wex/non-profit_organizations. The UTSA was adopted by the ULC in the 1970s and amended to its final form in the mid-1980s; it has now been ratified by 48 of the fifty (50) United States. Chapter 4 provides as a sample Virginia's adoption, at Va. Code Ann. §§59.1-335 *et seq.*, of the UTSA. *Id.* at p. 181 & n. 11.

[104] *See also* the Defend Trade Secrets Act of 2016, 18 U.S.C. §§1836 *et seq.* (Hereinafter "DTSA") *and* the Economic Espionage Act of 1996, 18 U.S.C. §§1831-1839 (hereinafter "EEA").

[105] *Id.* at pp. 174-240 *passim.*

[106] *Id.* at pp. 196-202.

[107] *Id.* This is a long addition, consisting of a new Chapter 4 Section C, "Typical Considerations of the Licensor," and 9 subsections; in addition, there are 16 sub-sub sections appended under the ninth and final subsection 9, "Additional Considerations," beginning with "a. Assignment" and ending with "p. Sponsored Research Opportunities." *Id.* Thus, there are a total of 25 new subsections added under Section C. *Id.*

[108] *Id.* at pp. 202-207.

[109] *Id.* For the Bayh-Dole Act Discussion, *see* pp. 202-05 & *passim*; *see also* 35 U.S.C. §§ 200 *et seq., as amended.* "The provisions of the Bayh-Dole Act…had an extraordinary effect on technology transfer in universities [after its passage in 1980]. Chapter 4 at p. 204.

[110] *Id.* at p. 204 & n.29; *Id.* at p. 205 & n.30. *See also* AUTM website at https://autm.net.

[111] First Edition, Chapter 4, had a subsection C.6.l "Other General Restrictions You Would Find in Most Other Licensing Agreements," *id.* at p. 177. In the Second Edition, Chapter 4, this has been simplified to subsection D.6.l "Other Restrictions," *id* at pp. 216-17 with some sub-subsections to explain in greater detail what the other restrictions are or might be. First Edition, Chapter 4 had a subsection C.8 "When Equity Is the Primary Consideration for the License, " *id.* at pp. 179-180; in the Second Edition, Chapter 4, this is renumbered at subsection D.8, the section title remains the same, but two sub-subsections D.8.1 "Equity" & D.8.2 "Activity" are added. *Id.* at pp. 219-220.

[112] First Edition. Chapter 4. Section C.9 at pp. 180-183.

[113] Second Edition. Chapter 4. Section D.9.a-h at pp. 220-223. The Introduction begins with a discussion of both the Bayh-Dole Act and the Trademark Clarification Act of 1984, 15 U.S.C. §§1501 *et seq.* (Hereinafter, the Trademark Clarification Act of 1984"). https://www.law.cornell.edu/uscode/text/15/1051. "The Trademark Clarification Act [of 1984] provides broader technology transfer authority in government-owned laboratories, permits those laboratories to enter into cooperative R & D agreements ["CRADAs"] with nonfederal entities, and requires employees to receive a fraction of resulting royalties." Chapter 4 at p.220.

[114] Chapter 4 at p. 223.

[115] *Id.* at p. 224. *Cited in* Second Edition, Chapter 4 as Section D.11.a "Academicians Want to Publish," *id.* & Section D.11.b. "Licensee Due Diligence," *id.*

[116] *Id.*, 35 U. S. C. §§ 102 (a) & (b) *as amended.* The AIA amended Section 102 because the USA went to a "first to file" regime, so the novelty test and statutory language have changed since the AIA; it is important to consult with patent counsel on these issues. The general statement in Chapter 4 is true; "Publication under patent laws is a very broad term. Any disclosure to a party that is not employed by the university or under an NDA may disqualify an invention for patent protection." Chapter 4 at p. 224. For a general discussion of the novelty requirements under Section 102, *see* Gene Quinn "The Novelty Requirements of 35 U.S.C. § 102" IPWatchDog Blog, https://www.ipwatchdog.com/2017/06/03/patentability-invention-patented/id=84071/. Just to recite the hornbook law, the three main bars pre- and post-AIA under Section 102 were public use, printed publication and offer for sale. There was and is a one year grace period to file for the inventor only, but under the AIA first-to-file regime it is not wise to wait to file at all post-AIA. Also, of course, the prior art bars remain. *Id.*

[117] *Id.*

[118] Chapter 4 at p. 224.

[119] Chapter 4, at pp. 182-185.

[120] *Id.* at p 186.

[121] *Id.* & Chapter 4, *passim*. Of course, it remains true that some scientists have more leverage in negotiations than others. So-called "superstar" scientists, such as Nobel Prize winners, of the sort that universities have to recruit and pay extra to maintain on their academic roster, certainly can leverage better terms.

[122] *Id.*, Chapter 4 at p. 186.

[123] *Id.* at pp. 186-87.

[124] *Id.* & Chapter 4, *passim*. Chapter 4 also takes note of 1) technology being put into the Public Domain (the classic case being insulin) and 2) manufacturing or sales restrictions. *Id.* at pp. 187-188. For example, under the Bayh-Dole Act, 35 U.S.C. §204, "products developed with federal funding and sold in the United States must have some substantial portion of

that product manufactured in the United States, to the extent practicable." *Id.*, *cited in* Chapter 4 at p.188 n.14.

[125] Second Edition, *passim.*

[126] It should be noted that a recent trend at universities is to rename and rebrand their offices of tech transfer, so as to make the job title sound more prestigious or elite; Tech Transfer at the Wyss Institute at Harvard University, for example, is termed the "Office of Technology and Business Development," https://wyss.harvard.edu/team/business-development-team/, while the University of Pennsylvania Tech Transfer office was renamed and rebranded as the "Penn Center for Innovation," https://www.pci.upenn.edu. Even AUTM has been rebranded in recent years; it has a new logo and a more aesthetically visual website. https://autm.net.

[127] For example, this reviewer enrolled in (and earned the highest grade in) Graduate Seminar classwork on Tech Transfer at the Wharton School in 1994 with Prof. Steve Sammut, who at that time was director of the University of Pennsylvania Tech Transfer Office (since renamed, *see supra*). This would be an example of some of highly relevant classroom experience; working in the tech transfer office, one would work with all the licensing agreements and forms and gain a day to day familiarity with them. As Chapter 4 and elsewhere in the Second Edition note, the University Perspective on Tech Transfer is not precisely that of the patent counsel representing the inventor or other actors party to the transaction. A pertinent development since 1994 has been the increasing professionalization of the AUTM, *cited supra*, which really was not such a distinct force back in the 1990s.

[128] Chapter 4 at pp. 239-240.

[129] Chapter 5.

[130] Chapter 6, *passim.*

[131] Chapter 16 at p.828 & n.24.

[132] *See* Chapter 7 *passim.*

[133] *Id.* at pp. 403-407, discussing the "Public Health and Bioterrorism Preparedness and Response Act of 2002," *as amended,* Pub. L. No. 107-188, 116 Stat. 594 *amending various provisions of* 42 U.S.C. 6A §§ 201 *et seq.* & the regulations at 42 C.F.R. pt.73. *as amended.* Id. *See also* *https://www.govinfo.gov/content/pkg/STATUTE-116/pdf/STATUTE-116-Pg594.pdf*

[134] *See* Chapter 9, *passim.*

[135] To the extent materials from First Edition, Chapter 10 are not brought forward to the Second Edition, then the First Edition may remain a relevant Desk Reference. On staying current with the FDA, there are many ways to do so now; the FDA has many web resources and outlets, and now even has twitter pages, where it publishes daily and even hourly its announcements and pronouncements on various matters. However, it is best to consult an expert in these matters.

[136] *See* Chapter 10, *passim.*

[137] Pub. L. No. 104-191, 110 Stat. 1936, *as amended.* (also referred to as "AHIPPA" and the "Kennedy-Kassebaum Act of 1996"). According to Chapter 10:

> On August 21, 1996, Congress enacted….HIPPA. Under authority granted by HIPAA, the U.S. Department of Health and Human Services ("HHS") issued regulations related to the use and disclosure of health information (the "Privacy Rule") and related to safeguarding the privacy, availability and integrity of health information (the "Security Rule"). (citations omitted). Second Edition, Chapter 10 at pp. 501-502.

Since the First Edition, Congress passed the Health Information Technology for Economic and Clinical Health Act of 2009, Pub. L. 111-5, *as amended* ("HITECH"), and additional modifications pursuant thereunder were implemented in 2013 by HHS regulation to both the Privacy and Security Rules, as noted in Chapter 10 at p. 502 & n.2 (original citations omitted).

[138] Chapter 10 at p. 558 & n. 102. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (Text with EEA relevance). https://eur-lex.europa.eu/eli/reg/2016/679/oj

[139] California Consumer Privacy Act of 2018, A.B. 375, *as amended*. Second Edition, Chapter 10 at pp. 567 *et seq.*

[140] Chapter 10 at pp. 501 *et seq.* & *passim.*

[141] Chapter 10 at p. 573.

[142] *Id.*, *passim* & "Key Acronyms Used" at *id.*, pp. 604-605. Also, acronyms IPPS & OPPS are utilized in Chapter 11 for Inpatient Prospective Payment System ("IPPS") and Outpatient Prospective Payment System ("OPPS"). *See id.* at pp. 596-597 & 604-605.

[143] *See* Chapter 12, *passim.*

[144] *See* "NEPA Environmental Review Requirements" at Environmental & Energy Law Program, website maintained by Harvard Law School, https://eelp.law.harvard.edu/2018/08/nepa-environmental-review-requirements/, which monitors and has monitored the deregulation of EPA over the past several years by the Trump Administration.

[145] TSCA, 15 U.S.C. §§2601 *et seq. as amended;* FIFRA, 7 U.S.C. §§ 136 *et seq. as amended*. *Cited in* Chapter 12 at p.607 & n.1 & 2 & *passim.*

[146] Chapter 13, *passim.* The FDA home page is at https://www.fda.gov

[147] *Id.* at pp. 707-708.

[148] *See* Chapter 14, *passim.*

[149] Chapter 14, *passim* & at pp. 723 *et seq.*

[150] **"**Bayer to Sell $9 Billion in Assets to Get Green Light for Monsanto Deal" *The Wall Street Journal.* ***https://www.wsj.com/articles/justice-department-approves-bayer-monsanto-deal-but-requires-asset-sales-1527611108*** (May 20, 2018). *See also* Chapter 14 at p.735 & n.49 (reference to Monsanto's dealing with EC/EU regulation of agricultural biotech products as of July 2013).

[151] *See* Chapter 15, *passim.*

[152] Chapter 15 at pp. 737-775 & *passim.*

[153] False Claims Act, 31 U.S.C. §§3729 *et seq., as amended.* ("FCA"). *Cited in* Chapter 15 at p. 775 & n.123.

[154] Chapter 15 at pp. 775-798 & *passim.*

[155] Chapter 20 at p.978.

[156] "Meta-Ethics" (or metaethics) are the study of how ethics are even possible. *C.f.* Sayre-McCord, Geoff, "Metaethics", *The Stanford Encyclopedia of Philosophy* (Summer 2014 Edition), Edward N. Zalta (ed.), https://plato.stanford.edu/archives/sum2014/entries/metaethics/ (Hereinafter, "Metaethics Article").

[157] On Utilitarianism, *See* Chapter 20 at p. 981 & its references to Jeremy Bentham & John Stuart Mill. To this list should be added Henry Sidgwick. *See* Henry Sidgwick. *The Methods of Ethics.* (1874). *See generally, passim,* Driver, Julia, "The History of Utilitarianism", *The Stanford Encyclopedia of Philosophy* (Winter 2014 Edition), Edward N. Zalta (ed.), https://plato.stanford.edu/archives/win2014/entries/utilitarianism-history/ (Hereinafter, "Utilitarianism Article"). The Utilitarian Article has excellent background and explanation of Bentham, Mill, Sidgwick and G.E. Moore. This Reviewer mentions Sidgwick, because in Prof. John Rawls' famous class on Ethics at Harvard, Philosophy 171, back in the 1970s, Rawls taught Sidgwick, not Bentham or Mill, as the classic exponent of Utilitarianism, to which his *Theory of Justice* was, of course, opposed. *C.f.* John Rawls. *A Theory of Justice.* (1971).

[158] For a longer, more philosophical and theoretical view on bioethics, *see e.g.* Arras, John, "Theory and Bioethics", *The Stanford Encyclopedia of Philosophy* (Winter 2016 Edition), Edward N. Zalta (ed.), https://plato.stanford.edu/archives/win2016/entries/theory-bioethics/ (Hereinafter, "Theory and Bioethics").

[159] Chapter 20 at p. 978, 980 & other references *passim. See also passim* Christos Yapijakis. "Hippocrates of Kos, the Father of Clinical Medicine, and Asclepiades of Bithynia, the Father of Molecular Medicine." 23 *In Vivo* 507 (2009) **https://www.ncbi.nlm.nih.gov/pubmed/19567383** *and* **http://iv.iiarjournals.org/content/23/4/507.long** On "First Do No Harm," there is dispute as to Hippocrates actually originating those exact words. *See Primum non Nocere*, ***http://www.eastridges.com/wesley/primum.html***

[160] *Id.*

[161] For example, the Hellenic Medical Society of NYC for years had a conference every summer at Kos. Another group which recently met at Kos was: 2nd HUMAN & TRANSLATIONAL IMMUNOLOGY CONFERENCE, 5/2/19-6/3/19. **https://www.humanimmunology.org**

[162] *See* Chapter 20 at pp. 985-987 & original sources cited therein, including weblinks to original sources.

[163] *See* Arthur J. Kyriazis. "Book Reviews." 27 *Biotech.L.Rep*. 227 (2008), *reviewing* D.L. Finegold *et al. BioIndustry Ethics*. (2005) *and* R. Bailey. *Liberation Biology: The Scientific and Moral Case for the Biotech Revolution.* (2005). (discussing *inter alia* the history of eugenics in the USA). https://www.liebertpub.com/doi/pdfplus/10.1089/blr.2008.9949

[164] Chapter 20 at pp. 987-993 & original sources and cases cited therein.

[165] *Id., cited in* Joyce, Richard, "Moral Anti-Realism", *The Stanford Encyclopedia of Philosophy* (Winter 2016 Edition), Edward N. Zalta (ed.), https://plato.stanford.edu/archives/win2016/entries/moral-anti-realism/ (Hereinafter, "Moral Anti-Realism Article").

For more on Mackie's arguments on moral skepticism and moral error theory, *see* https://plato.stanford.edu/entries/moral-anti-realism/moral-error-theory.html (Hereinafter, "Mackie Arguments").

[166] *See* Moral Anti-Realism Article, *cited supra*, *passim.* *See also* "Moral Nihilism," and original sources, books, articles cited therein. https://en.wikipedia.org/wiki/Moral_nihilism#Argument_from_queerness
See also "The Euthyphro Problem", *cited in* Metaethics Article, *cited supra*:

> And, as Plato emphasized in *Euthyphro*, one is also left with the difficulty of explaining why God's commands are authoritative.
>
> One plausible answer might be that God's perfect knowledge of right and wrong, or God's own moral perfection, explains why his commands serve legitimately as standards for us. But that answer assumes that standards of morality exist independently of God's will (either as objects of his knowledge or as standards in light of which He counts as morally perfect), in which case speaking of morality as consisting of God's commands will not explain the origin or nature of these independently existing standards.

And so on. This leads to a paradox of circular reasoning, known as the problem of the criterion, e.g. a thing is right because God says so, but God is God because we say so, and thus we are saying that the thing is right.

[167] Thomas S. Kuhn. *The Structure of Scientific Revolution.* (1962).

[168] W.V.O. Quine. "Two Dogmas of Empiricism." 60 *The Phil. Rev.* 1 (1951).

[169] Richard Rorty. *Philosophy and the Mirror of Nature*. (1979)

[170] Immanuel Kant. *Critique of Pure Reason*. (1781).

[171] This is known as "constructivist ethics" or "constructivist meta-ethics." It reflects an agreement by a group, or sub-group, that we will agree upon a code or set of rules (or meta-rules) to govern our conduct amongst ourselves. The main exponents of this view are John Rawls and Immanuel Kant. Bagnoli, Carla, "Constructivism in Metaethics", *The Stanford Encyclopedia of Philosophy* (Winter 2017 Edition), Edward N. Zalta (ed.), https://plato.stanford.edu/archives/win2017/entries/constructivism-metaethics/

[172] Chapter 20 at p. 994 & n.38, *citing The Nuremberg Code, reprinted in* Jay Katz. *Experimentation with Human Beings.* (1971) at p. 305.

[173] Chapter 20 at pp. 994-995 and original sources cited therein.

[174] Chapter 20 at pp. 997-998. To demonstrate how much things changed from 1976-2020, the reviewer was a student in Prof. Walter Gilbert's Introduction to Molecular Biology class in the spring of 1977 at Harvard University (Prof. Naomi Pierce, then a grad student, was in charge of the lab sections, and Nobel Laureate E.O. Wilson had taught the first semester, Introduction to Biology/Ethology). (Gilbert would get his Nobel Prize a couple of years later).

Everything Dr. Gilbert taught us was about plasmids, vectors and recombinant DNA—stuff that was completely new to all of us sitting there listening. In point of fact, we were getting the very first version of biotechnology. Less than a year later, Gilbert would co-found Biogen, Inc., which later would become Biogen Idec, now a Fortune 500 company with more than one billion dollars in revenue and a standard case study in first generation biotech company growth.

But the initial responses to rDNA research were cool; Gilbert and Biogen ran into regulatory issues locally, as the Mayor of Cambridge, MA was reluctant to allow recombinant DNA research in his city, and the regulatory snafu had to be resolved federally, invoking pre-emption of the local Cambridge, MA regulatory scheme. *See* Second Edition, Chapter 20, Gary E. Merchant, Robyn S. Shapiro & Hugh B. Wellons, "Bioethics" (Hereinafter "Chapter 20");

> In 1977, the city council of Cambridge, MA held hearings on rDNA research at the city's universities [Harvard & MIT] and created the Cambridge Biohazards Committee to protect residents from potential health risks. Elsewhere, critics voiced concerns, arguing that rDNA research was an attempt to upset the order of nature by manipulating the code of life….
>
> Ultimately, the controversy about whether and how to regulate rDNA was resolved, at the federal level, with NIH rDNA guidelines, released June 23, 1976, and the establishment of the NIH's Recombinant DNA Advisory Committee ("RAC"). The NIH guidelines remain in force today, and continue to be overseen by the RAC. To date, this approach has preserved scientific freedom and the public's health, and in the face of current debates over stem cell research, genetic cloning, and genetically modified food, many herald it as an example of creative management of risks and ethical conflicts raised by advances in science. *Id.* at pp. 997-998. (original citations & footnotes omitted).

See also Chapter 20, "Regulation of Recombinant DNA Research" at pp. 996-998 *passim* & sources cited therein. This is a very important discussion of what turned out to be a seminal, critical phase of the biotechnology revolution. As it turns out, this Reviewer was a witness, not merely an observer, to what truly was mass hysteria in the local Cambridge, MA community over what was merely scientific progress in an orderly manner.

Fortunately for Dr. Gilbert & Biogen, NIH stepped in with an rDNA regulatory regime, and thereafter followed the Bayh-Dole Act of 1980, the revolution in tech transfer relationships between universities and the private sector, and the other developments in biotech, cited *supra & infra.*

[175] Chapter 20 at p. 1016.

[176] The Reviewer would like to thank the ABA Section of Science & Technology Law and its past Section Chair Hugh B. Wellons, Esq. for providing a complimentary copy of the Second Edition and further affording the Reviewer an opportunity to write this Review.