Building an IP Strategy for Life Science Entrepreneurs

15th Annual Biotechnology Entrepreneurship Boot Camp

Raymond A. Miller

June 2, 2019

Pepper Hamilton LLP
Attorneys at Law

Overview of Discussion

- Intellectual Property 101
  - Basics
  - IP Strategy
  - Regulatory Exclusivity
- Example of complex IP and regulatory considerations
  - Compounding pharmacies
- Case Law impacting pharmaceutical development
- Pepper Hamilton experience

IP is an important part of the story for early stage companies

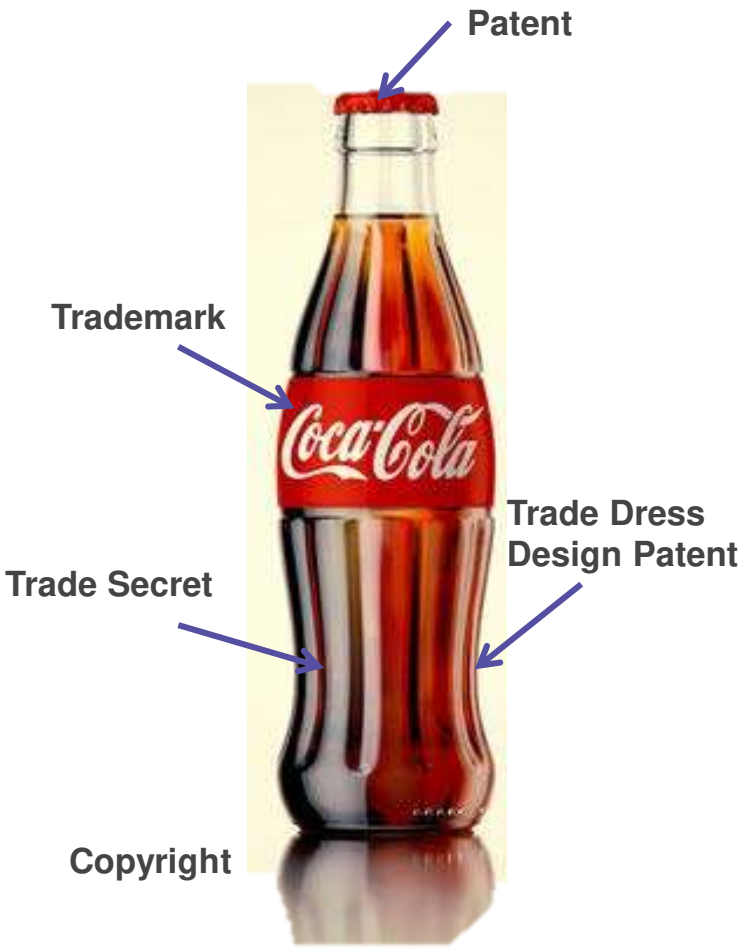
- The ultimate value of IP is to provide exclusivity to a market position
  - A patent is most valuable where there is a market or will be a market
  - IP can help to create a position that prevents advancement of competitors (i.e. exclusivity)
  - Exclusivity can give ownership of the market category
- Intellectual property (IP) can exclude others from making, using or selling your creative work
- Ability to formulate and articulate your IP strategy is critical to successfully obtaining investments, strategic partnerships and licensing deals.

Intellectual Property 101

Pepper Hamilton LLP
Attorneys at Law

Main Types of IP

- Patent: novel, non-obvious and useful processes, products, or ornamental design
- Trademark: Name, design, symbol, word(s) or other source identifier of goods or services
- Copyright: original work of authorship fixed in a tangible medium
- Trade Secret: Information kept confidential which has commercial value due to its secrecy
- Regulatory Exclusivity provides incentives to develop drugs and biologics



Patents

- A property right granted for an invention by the patent office
  - Confers the right to exclude others from making, using, offering for sale or importing the patented invention
  - Does not confer the exclusive right to practice the invention
- 3 types of patents:
  - Utility: functional components of a product or process
  - Design: ornamental design of useful objects
  - Plant: new varieties of living plants
- Anatomy of a Patent:
  - Claims: define the legally enforceable metes and bounds of the patent (i.e. property lines)
  - Drawings: may be required to understand
  - Specifications: provide context for interpreting the claims – everything else. The claims can be considered part of the specification

Trademark / Service Mark

IP Rights

- Name, design, symbol, word(s) or other device
- Represents the goodwill in a company's goods or services
- Rights can be registered with the USPTO or established by use in commerce
  - ® can be used after federal registration; no legal requirement for marking
- Rights are territorial
- Business name can also be considered a potential trademark/service mark

Copyright

IP Rights

- Original work of authorship
  - Non-functional expression
  - Original to author and independently created
- Fixed in a tangible medium
  - For example, a photograph on paper or in digital format, video or sound recordings in digital format
- Includes
  - Literary works
  - Musical works
  - Pictorial, graphic and sculptural works
  - Audiovisual works
  - Sound recordings

Trade Secrets

- Information that is not disclosed outside of an obligation of confidentiality
  - Formula, recipe, or manufacturing process
  - Software source code
  - Business information (sales data, market intelligence)
  - Customer lists
- Has commercial value due to its secret nature

IP Strategy

- The ability to formulate and articulate a strong IP strategy is critical to success obtaining investments, strategic partners and third party licensing

- A strong strategy will:
  - Use a layered approach with a combination of patents, copyrights, trademarks, and trade secrets
  - Dovetail patents with market and regulatory exclusivity

IP Portfolio

- Map and inventory all company/technology IP, both current and potential future IP
- Identify core patents and evaluate strengths and weaknesses to build the portfolio around these assets
- Assess whether the IP reflects current protocols: product drift should be assessed regularly

IP Ownership

- Assignments from each inventor must be properly executed and recorded

- Exclusive rights are directly proportional to the strength of the licensed patents
  - Only effective if the patents exclude others from making, using, selling or otherwise commercializing a competitive product

Patent Term

- Utility and Plant patents:
  - 20 year terms calculated from the filing of the earliest non-provisional application to which they claim priority
  - Patent term adjustment (PTA): delay by USPTO
  - Patent term extension (PTE): time to go through FDA
- Extending patent terms to the maximum can provide longer protection than their natural expiry
- Design patents:
  - 15 year terms calculated from the day they are granted

Patent Term Adjustment

- Provides extension on the standard patent term based on delays caused by the USPTO during the examination process.
- Types of delays:
  - Promptness of responses by the USPTO
    - Provide at least one notification not later than 14 months after filing
    - Respond to a reply/appeal within 4 months after date on which reply/appeal is filed
    - Act on an application within 4 months after decision by the PTAB or Federal Court (where allowable claims remain)
    - Issue a patent within 4 months after the date on which issue fee was paid and all requirements satisfied
  - No more than 3 years of application pendency
  - Derivation proceedings, secrecy orders, and appeals

Patent Term Extension- General

- PTE only available for a patent that has been issued during clinical development and/or regulatory review period **for the first approved commercial use** of a drug, biologic or medical device product. 35 U.S.C. § 156
  - patent claims product, method of using a product or method of manufacturing a product
  - term of patent not expired before PTE application submitted
  - term of patent not previously extended
  - first permitted commercial marketing or use of product under which regulatory review period occurred
  - must submit application within 60 days of FDA approval
- Extension = ½ clinical development time + NDA/BLA/PMA review/approval time
  - Max extension is 5 years; and 14 years total patent term from FDA approval

Products Eligible for PTE

- Application submitted by the owner of the patent or its agent
  - patent owner or agent must be the holder of regulatory approval
  - the marketing applicant must serve as the patent owner's agent if it applies for a PTE
- The "product" is the active ingredient, including or any salt or ester of the active ingredient
  - *e.g.*, if a salt has been previously approved, a patent on its **acid** is not eligible for PTE (same product);
  - if an acid has been previously approved, a patent on its **salt or ester** is eligible for PTE (different products);
  - *and* if only the salt of an acid has been previously approved, an **ester of the same acid** is eligible for PTE (different products)
- Combination product where both components were previously approved is not eligible (*e.g.*, hydrocodone/ibuprofen combination not eligible); combination where only one component was previously approved is eligible, but only as to patent on previously unapproved component
- Class III medical devices are eligible (devices receiving review under FDCA section 515); Class I and II devices are not.

Rights Derived from PTE

- Term of the entire patent is extended, not just the individual claims
- But only as to the FDA-approved uses, not other commercial uses
- Extension applies to any new salt or ester of the acid, but not vice-versa (if patent otherwise encompasses the same)

Calculating the Regulatory Review Period

- Extended patent term will be the shortest of:
  - RRP – PGRRP – DD – ½(TP-PGTP);
    - RRP = regulatory review period
      - If multiple INDs filed, begins on the date of first exemption of the approved product (even if different indication)
    - PGRRP = pre-grant regulatory review
    - DD = time during which applicant did not act with due diligence
    - TP = regulatory review period which is testing phase
    - PGTP = pre-grant testing phase
  - 14 years of total exclusivity; or
  - 5 years from end of patent term under 35 U.S.C. § 154.

Types of Regulatory Exclusivities available in the United States

NCE Exclusivity

- NCE: New Chemical Entity
- Any drug with an active moiety that has not been previously approved by FDA in a NDA
  - active moiety- molecule or ion responsible for the drug's physiological or pharmacological action (not salt or ester)
  - special qualifiers: fixed dose combos, enantiomers, non-ester prodrug, poorly characterized mixtures
- For 5 years, FDA may not *review or approve* an ANDA or 505(b)2 for same active moiety (regardless of indication)
  - 30 months average ANDA approval time
- However, if there is an Orange Book (OB) Listed patent, ANDA/505(b)(2) *may* be submitted with Para IV Cert at year 4
  - Recall: If Innovator asserts OB Listed patent within 45 days of Para IV Cert, approval of ANDA/505(b)(2) stayed until 30 months from cert or 7 ½ years from NDA approval (if brought in Y4) 21 CFR 314.07(b)(3)(i)(A) and (B)
- While unlikely, NDA may be reviewed and approved by FDA during this time

Clinical Investigation Exclusivity

- Any drug that has been previously approved by FDA, but the application contains a new clinical investigation that was necessary for approval
  - e.g., new indication, dosage form, script to OTC
  - NDA or supplemental NDA
  - no bioavailability study
- For 3 years, FDA may not *approve* an ANDA or 505(b)2 application for same active moiety containing the new clinical investigation
  - FDA can review during this time
- ANDA/505(b)(2) may be submitted at any time
- If Innovator asserts OB listed patent within 45 days of Para IV Cert, approval of 505(b)2/ANDA stayed 30 months from cert (non-NCE)
  - Can run concurrently with 3 year CI Exclusivity
  - 30 months average ANDA approval time in 2012

Orphan Drug Exclusivity

- Any drug intended to treat a disease that affects less than 200K U.S. citizens ("medically plausible" subset)
- For 7 years, FDA may not *approve* a NDA, ANDA or 505(B)2 application for same active moiety for the same indication
  - FDA can review during this time
- However, FDA can review and approve if "clinical superiority"
  - only after any applicable NCE exclusivity expired
- FDA can review and approve same active moiety for different indication
  - Could be used off-label for the Orphan disease

Pediatric Exclusivity

- If Applicant conducts a study in pediatric population as requested by FDA through a formal Written Request

- *6 month add-on* to any *existing* marketing and Orange Book listed patent exclusivity
  - the study itself may entitle it to CI exclusivity
  - attaches to all of the applicant's products containing the active moiety (all dosage forms, all indications)
  - attaches to the END of exclusivity

QIDP Exclusivity

- QIDP: Qualified Infectious Disease Product
  - covers antibiotics and antifungals
- Any drug that is designated as a qualified infectious disease product when application filed
  - e.g. resistant gram positive pathogens, multi-drug resistant gram negative bacteria (Pseudomonas), multi-drug resistant tuberculosis, C diff
  - once a drug is designated as a QIDP, can't revoke
- The 5 year exclusivity of NCE, the 3 year exclusivity of CI or the 7 year exclusivity for OD is *extended an additional 5 years*
- Fast-track review and approval

IP 101: Summary

- Therapy should drive IP and be tracked in patent claims
- An integrated strategy including IP and regulatory exclusivity is strongest
- Patent Term Extension (PTE) available for time in clinical trials while patent is issued
- Keep in mind:
  - Grant of a patent should be viewed as a milestone, not a golden ticket –vigilance is needed
  - Regulatory Exclusivity without any patent coverage does provide an opportunity for ROI

Example: Pharmacy Compounding- an emerging concern for specialty pharmaceuticals

Insights: A look into the complexity of developing an integrated IP and regulatory strategy to protect company assets

Why Care about Pharmacy Compounding Now?

- Compounding pharmacies
  - Pharmacies that prepare compounded, personalized medications based on a practitioner's specific prescription
- Emergence of telemedicine, personalized medicine and integrated care is increasing the demand for personalized prescriptions, which are filled by compounding pharmacies
- Creating a challenge to pharmaceutical manufacturers:
  - Compounding pharmacies don't require FDA approval
  - Can be tricky to protect against patent infringement

Compounding Pharmacies

- Competitive concerns raised by Innovators, VCs, and investors
  - Annual Growth Rate of ~ 9%; expected to reach $14–20B by 2020, ~2% of pharmaceutical market
  - Diverting clinical trial candidates
  - Adverse events- reporting, impact on reputation
  - Impact on innovator exclusivity
  - Impact on innovator pricing, consumer expectations
- Creation of new 503B Outsourcing Facilities
  - 503A- traditional compounding pharmacies
    - make each script on demand for an individual
  - 503B- outsourcing facilities-quasi-drug manufacturers
    - batch produce modified versions of marketed drugs

503A and 503B- Key Parameters

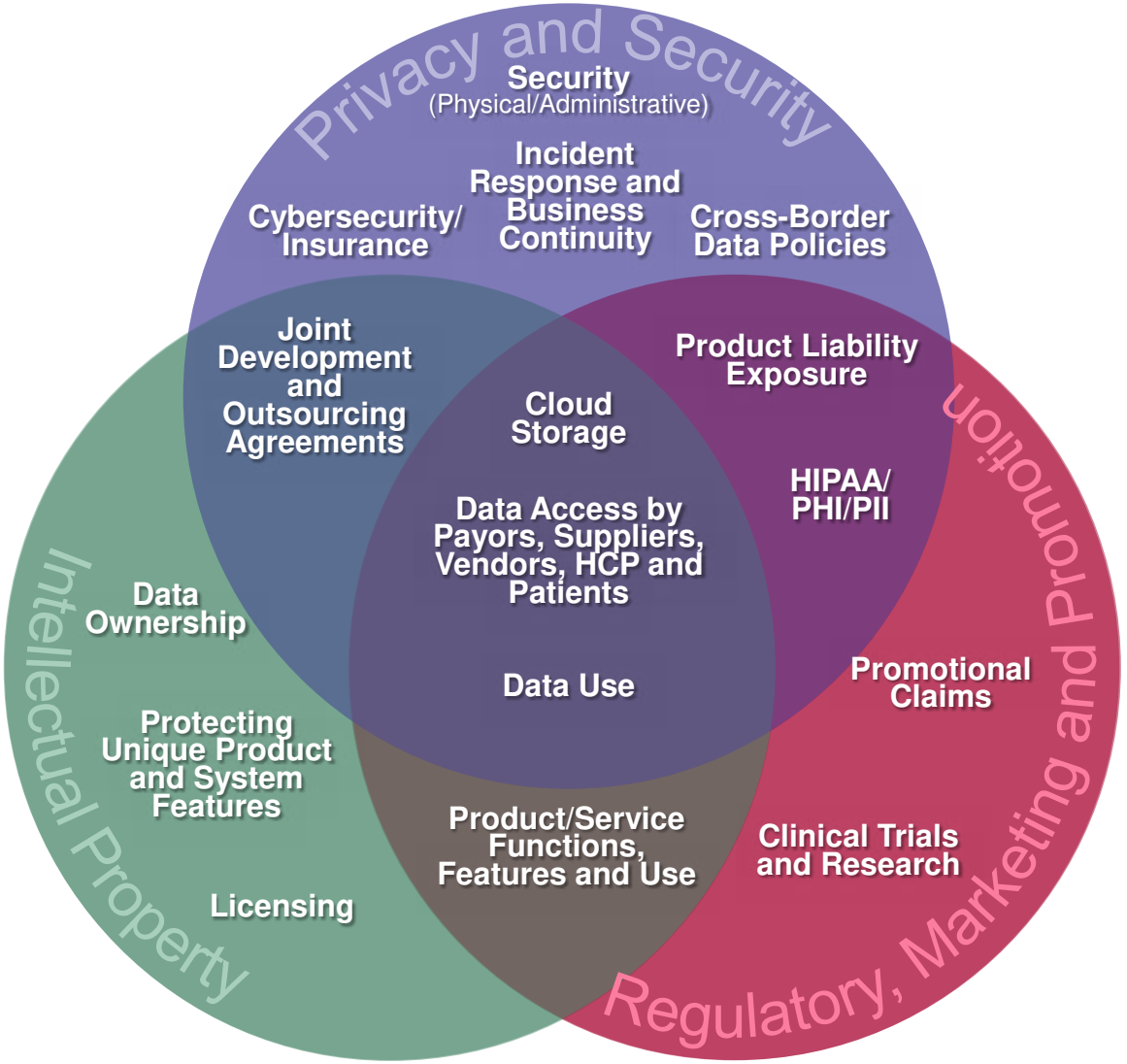
	503A	503B
Types of compounders	Licensed pharmacist or physician	Licensed pharmacist (or direct supervision)
Location of compounding	Pharmacy or federal facility	Outsourcing Facility
Prescription	Valid script for patient required, indicating necessary for patient (or in limited quantities, based upon history)	No script required, unless dispense directly to patient
Bulk Drug Substances	• Complies with USP compounding chapter • If USP/NF monograph, complies; if not, is component of FDA approved drug; if not, on FDA 503A Bulk List • Manufactured by registered establishment with CoA	• On FDA 503B Bulk List or Shortage List • If USP/NF monograph, complies • Manufactured by registered establishment with CoA

503A and 503B- Key Parameters

	503A	503B
Essentially Copies	Not compound regularly or in inordinate amounts any drug products that are essentially copies of commercially available drug product	Drug is not essentially a copy of one or more approved drugs -if OTC monograph drug, shortage is not an exception
Interstate Distribution	Limited to 5% or less of the total scripts dispensed by such pharmacy, unless state has MOU with FDA	No limits
Other	Not Applicable	• CGMP, federal registration, reporting, AE reporting, labeling
Exempt from	• 502(f)(1) labeling with adequate directions for use • 505 NDA requirements • 501(a)(2)(B)- cGMP	• 502(f)(1) labeling with adequate directions for use • 505 NDA requirements • 582 drug supply chain security

Integrated Healthcare Requires Integrated Counseling

- Pepper has created an interdisciplinary team of practitioners to address this important emerging issue
- What tools are available to address concerns?



Pepper Hamilton LLP
Attorneys at Law

Changes in case law and government regulations impacting pharmaceutical development

Pepper Hamilton LLP
Attorneys at Law

Recent Developments Impacting Pharmaceuticals

- Experimental Use (*Barry v Medtronic* - Fed Cir 2019) – "ready for patenting" "reduced to practice" "work for its intended purpose"
- Method of Use Claims (*Vanda v West Ward* – Fed Cir 2018) – Patent eligibility addressed – Method of Treatment are outside of Mayo because "applying" natural law; still be aware of Mayo
- On Sale Bar – (*Helsinn v Teva* - S. Ct. 2019) – new AIA provisions of "otherwise available to public" did not change "on-sale" bar and secret sales are sales
- Patent Term Adjustment – (Two cases involving *Novartis* Fed Cir 2018) - Gilead v Natco (Fed Cir 2014) raised the issue that ODP could be applied to earlier issued patent; and Magna suggested PTA was at risk
- Government Funding – May 2018 – Changes to Bayh-Dole require stricter reporting and errors may lead to clouding of title – no longer a 60 day mea culpa

Pepper Experiences of Integrating Patent & Regulatory Exclusivity

Pepper Hamilton LLP
Attorneys at Law

Case Study: Ampyra® (dalfampridine)

Ampyra (dalfampridine) 10 mg extended release tablet for oral administration, twice daily, to improve walking in patients with multiple sclerosis

- NDA Approved 1/22/2010
- NCE- 1/22/2015
- Orphan Drug- 1/22/2017
- 4 Orange Book listed patents (2024-2027)
  - 1 with PTE
  - Generic entry after OB listed patents found invalid in 2018

Case Study: Rhofade® (oxymetazoline)

Rhofade (oxymetazoline)1% cream for topical administration once daily for the treatment of persistent facial erythema associated with rosacea in adults

- NDA Approved 1/18/2017
- CI- 1/18/2020
- 5 Orange Book listed patents (2024-2031)
  - no PTE

Case Study: Eskata® (hydrogen peroxide)

Eskata (hydrogen peroxide) 40% topical solution for the treatment of seborrheic keratoses that are raised

- NDA Approved 12/14/2017
- CI- 12/14/2020
  - NCE reconsideration request pending before FDA exclusivity board
- 4 Orange Book listed patents (2022-2035)
  - PTE application pending

Case Study: Solosec® (secnidazole)

- Solosec (secnidazole) 2 g granules for oral administration for the treatment of bacterial vaginosis in adult women

- NDA approved 9/15/2017
- NCE + GAIN- 9/15/2027
- Currently, no Orange Book listed patents

Questions & Answers

Capabilities

Best Lawyers

More than 70 lawyers listed, including 5 as **Lawyer of the Year**

100+

lawyers highly rated by **Super Lawyers** and **Rising Stars**

SERVICES

BUSINESS
INTELLECTUAL PROPERTY
GOVERNMENT REGULATION
INTERNATIONAL
LITIGATION

INDUSTRIES

CONSTRUCTION LAW
EDUCATION COUNSELING, LITIGATION AND INVESTIGATION
ENERGY
FINANCIAL
FOOD, ALCOHOL AND BEVERAGE
HEALTH CARE
INVESTMENT FUNDS
LIFE SCIENCES
MEDIA, COMMUNICATIONS AND ENTERTAINMENT
NONPROFIT ORGANIZATIONS AND FOUNDATIONS
PHARMACEUTICAL AND MEDICAL DEVICE
RETAIL
TECHNOLOGY
TRANSPORTATION

Global Reach

INTERNATIONAL NETWORK

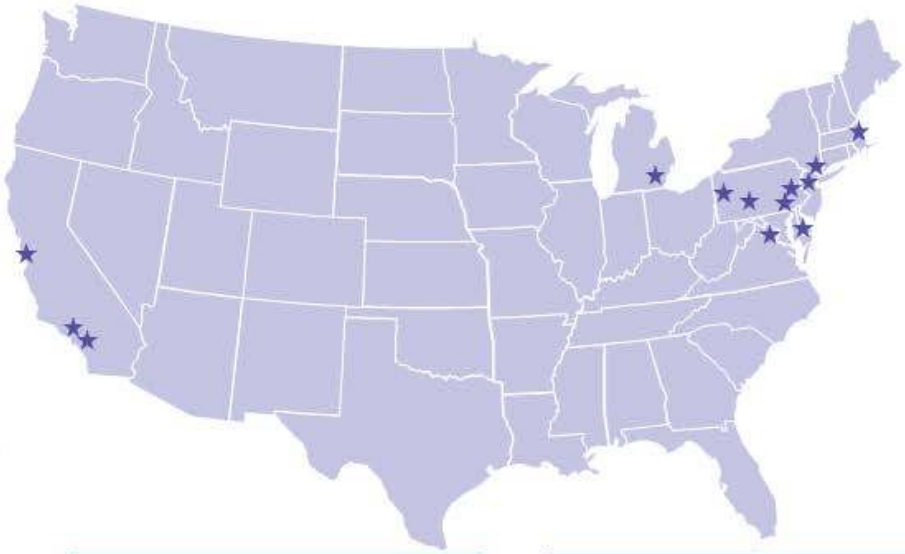
Pepper Hamilton is the exclusive member firm in Pennsylvania for **Lex Mundi** — the world's leading network of independent law firms with in-depth experience in 100+ countries worldwide.

Through the Lex Mundi global network, we can provide our clients with preferred access to more than 21,000 lawyers around the world — all from a single point of contact.

Individually, each Lex Mundi member firm is a leader in its local market. Collectively, Lex Mundi firms provide global legal resources with unmatched depth and breadth. Working with other Lex Mundi firms, we are able to seamlessly handle our clients' most challenging cross-border transactions and disputes.

Locations

BERWYN
BOSTON
DETROIT
HARRISBURG
LOS ANGELES
NEW YORK
ORANGE COUNTY
PHILADELPHIA
PITTSBURGH
PRINCETON
SILICON VALLEY
WASHINGTON
WILMINGTON



Legal 500

Recommended firm for **Construction**, **Product Liability** and **White Collar Criminal Defense**

500+ lawyers

13 offices in U.S.

125+ years of serving clients

Pepper Hamilton LLP
Attorneys at Law

For more information, visit

www.pepperlaw.com

Raymond A. Miller
412-454-5813
millerra@pepperlaw.com

N. Nicole Stakleff
412-454-5869
staklefn@pepperlaw.com

Pepper Hamilton LLP
Attorneys at Law