

Addictive Drugs: Science, Regulation & Policy Consulting

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Consulting as a Great Balancing Act

Time, Income, Service, Family, Social, Personal, Health

Non Revenue Activities

Organizations

WHO

NIH

FDA

CDC/Surgeon General

Service to Institution

Company (PinneyAssociates)

Academic (Johns Hopkins)

Consulting business development

Lecturing/teaching

Advising/mentoring

Publishing

Manuscript reviewing

Research collaborations

Family/Social/Personal/Health

Revenue Activities

Major

Pharmaceutical Consulting

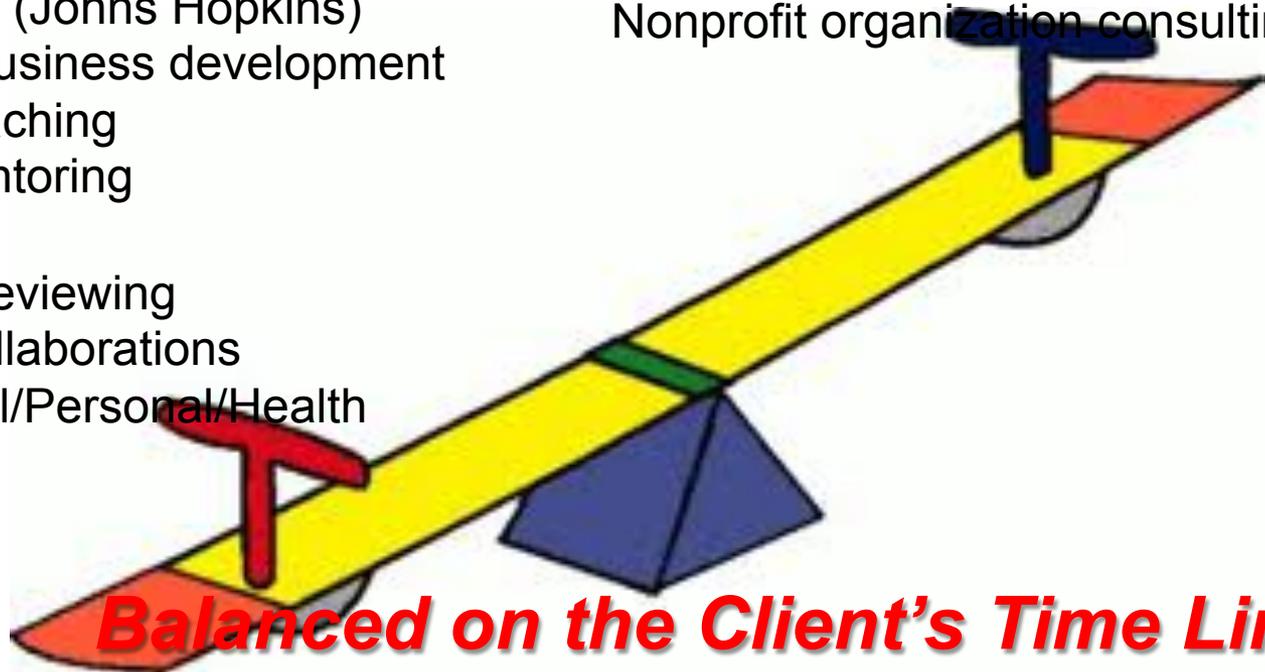
Legal consulting

Minor

Federal Contracts/Grants

CME lecturing and writing

Commissioned reports & editing
Nonprofit organization consulting



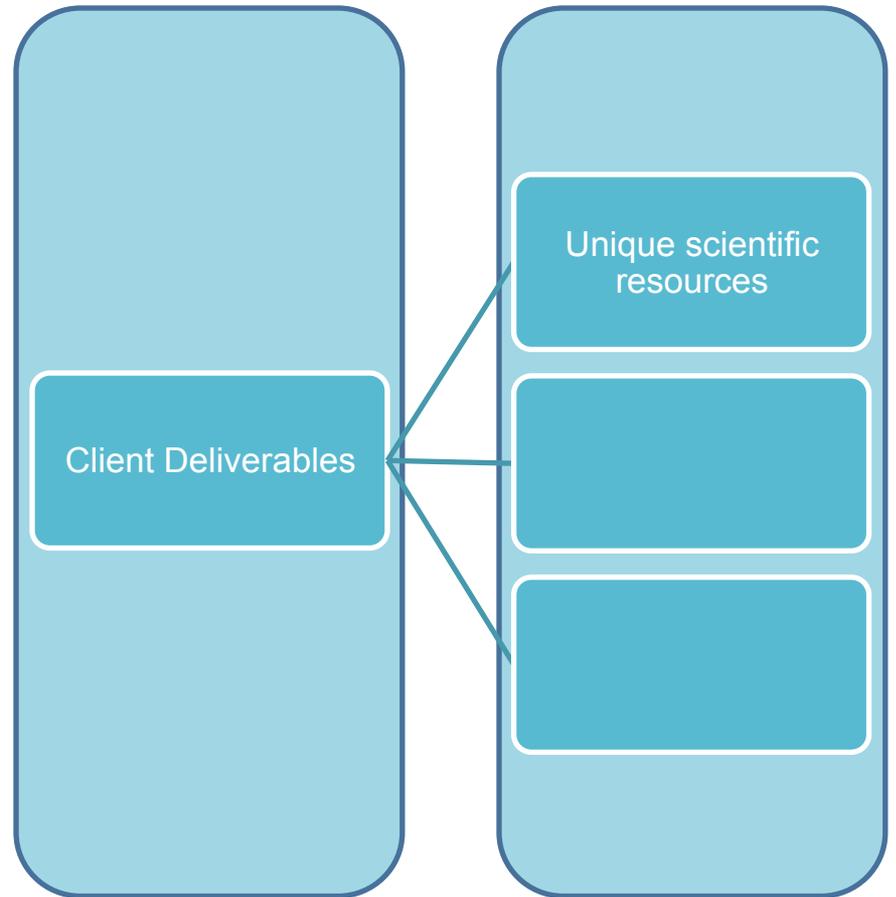
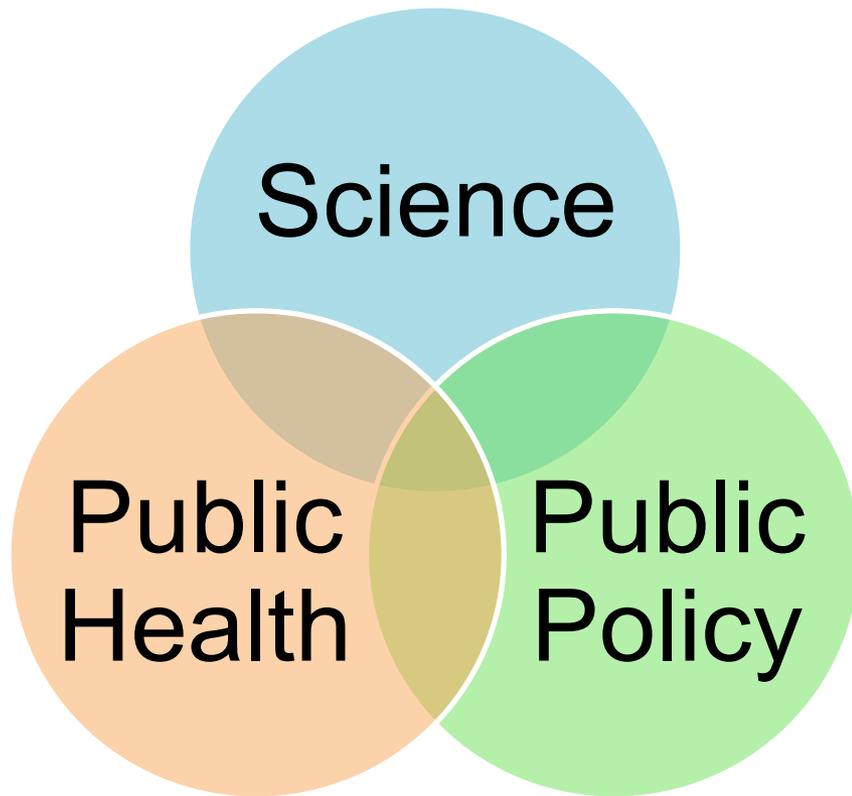
Balanced on the Client's Time Line



PinneyAssociates: What We Are & Do

- A science-based health consulting firm with unique resources and broad experience in medical, regulatory and public health aspects of pharmaceutical products
- Offers critical support to consumer and pharmaceutical clients across the product lifecycle
- Provide guidance to nonprofit organizations, governmental agencies, WHO, World Bank, etc.

PinneyAssociates



Knowledge Areas

- Experience across a broad spectrum of Rx and OTC product categories

Pain	Dermatology	Women's Health
Infectious Disease		
Addiction	Cholesterol	Gastro-intestinal
Smoking Cessation	Overweight & Obesity	Mental Health
Stimulants	Anti-epileptics	Sleep Aids

PinneyAssociates

- A 26 person core team of experienced scientists, policy experts, researchers, and analysts plus:
 - A multidisciplinary pool of scientific and medical experts from leading institutions
 - A broad network of scientific and medical researchers, practitioners, specialists, and regulatory and policy consultants

PinneyAssociates Teams

- Nine interdisciplinary client service teams
 - Pharmaceutical Risk Management
 - Over-The-Counter Strategic Services
 - Strategic Communications
 - Issues Management
 - Marketing Strategy
 - Clinical Pharmacology
 - Clinical and Behavioral Research
 - Data Management and Statistical Analysis
 - Human Abuse Liability Testing

Main Revenue Services Include:

- Issues (public health, abuse, benefit risk) assessment
- Due diligence on new pharmaceuticals
- Design and oversee studies
- Publications
- Secure product approvals
- Develop regulatory documents
- Develop appropriate labeling
- Defend marketed products
- Interpret risk management data
- Develop and Implement Risk Management/REMS
 - Surveillance, including internet monitoring
 - Interventions and field follow-up
 - Regulatory filings

Science to Regulation & Policy

Non Profit & Public Health Support

- Surgeon General's Reports
- FDA Tobacco Regulations
- FDA Guidance Documents, e.g. Abuse Potential...
- World Health Organization
 - Reports: Regulating the Dependence Potential and attractiveness of Tobacco Products
 - Specific product reports:
 - Waterpipes
 - Electronic Nicotine Delivery Systems (ENDS)
- Institute of Medicine Reports
- National Institute on Drug Abuse and National Cancer Institute Reports
- Congressional testimony and proceedings

www.pinneyassociates.com



Company Principals

John M. Pinney, President

- Internationally recognized authority on:
 - disease prevention and health promotion
 - pharmaceutical research and development
 - marketing and market research
 - public policy and regulation
 - substance abuse
- Co-founded and served as Executive Director of Harvard University's Institute for the Study of Smoking Behavior and Policy

Joe Gitchell, Vice President Program Operations, Director of Marketing Strategy

- Expertise in OTC switches, coordinating national health policy conferences, and marketing plans for products in the US, EU, Latin America, and Asia
- Leads efforts supporting regulatory approvals, conducting public policy analysis, developing marketing approaches, devising, refining and defending claims (including extensive claims challenge support) and providing input on strategic market opportunities and directions

Company Principals

Jack E. Henningfield, Ph.D., Vice President, Research and Health Policy

- Over 35 years of experience in the assessment of CNS acting drugs
- Professor of Behavioral Biology at Johns Hopkins University School of Medicine
- At NIDA, Jack has served as Chief of Clinical Pharmacology Research Branch, Chief of the Biology of Dependence and Abuse Potential Assessment Section, Coordinator of the Addiction Research Center's Minority Recruitment and Training Program, and Chief of its Human Performance Laboratory
- Has authored or co-authored over 400 published papers

Sidney H. Schnoll, M.D., Ph.D., Vice President, Pharmaceutical Risk Management Services

- Internationally recognized expert in addiction and pain management with over 30 years of experience in academic medicine and has consulted clients on regulatory and scientific strategy as well as development, implementation, and assessment of risk management activities
- Developed the RADARS® System at Purdue Pharma L.P. to study the abuse and diversion of prescription opioids
- Has served on numerous committees and boards including the FDA's Drug Abuse Advisory Committee, NIH study sections, National Board of Medical Examiners test development committees, and a board member of the College on Problems of Drug Dependence

Company Principals

Saul Shiffman, Ph.D., Senior Scientific Advisor

- Clinical and health psychologist in the fields of behavior change, development of behavioral and educational interventions, self-management and self-control, field research methodology, addiction and statistical analysis
- Authored or co-authored over 250 published papers
- Presented widely in medical and scientific forums
- Advised organizations including FDA
- Professor in the departments of psychology and pharmaceutical science at the University of Pittsburgh

Mitchell Zeller, J.D., Vice President, Policy and Strategic Communications

- Over 25 years of regulatory, legislative and communications experience
- Leads domestic and global efforts around strategic communications and health policy on the regulation of pharmaceuticals and tobacco products
- Served as associate commissioner and director of FDA's Office of Tobacco Programs from 1993 to 2000
- Honored with the Secretary's Award for Distinguished Service and the National Public Affairs Special Recognition Award from the American Heart Association

Team Directors

Reginald Fant, Ph.D., Director, Clinical Pharmacology and Risk Management

- Clinical pharmacologist with expertise in drug abuse liability, developing risk management plans and post-marketing surveillance reports

Lucy Owen, D.Phil., Co-Director, Issues Management

- Public health expert with extensive background in women's reproductive health and family planning, smoking control/cessation, and pain management

Janine Pillitteri, Ph.D., Director, Clinical and Behavioral Research

- Health psychologist with expertise in questionnaire design and testing, research design and data analysis, and health promotion and behavior

Team Directors

Mark Sembower, Ph.D. Director, Data Management and Analysis

- Biostatistician with expertise in statistical analysis and data management of clinical trials, public access datasets, and consumer surveys

Christine T. Sweeney, Ph.D., M.P.H., Co-Director, Issues Management

- Behavioral epidemiologist with expertise in cancer prevention and control, health promotion and disease prevention, and behavioral risk factors for chronic disease

Lisa M. Zapawa, M.D., M.P.H., Co-Director, Issues Management

- Public health expert with extensive background in women's reproductive health and family planning, smoking control/cessation, and pain management

Science and Policy Advisors

Edward J. Cone, Ph.D.

- Recognized worldwide for expertise on the chemistry and pharmacology on drug abuse

Nabarun Dasgupta, M.P.H.

- Quantitative epidemiologist specializing in researching the use and nonmedical use of prescription opioid pain relievers and heroin

George Quesnelle

- Former President of GSK Consumer Healthcare North America with more than 20 years of prescription-to-OTC switch experience including Nicorette, NicoDerm CQ, and alli

Karen L. Sees, D.O.

- Over 21 years experience in substance abuse treatment, research, and pain management

Example of a Major Service Area:
The Regulatory Challenges of Pain
Medications and Abuse



Pain, Therapy, and Public Health

- Undertreated pain is a public health problem (IOM, 2011)
 - Public pressure on FDA to expeditiously approve potentially helpful drugs
- Opioid analgesics involved in abuse, diversion, and opioid-related deaths
 - Public pressure for FDA to “do something”, e.g., not approve new drugs

Pain Rx: Issues & Opportunities

- Patient, doctor, public health and political pressures may require new entities and formulations
- Addiction concerns are an opportunity to develop products that are scheduled or labeled differently than equi-effective existing CII drugs
- FDA has announced support of tamper-deterrent and less abusable analgesic development

The Challenge of Pain Medications for FDA and Sponsors

- Challenge to Pharma: More effective and less reinforcing medications
- Challenge to FDA: Balance problem of under-treated patients with opioid abuse & overdose
- Challenge to Abuse Liability Assessment (AL): Provide data to differentiate less abusable medications with less restrictive scheduling and/or labeling than equi-effective approved drugs – recent CEO Comment (See Dasgupta et al., DAD, 2011)

The Historical Search for Non Addictive Analgesics – the beat goes on.....

The College on Problems of Drug Dependence was founded in 1929 to develop non-addictive pain relievers to replace morphine

- Addiction Research Center (ARC) at the Lexington KY federal penitentiary
- National Institute on Drug Abuse, Intramural Research Program
- Universities :Michigan, Medical College of VA, Hopkins, Harvard...

Where is FDA Now?

See AdCom next Monday-Tuesday

- Concerned about fueling abuse
- Fearful of backlash from pain sufferers
- Trying to find effective REMS that assures access, including class REMS such as ER/LA and TIRF
- Encouraging advances in potential abuse and tamper deterrence by scheduling and labeling differentiation (e.g., Oxecta, Embeda, Concerta, Nucynta, Opana ER, new OxyContin, Suboxone, Vyvanse)
- Finalizing the Draft Guidance on Abuse Potential Assessment, and developing guidance for 'Abuse/Tamper Resistance'

Guidance for Industry: Assessment of Abuse Potential of Drugs - Draft Guidance (FDA, 2010)

- Based on the state of the science, including special conferences of the CPDD
- Explains the role of AL studies in drug scheduling
- Provides current thinking on studies to consider in influencing scheduling and other abuse related labeling decisions

FDA Drugs Tab: www.fda.gov/Drugs

Medication Guides, Drug Shortages, Drug Safety Communications and Other Safety Announcements
Development & Approval Process (Drugs)
Conducting Clinical Trials, Types of Drug Applications, Forms and Submissions Requirements, Labeling Initiatives, Drug and Biologic Approval Reports

Research by FDA Staff to Evaluate and Enhance the Safety of Drug Products
Resources for You
For Consumers, Health Professionals, Industry

Approvals & Clearances

- This Week's Drug Approvals
- Drug and Biologic Approval Reports
- Search Drug Approvals by Month Using Drugs@FDA

Stay Informed

- What's New (Drugs)
- E-mail Alerts, News Feeds, Podcasts, Webinars, and Widgets on Drug Topics
- Meeting Presentations

Contact FDA

Toll Free
(855) 543-3784, or
(301) 796-3400
druginfo@fda.hhs.gov

Human Drug Information
Division of Drug Information (CDER)
Office of Communications
Feedback Form
10001 New Hampshire Avenue
Hillandale Building, 4th Floor
Silver Spring, MD 20993

Resources for You

- Consumers
- Healthcare Professionals
- **Industry**
- About the Center for Drug Evaluation and Research
- Buying Medicines Over the Internet
- Counterfeit Medicine
- CDERLearn
- Report a Problem

Search Drugs

SEARCH

News and Announcements

- FDA takes action against thousands of illegal Internet pharmacies
- FDA Drug Safety Communication: Ongoing safety review of Parkinson's drug Mirapex (pramipexole) and possible risk of heart failure
- FDA Drug Safety Communication: Rare cases of serious burns with the use of over-the-counter topical muscle and joint pain relievers

➤ [More News and Announcements](#)

Drug Safety

- Buying & Using Medicine Safety
- Drug Safety Communications
- **Index to Drug-Specific Information**
- **Medication Guides**
- Medication Health Fraud
- Postmarket Drug Safety Information for Patients and Providers

Program Areas

Leads you to REMS, Guidances, Approval Histories

Quick link to Drug Safety Info

Quick link to MedGuides

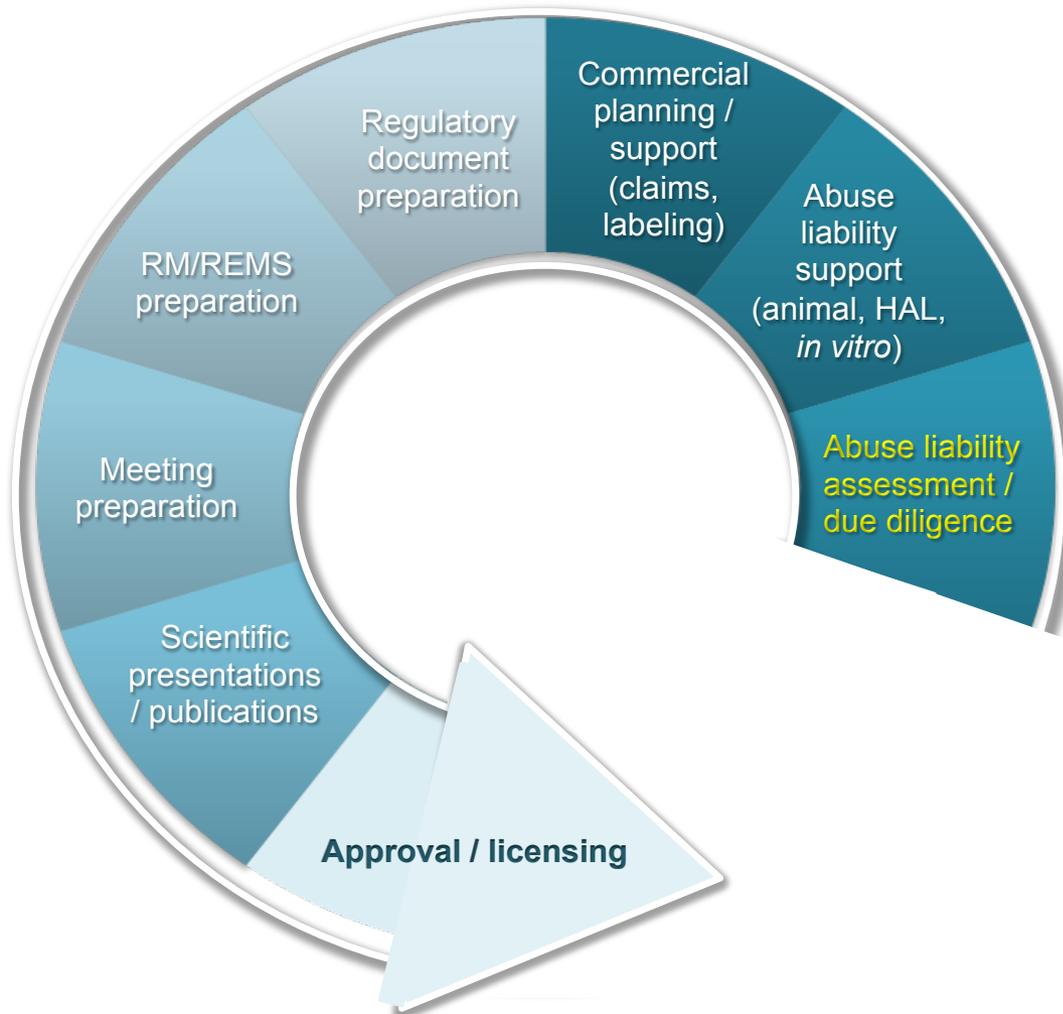
PinneyAssociates's Services



Pinney Associates Risk Management and Abuse Liability Services: Life Cycle



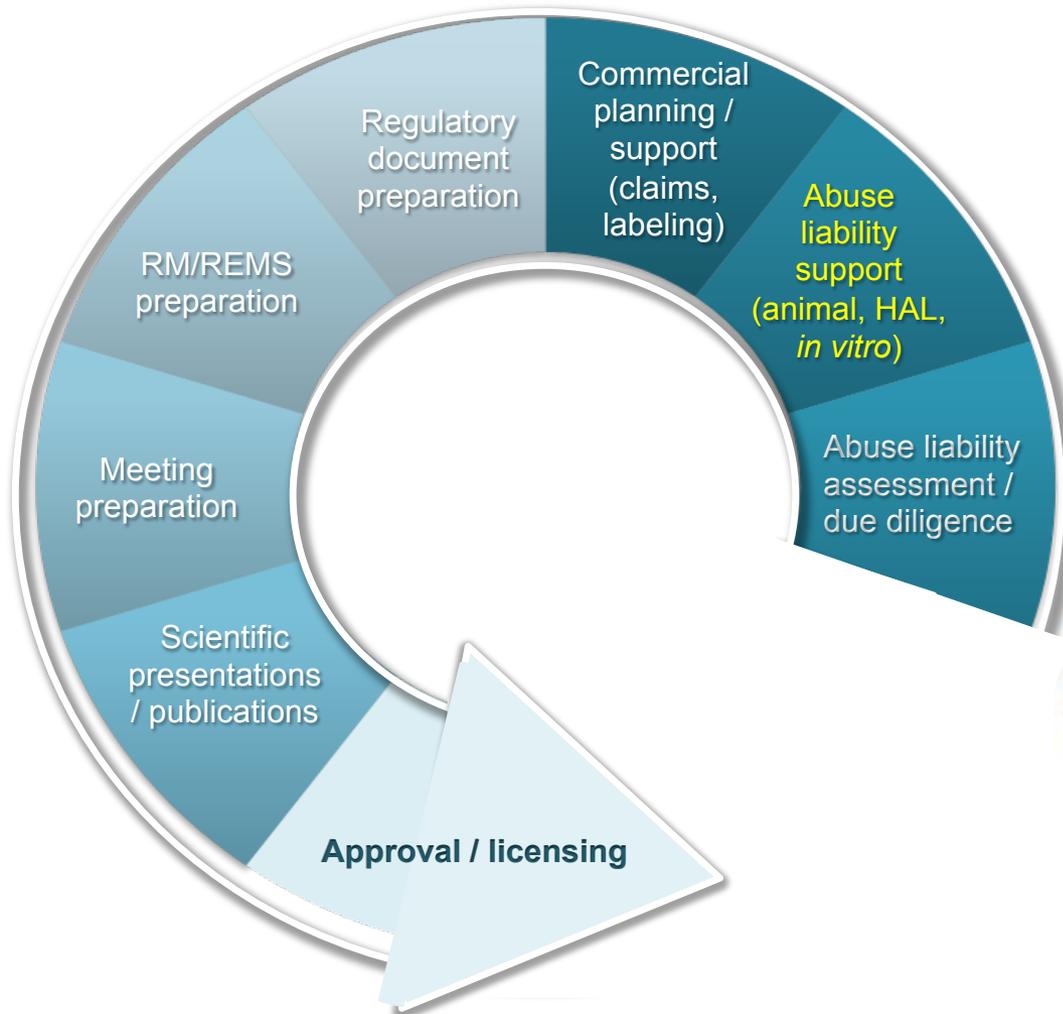
Pinney Associates Risk Management and Abuse Liability Services



Abuse Liability Issues Assessment and Due Diligence

- **Goals**
 - Provide sponsor and potential partners/backers with assessment of abuse liability issues relevant to approvability, scheduling, labeling and risk management
 - Identify potential gaps in science base
- **Approach**
 - Understand goals of sponsor regarding timeline, scheduling, labeling, and market position
 - Assess AL data including chemistry, *in vitro*, nonclinical, clinical, and formulation integrity
 - Review and assess correspondence with FDA and DEA
 - Recommend potential development and regulatory strategies to meet the needs and goals of the sponsor
 - Work with sponsor to identify critical studies, potential designs, and implement timelines to address near and longer term goals of sponsor and potential partners

Pinney Associates Risk Management and Abuse Liability Services



Abuse Liability Support

- *In vitro* tamper testing support
 - Tamper testing protocol design review and recommendations (or preparation)
 - Protocol implementation
 - Data interpretation
- Human abuse liability (HAL) assessment support
 - HAL study design and statistical plan
 - Data interpretation and final study report
 - Presentation and defense of HAL study findings with regulatory authorities
 - Presentation and publication of HAL study data

In Vitro Formulation Testing for Tamper and Abuse Deterrence

- Tamper resistant/deterrent formulations are major hot area of drug development in recent years
- *In vitro* studies are less costly commitments than HAL studies
- They are understood to be vital to conduct at early stages to guide further developmental commitments and testing as well as to understand potential market value and licensing opportunities
- They have great potential to feed considerable additional abuse liability service work

Examples of Tamper Methods Tested

- Assessment of cutting/crushing/powdering
Cutting with knife, crushing with spoon, powdering by grinding or milling
- Solvents to be tested
Water, saline, ethanol (40%, 95%), acetone, ethyl acetate, ether, methylene chloride, hexane, lighter fluid, paint thinner, vegetable oils
- Temperatures to be tested
Ambient, 95°C, reflux
- pH to be tested
Acid, neutral, basic
- Timeframes
-5 min, 15 min, 30 min, 1 hr, 2 hr, 4 hr, 8 hr, 12 hr, 24 hr

(Fant, Cone, & Henningfield. Presented at the College on Problems of Drug Dependence, June 2011)

HAL Study Design Begins With The Sponsor's Goals

- Scheduling: Nonscheduled status or less restrictive scheduling than predecessor or competitor?
- Labeling: Differentiating labeling, perhaps including HAL study findings?
- Postmarketing: Less burdensome risk management/REMS than competitors?
- Commercial targets: Competitive products, potential patients, prescribers, and/or payers?

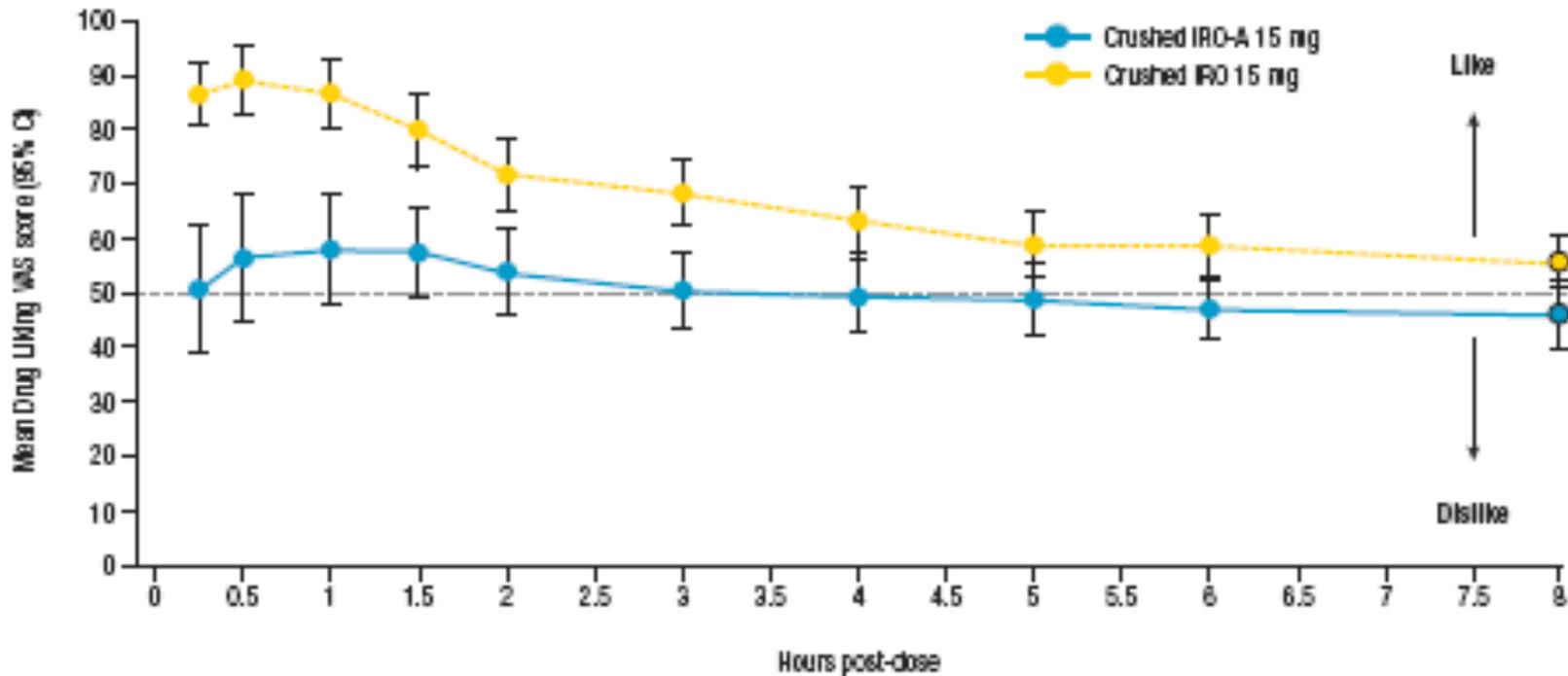
CEO: "If this drug does not look less addictive in the HAL we will kill it! The world does not need just another opioid analgesic and I would not be able to get the 150million for the next phase of development. Do you see why I am nervous about this study?"

Scientific and Registration HAL Studies

Characteristic	Scientific HAL	Registration HAL
Number of subjects	8-12	20-40
HAL Measures	3-6	10+
Population	Less representativeness	Gender balanced, relevant minorities
Cost	0.5-0.75 million	2 million+
Time	3-6 months from “go” to report	8-12 months from “go” to report
Study provides	<p>Early strong signal of the likely outcome of a registration HAL and basis for diligence and label “claims</p> <p>May guide other drug development decisions including registration HAL design</p>	Often acceptable HAL assessment for the NDA

E.g., Formulation Benefit: Drug Liking was lower for Oxecta than Roxicodone

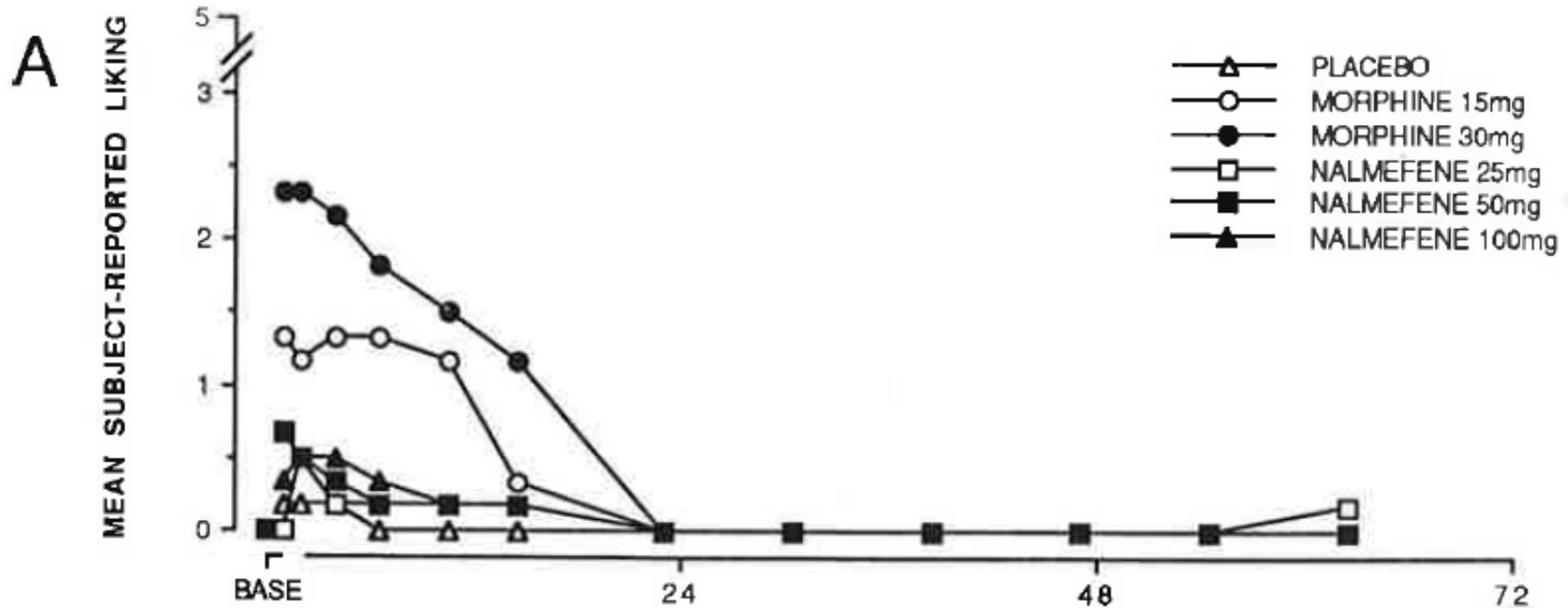
IRO-A: Oxecta
IRO: Roxicodone



(Rolleri, Faulknor, Schoedel, Pixton, Chen, Bass, & Sellers. Presented at the American Academy of Pain Management, September 2011)

Nalmefene (CII opioid to nonscheduled)

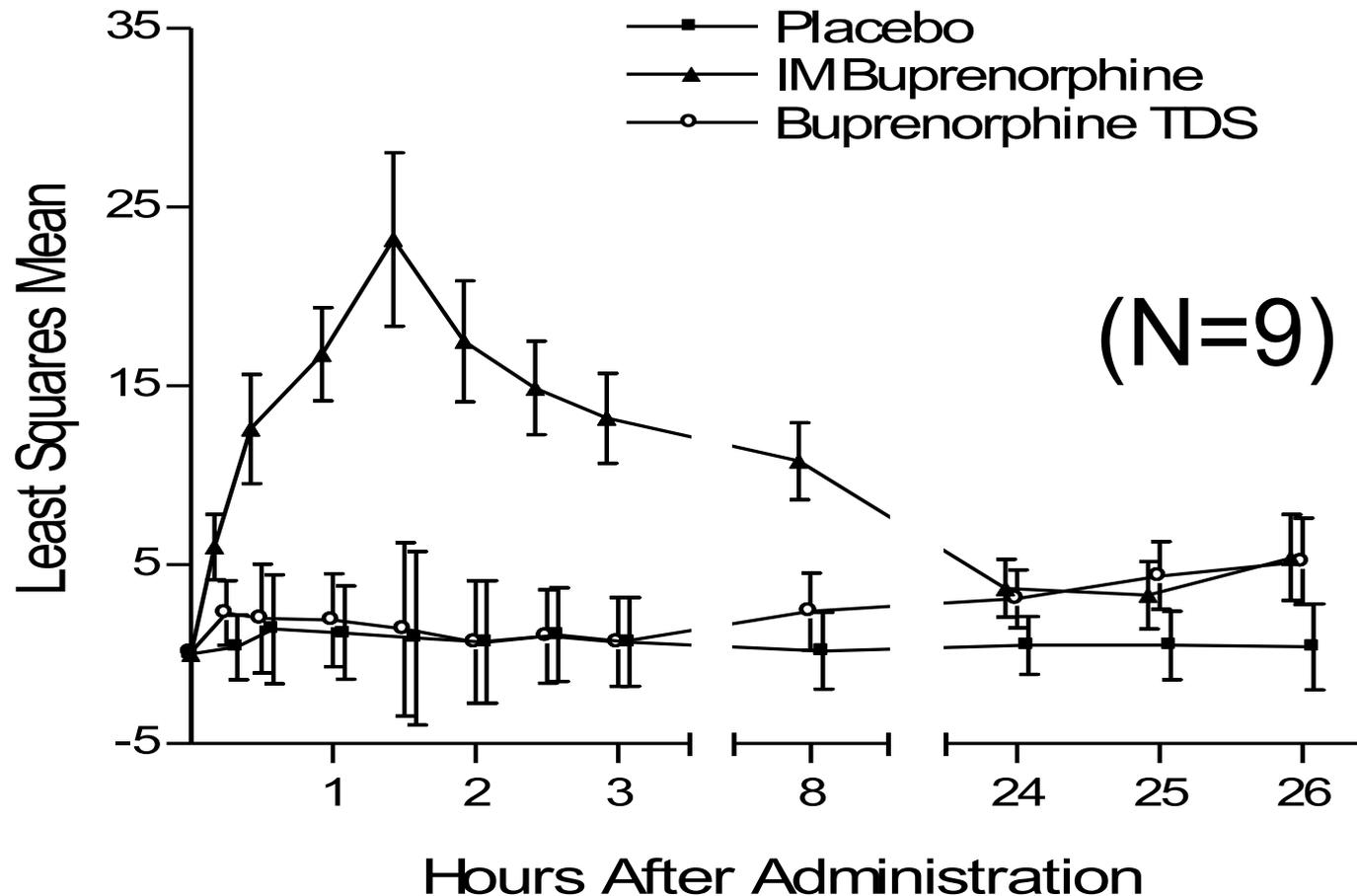
(Fudala, Heishman & Henningfield, 1991)



(N=6)

Speed of onset benefit: Transdermal Buprenorphine (Becker et al., 2001)

Drug Liking



An Issue That is Sure to Emerge: What if We Had a Formulation That is --

- highly resistant to ALL known methods of tampering
- slowly delivers drug over an extended period, or releases drug only to the individual's prescription

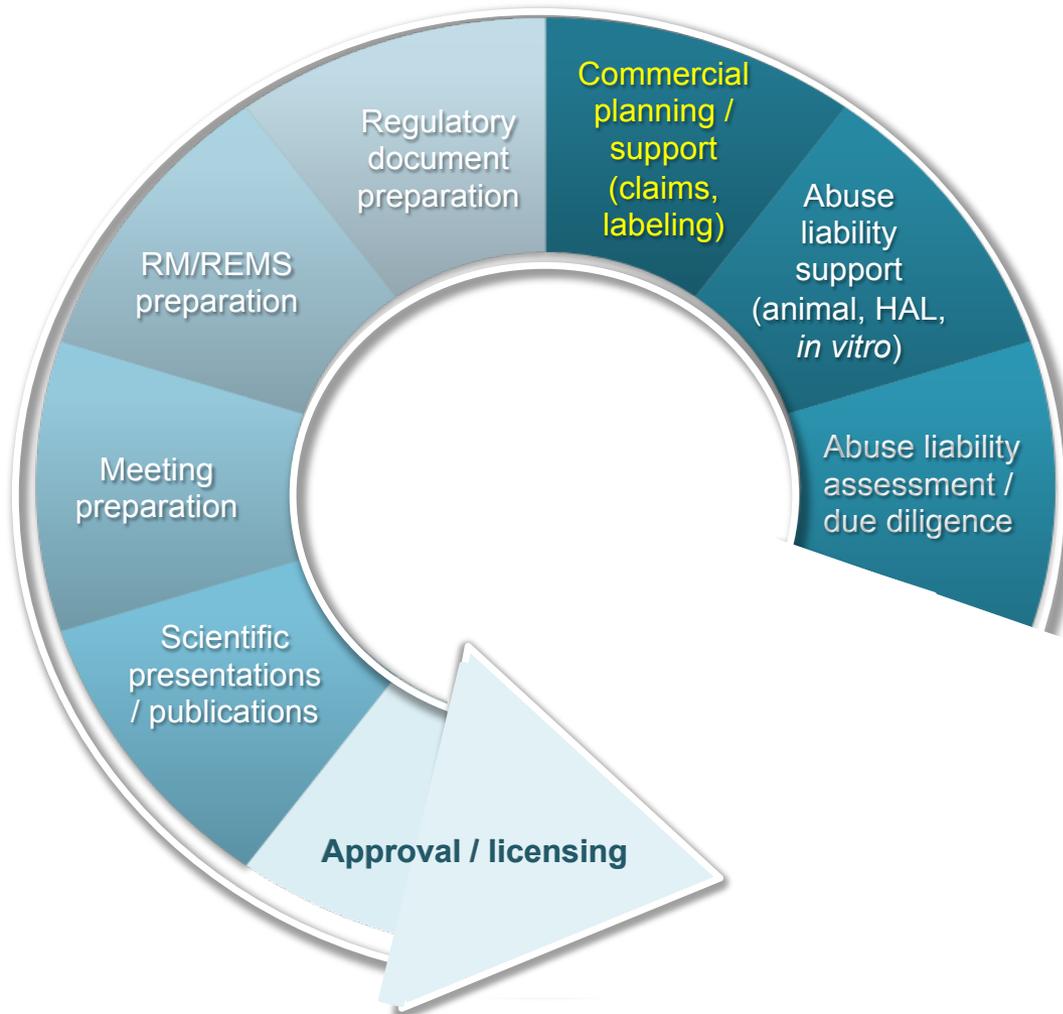


Should it – could it – be scheduled less restrictively than conventional formulations of the same Active Pharmaceutical Ingredient (API)?

This pushes the bounds of the CSA

How about differentiation by labeling “claims” or less restrictive REMS?

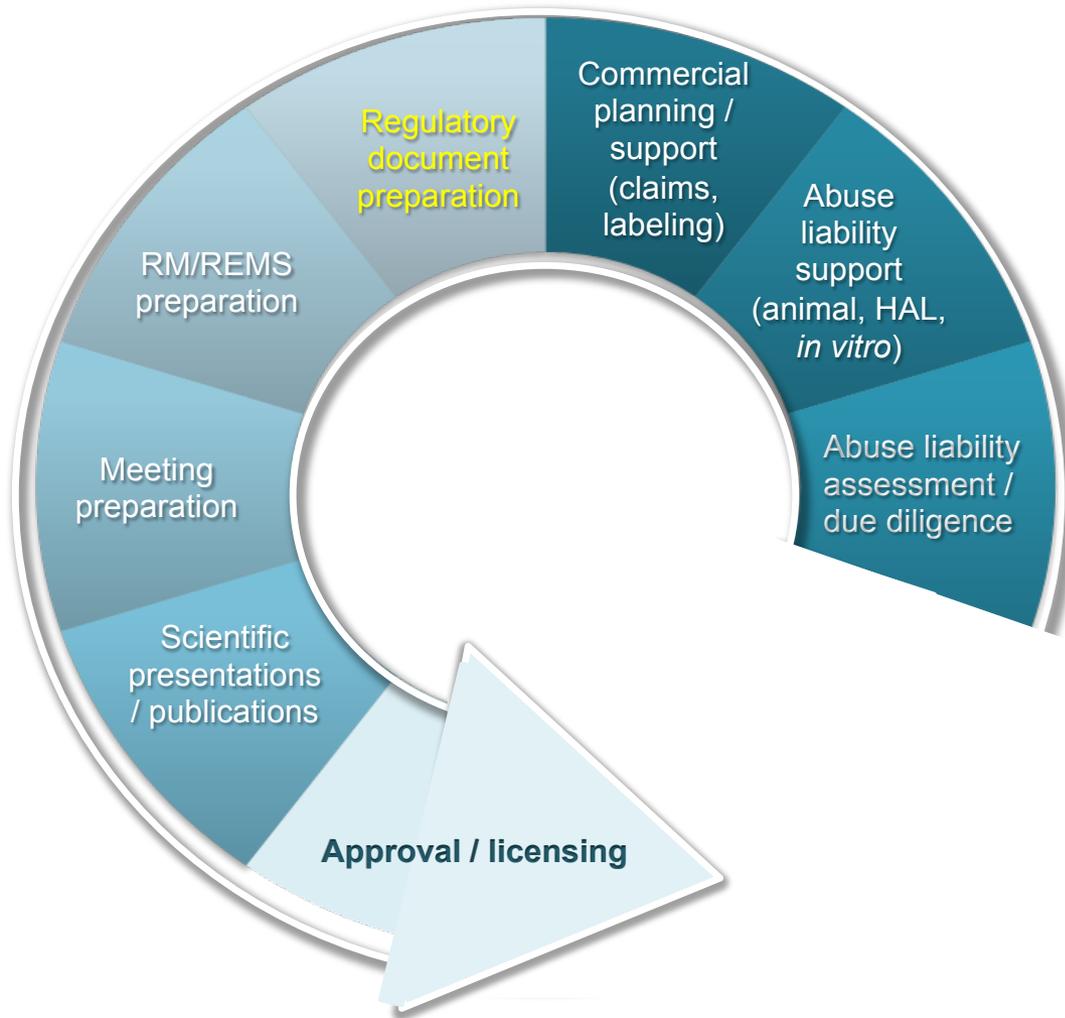
Pinney Associates Risk Management and Abuse Liability Services



Commercial Planning / Support

- Market analysis
- Differentiated positioning and claims development
- Claims refinement and defense against potential competitor challenges
- Preliminary stakeholder engagement planning
- Engagement and representation before potential licensees and/or investors

Pinney Associates Abuse Liability Services



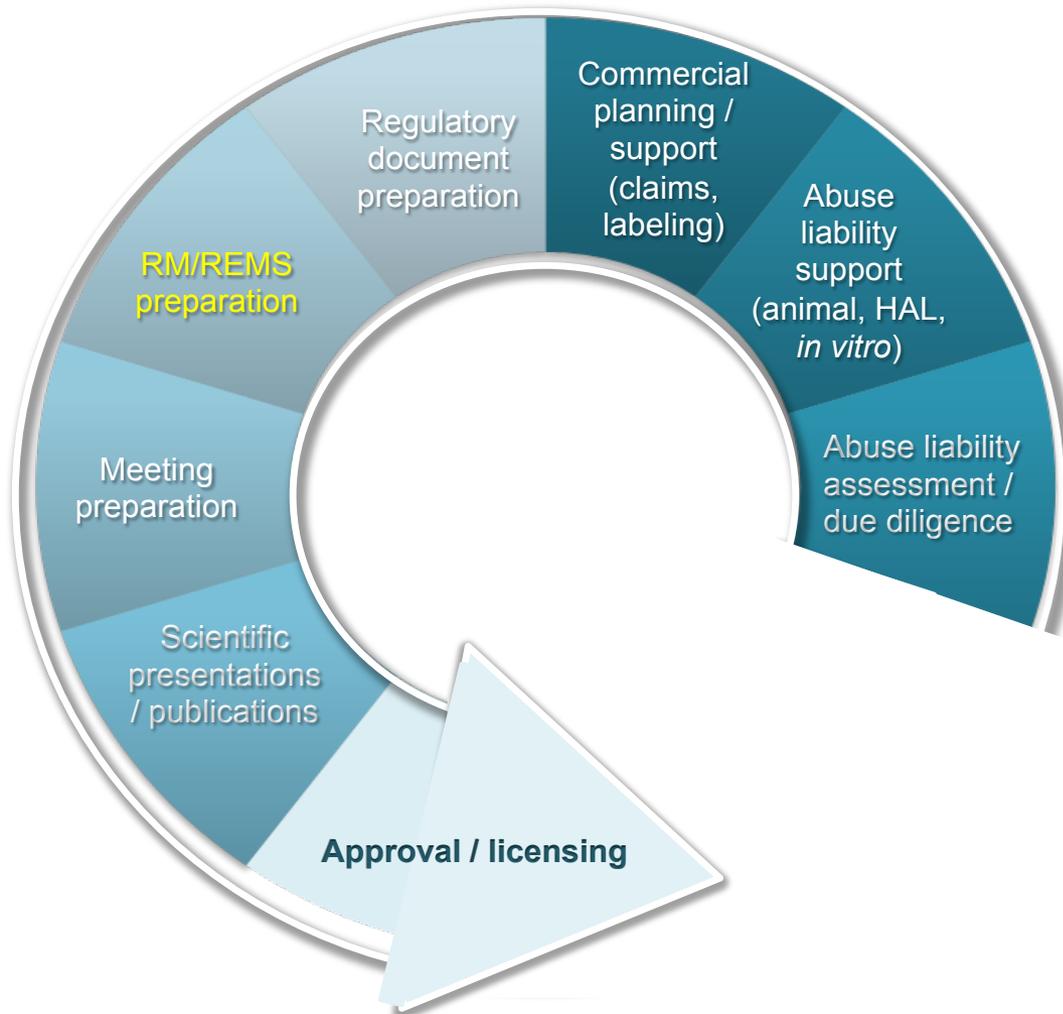
Regulatory Document Preparation

- Abuse potential section of the NDA and 8-factor abuse liability assessment
- Sections of the Integrated Summary of Safety (ISS) related to abuse potential
- Risk Assessment/Evaluation (and Mitigation Strategies – aka REMS)

The 8 Factors – required for scheduling

1. Actual or relative potential for abuse – *this is where HAL data are considered – as one component in one factor but these data are heavily weighted*
2. Scientific evidence of its pharmacological effect
3. Current scientific knowledge regarding drug
4. History and current pattern of abuse
5. The scope, duration, and significance of abuse
6. Risk to public health
7. Psychic or physiological dependence liability
8. Immediate precursor of substance controlled

Pinney Associates Abuse Liability Services



PinneyAssociates Risk Management Approach

Understand objectives so as to define risk management concepts in relation to product strategy



Assess fully the benefits of a product in order to properly contextualize risk

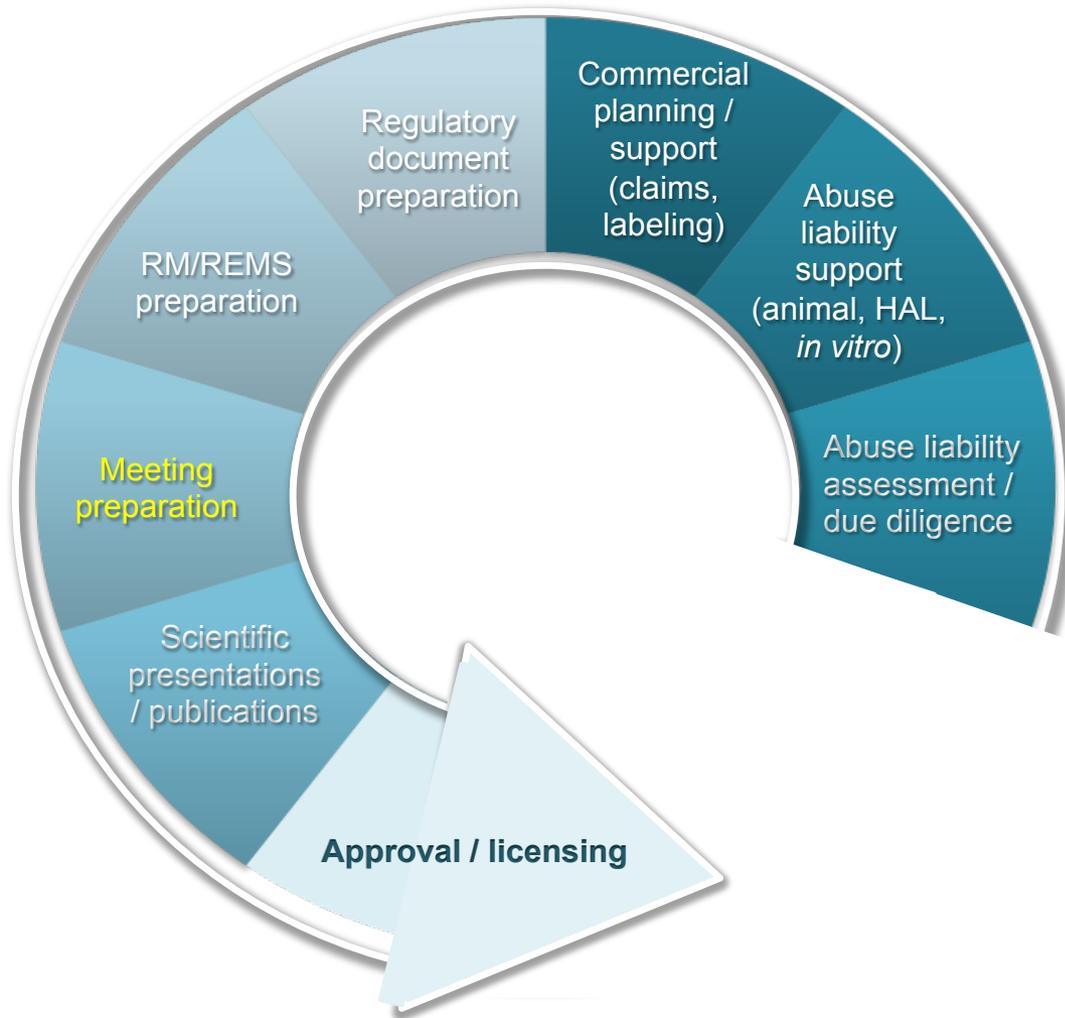


Work to identify potential problems and develop effective strategies and tools to address them before they arise



Design a REMS that can easily be adapted to include new products in sponsors pipeline

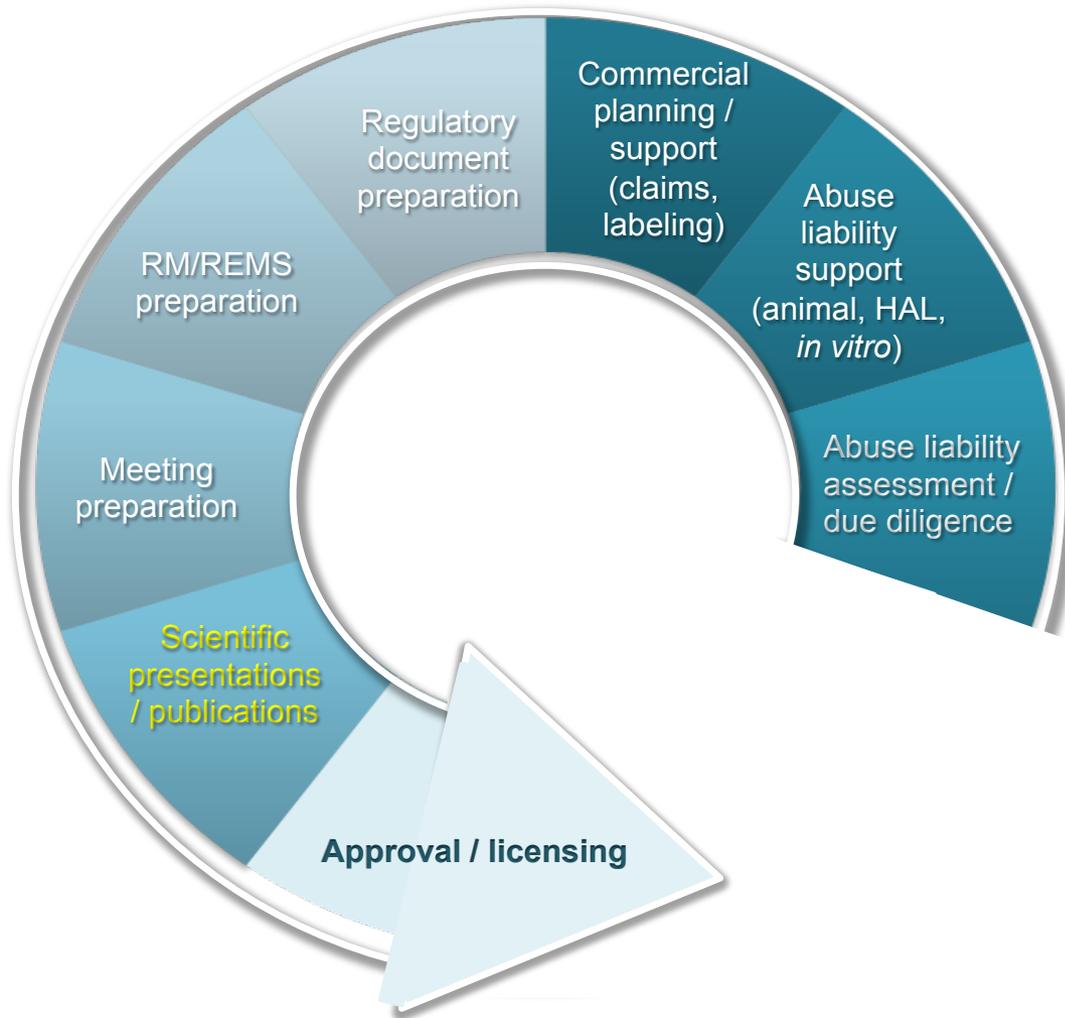
Pinney Associates Abuse Liability Services



Meeting Preparation

- FDA Division/CSS & FDA Advisory Committee
 - End of Phase II meeting
 - Pre-NDA meeting
 - Advisory Committee meeting
- Potential licensee and/or investor meetings
- Develop briefing materials, Q&A books
- Convene mock advisory meetings

Pinney Associates Abuse Liability Services

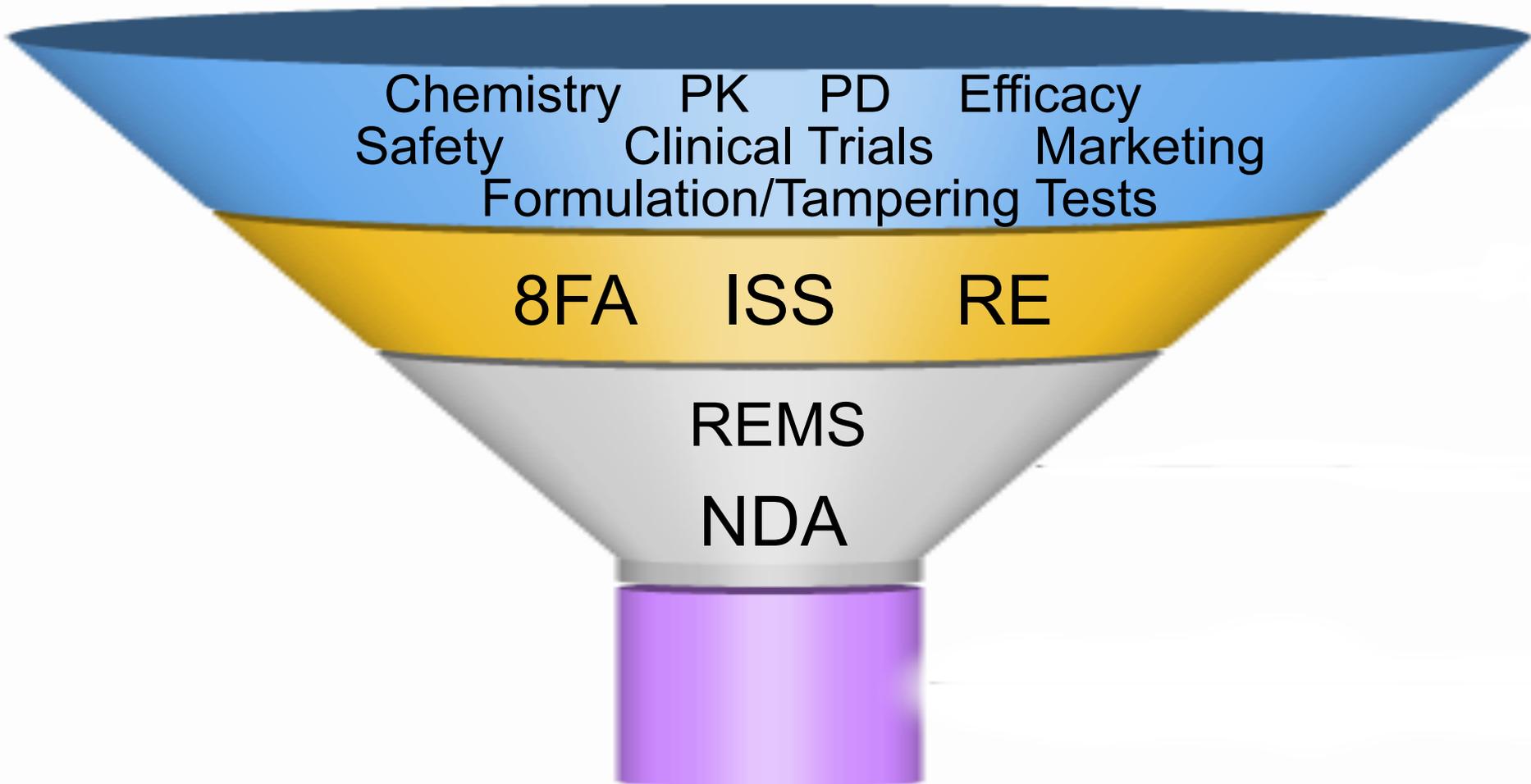


Scientific Presentations / Publications

- Conference preparation and presentation
 - Abstracts
 - Posters
- Manuscript preparation

Approval / Licensing

- FDA approval
 - Least restrictive scheduling
 - Favorable labeling and claims
 - Minimal post marketing requirements
- Licensing & other commercial opportunities
 - this is often the goal of smaller biotech and pharmaceutical development companies with limited capabilities in approval and marketing



Approval – Labeling and
Scheduling
Marketing

Support, Claims, Surveillance, REMS

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Company (PinneyAssociates)

Academic (Johns Hopkins)

Consulting business development

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Revenue Activities

Major

Pharmaceutical Consulting

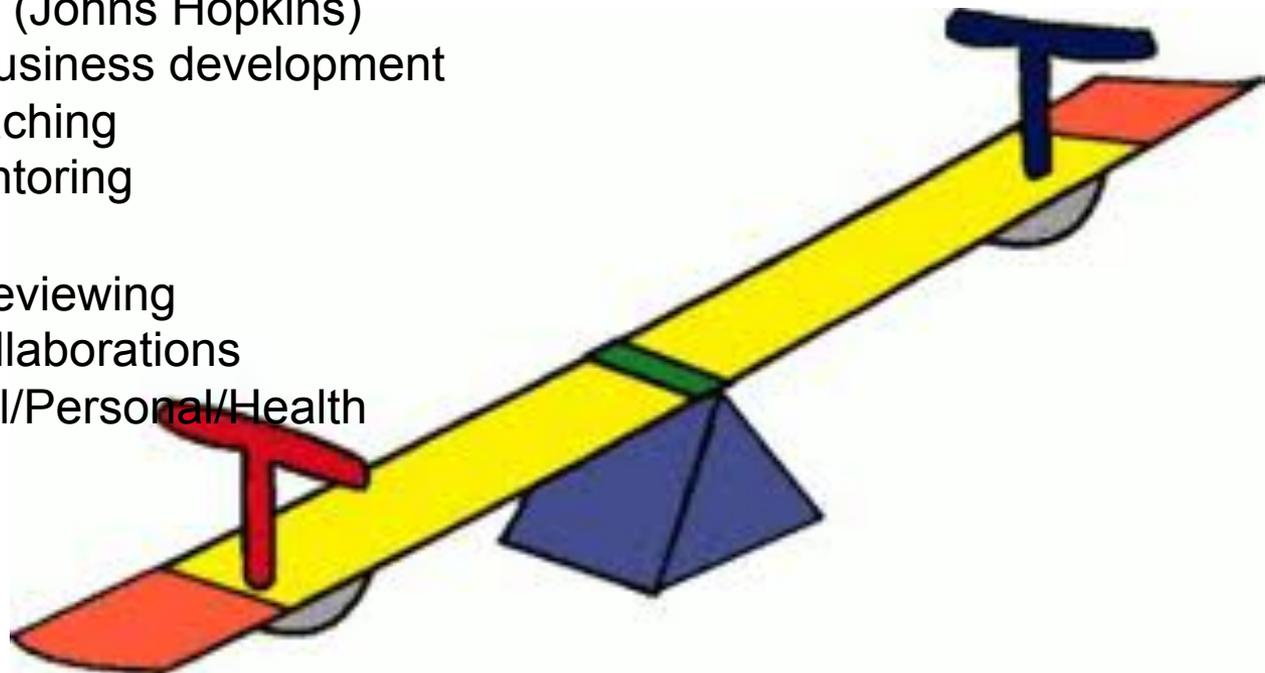
Legal consulting

Minor

CME lecturing and writing

Commissioned reports & editing

Nonprofit organization consulting



Discussion

