

Applied Cannabis Research within VA: An Overview & Successful Example

Clinical Science Research & Development Service

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VA

U.S. Department of Veterans Affairs
Veterans Health Administration
Office of Research & Development

Introduction

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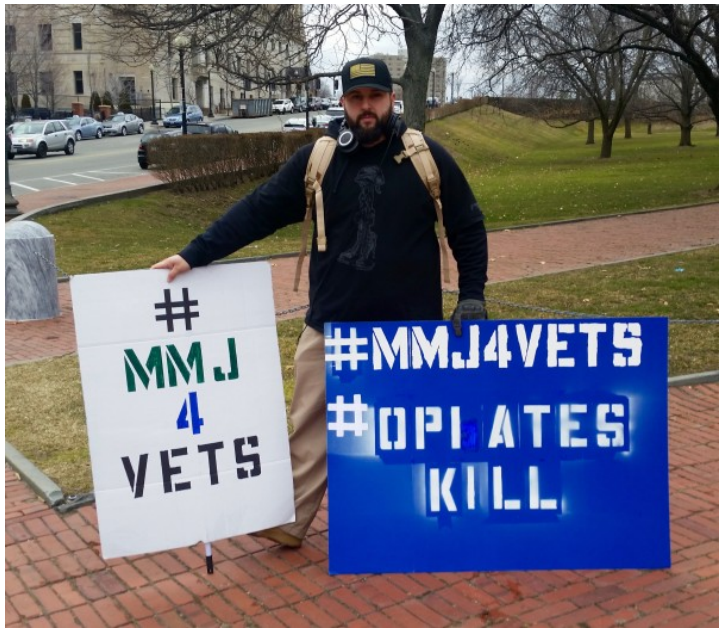
Overview of Webinar

- Office of Research & Development and Cannabis Research
- Mechanisms of Support
- Design Considerations
- Procedures
- Q&A

Veterans and Cannabis



ORD & Cannabinoid Research

1. YES, it's allowed! Under the Controlled Substance Act, research with cannabis is permissible with regulatory approvals
2. Currently funded by VA Office of ORD:
   - Clinicaltrials.gov Registration# NCT03518801

Mechanisms of Support

1. VA CSR&D Merit
2. VA PTSD Psychopharmacology Initiative

Design Considerations

1. Aims
   - Determine how Veterans currently use cannabis
     - Does it help or hurt?
   - Develop cannabinoid-based pharmacotherapy
2. Study Drug
   - Whole plant cannabis versus single molecule formulation
   - Plant-derived versus synthetic
3. Formulation
   - Method of administration
     - Oral, sublingual, smoked/vaporized, topical

An Example: CBD-PE Study

- **Design:** Prospective, randomized controlled investigation testing CBD as adjunctive pharmacotherapy
- **Methods:**
  - N = 136 military veterans
  - 16 weeks drug or placebo
    - dose: 600mg CBD daily, oral
    - 12 sessions PE therapy

Sources of Drug

1. NIDA Drug Supply
2. Traditional Drug Development Process
3. FDA-approved Medications

NIDA Drug Supply Program

Bulk Marijuana

Bulk marijuana is currently available in the following general categories, and due to recent interest its strength is being provided for both THC and CBD as Low (<1%), Medium (1-5%), High (5-10%), and Very High (>10%). Bulk marijuana has small amounts of other cannabinoids (CBC, CBG, CBN, and THCV) which are reported in the batch specific details.

- **Placebo marijuana (produced by solvent extraction)**
  - THC (0%) / CBD (0%)
- **Low THC varieties**
  - Low THC (<1%) / Medium CBD (1-5%)
  - Low THC (<1%) / High CBD (5-10%)
  - Low THC (<1%) / Very High CBD (>10%)
- **Medium THC varieties**
  - Medium THC (1-5%) / Low CBD (<1%)
  - Medium THC (1-5%) / Medium CBD (1-5%)
  - Medium THC (1-5%) / High CBD (5-10%)
  - Medium THC (1-5%) / Very High CBD (>10%)
- **High THC varieties**
  - High THC (5-10%) / Low CBD (<1%)
  - High THC (5-10%) / High CBD (5-10%)
  - High THC (5-10%) / Very High CBD (>10%)
- **Very high THC varieties**
  - Very High THC (>10%) / Low CBD (<1%)

Marijuana cigarettes

The following represents the existing stocks of manufactured marijuana cigarettes, which will be made available to the research community until depleted. Please note that NIDA does not plan to manufacture marijuana cigarettes in the near future. Only bulk marijuana will generally be available for research

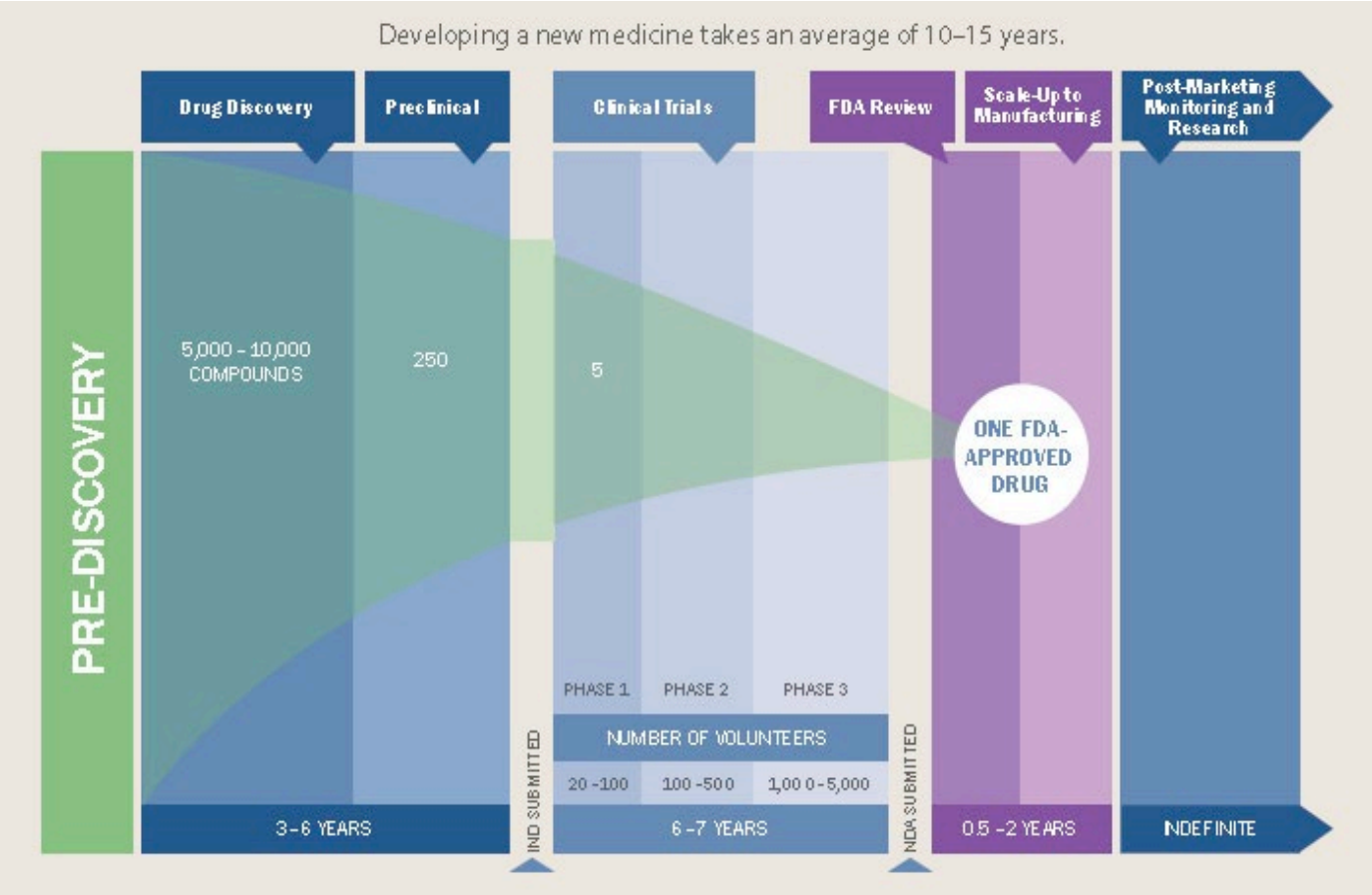
Table 1 - Marijuana Cigarettes (RTI)

Batch No.	THC	CBD	%THC	%CBD	%CBC	%CBG	%CBN	%THCV
12792-1208-77	Medium	Low	2.000	0.020	N/A	N/A	0.470	N/A
10074-0301-97	Medium	Low	2.800	0.080	N/A	N/A	0.220	N/A
12792-0109-120	Medium	ND	3.600	ND	N/A	N/A	0.270	N/A
12792-0109-146	High	ND	5.600	ND	N/A	N/A	0.400	N/A
10604-0203-95	High	ND	6.700	ND	N/A	N/A	0.490	N/A
12944-0509-105	Placebo	Placebo	0.002	0.001	N/A	N/A	0.004	N/A

Legend - Low = <1%; Medium = 1-5%; High =5-10%; ND = Not detected, N/A = Not available
Note: %THC contents may vary with time and storage conditions. Therefore researchers should inquire about latest THC strength before submitting their request.

NIDA Drug Supply Program Director, Dr Rik Kline at rkline@nida.nih.gov

Traditional Drug Development Process



Traditional Drug Development Process

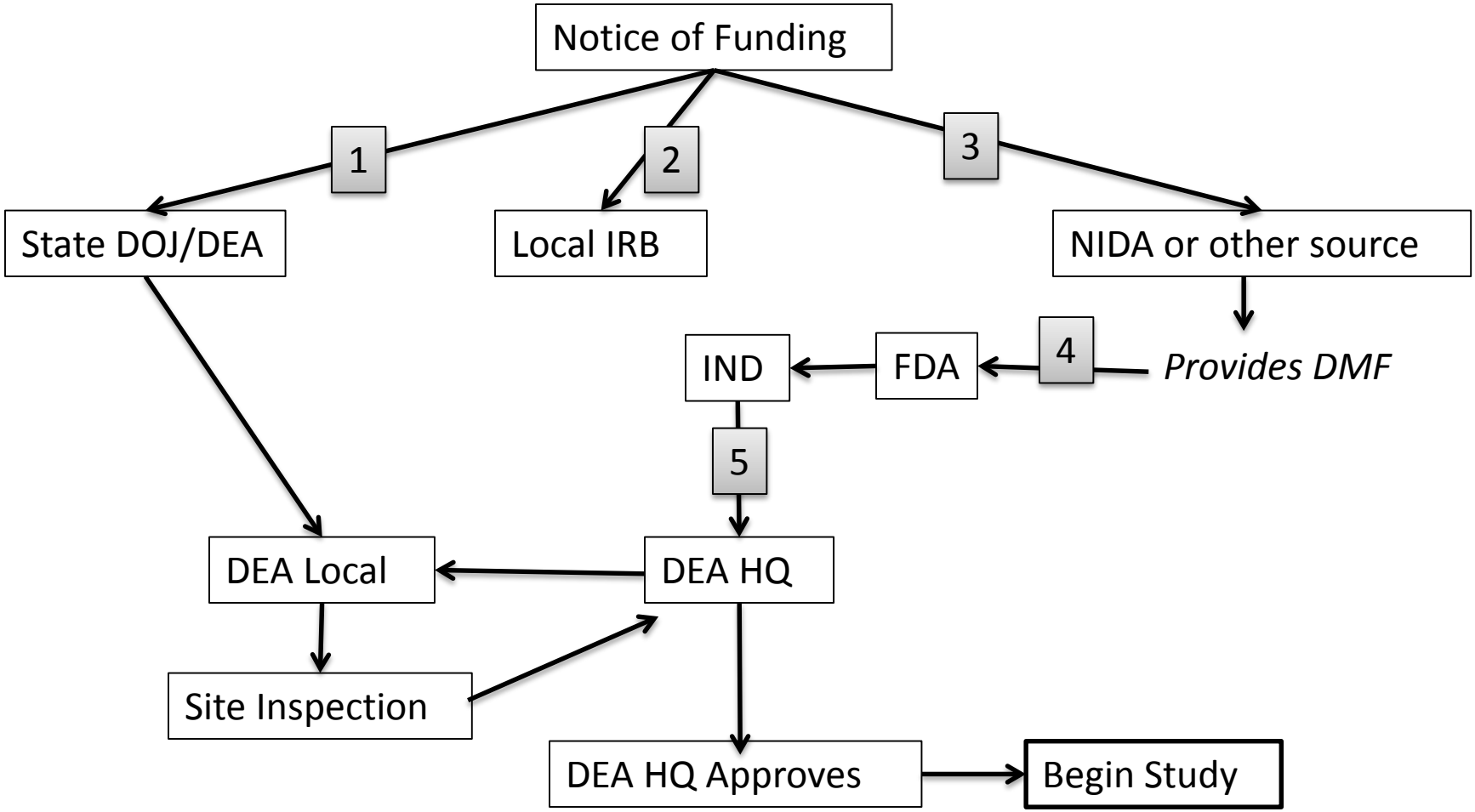
- Must have sufficient data in Drug Master File (DMF) for FDA to approve Investigational New Drug (IND)
  - In-vivo
  - Preclinical
  - Safety & Dosing
- Company/Manufacturer must have DEA Schedule-1 license to manufacture and transport

FDA Approved Cannabinoids

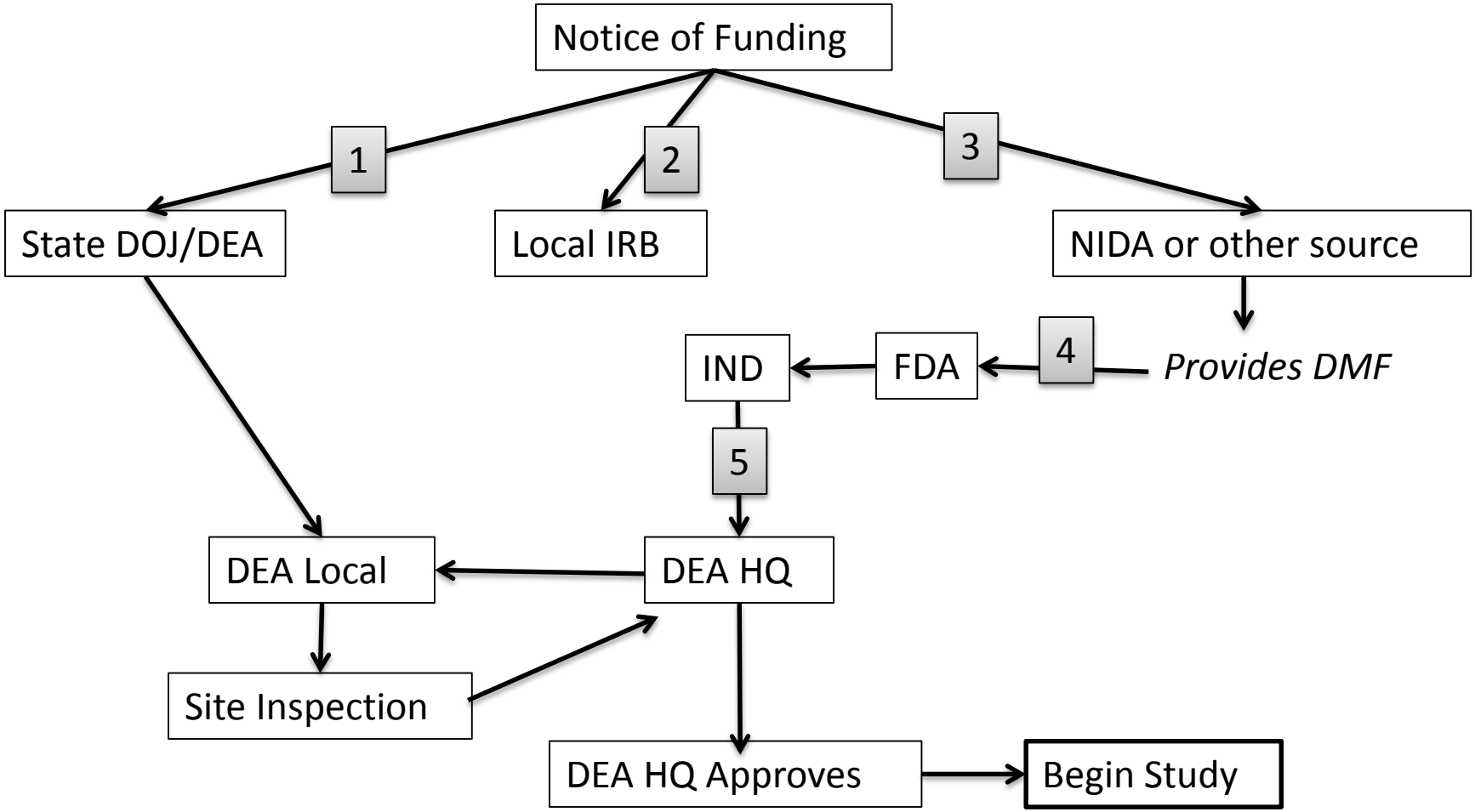
- Epidiolex – botanically derived CBD extract
- Marinol & syndros (dronabinol)– synthetic functional analogue of THC
- Cesamet (nabilone) – synthetic functional analogue ofTHC

Other Options?

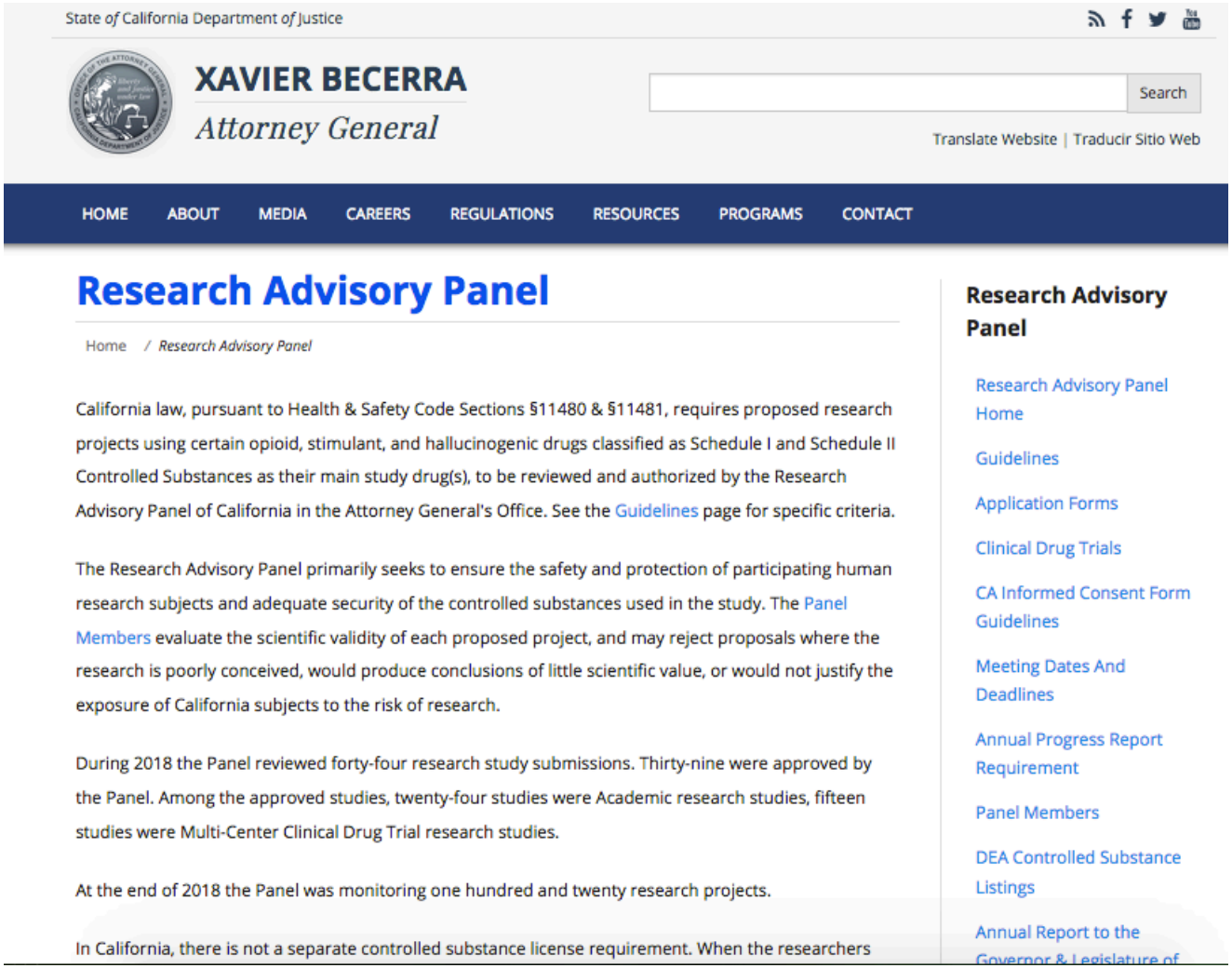
Process of Approval ~ 6-12 mo.



Process of Approval ~ 6-12 mo.



DOJ Approval by State



State of California Department of Justice

XAVIER BECERRA
Attorney General

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Research Advisory Panel

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California law, pursuant to Health & Safety Code Sections §11480 & §11481, requires proposed research projects using certain opioid, stimulant, and hallucinogenic drugs classified as Schedule I and Schedule II Controlled Substances as their main study drug(s), to be reviewed and authorized by the Research Advisory Panel of California in the Attorney General's Office. See the Guidelines page for specific criteria.

The Research Advisory Panel primarily seeks to ensure the safety and protection of participating human research subjects and adequate security of the controlled substances used in the study. The Panel Members evaluate the scientific validity of each proposed project, and may reject proposals where the research is poorly conceived, would produce conclusions of little scientific value, or would not justify the exposure of California subjects to the risk of research.

During 2018 the Panel reviewed forty-four research study submissions. Thirty-nine were approved by the Panel. Among the approved studies, twenty-four studies were Academic research studies, fifteen studies were Multi-Center Clinical Drug Trial research studies.

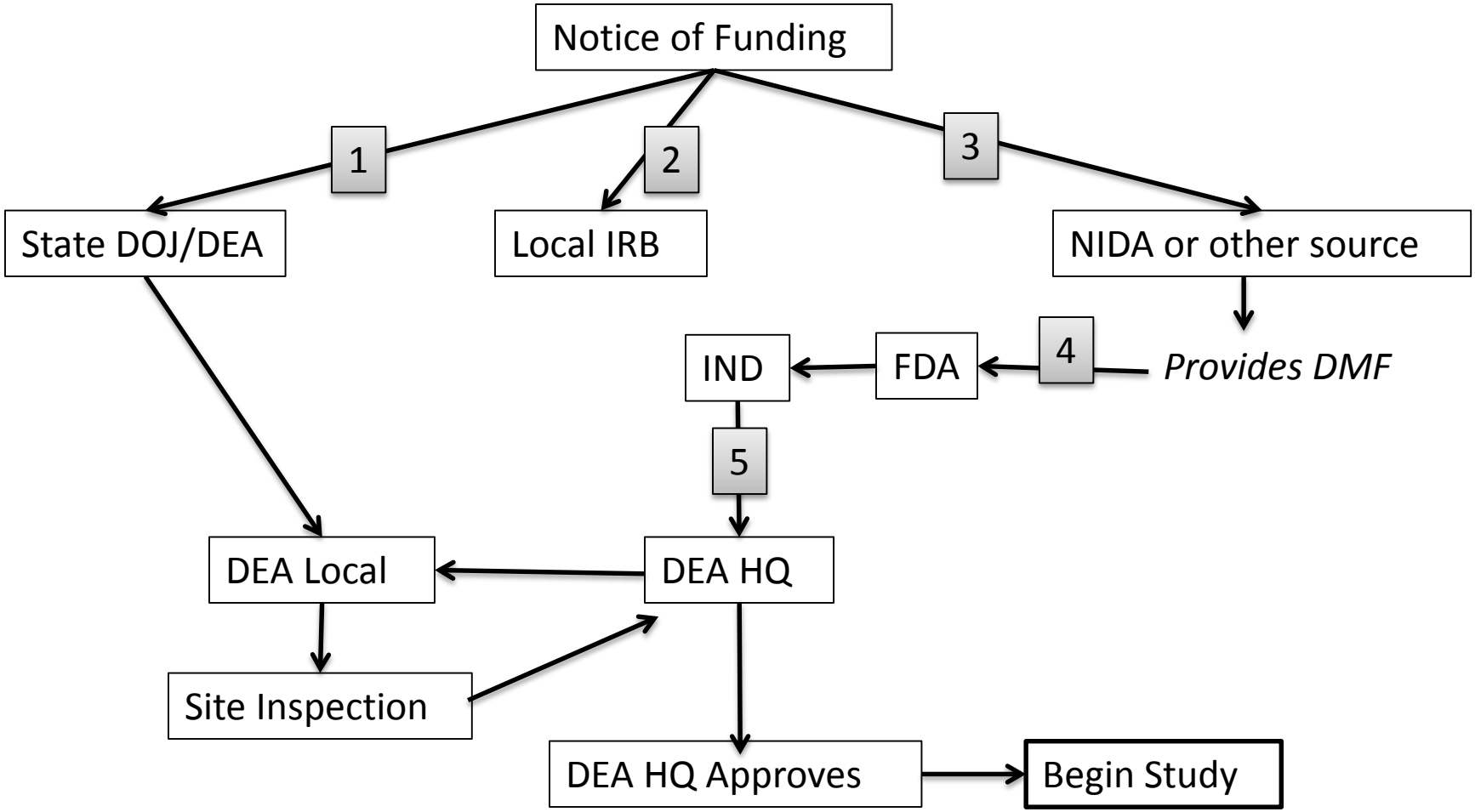
At the end of 2018 the Panel was monitoring one hundred and twenty research projects.

In California, there is not a separate controlled substance license requirement. When the researchers

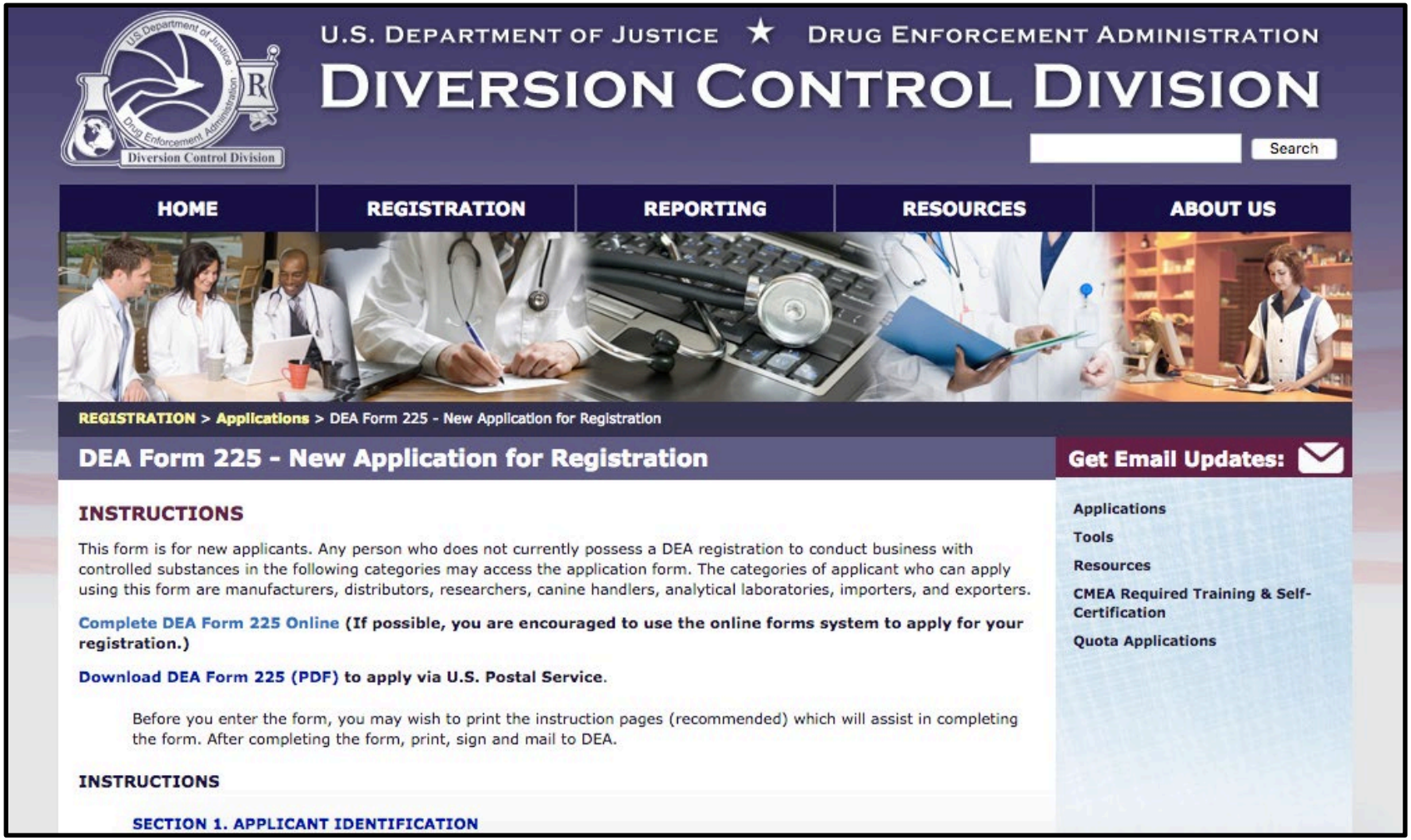
Research Advisory Panel

- Research Advisory Panel Home
- Guidelines
- Application Forms
- Clinical Drug Trials
- CA Informed Consent Form Guidelines
- Meeting Dates And Deadlines
- Annual Progress Report Requirement
- Panel Members
- DEA Controlled Substance Listings
- Annual Report to the Governor & Legislature of

Process of Approval ~ 6-12 mo.



DEA Schedule-1 Registration



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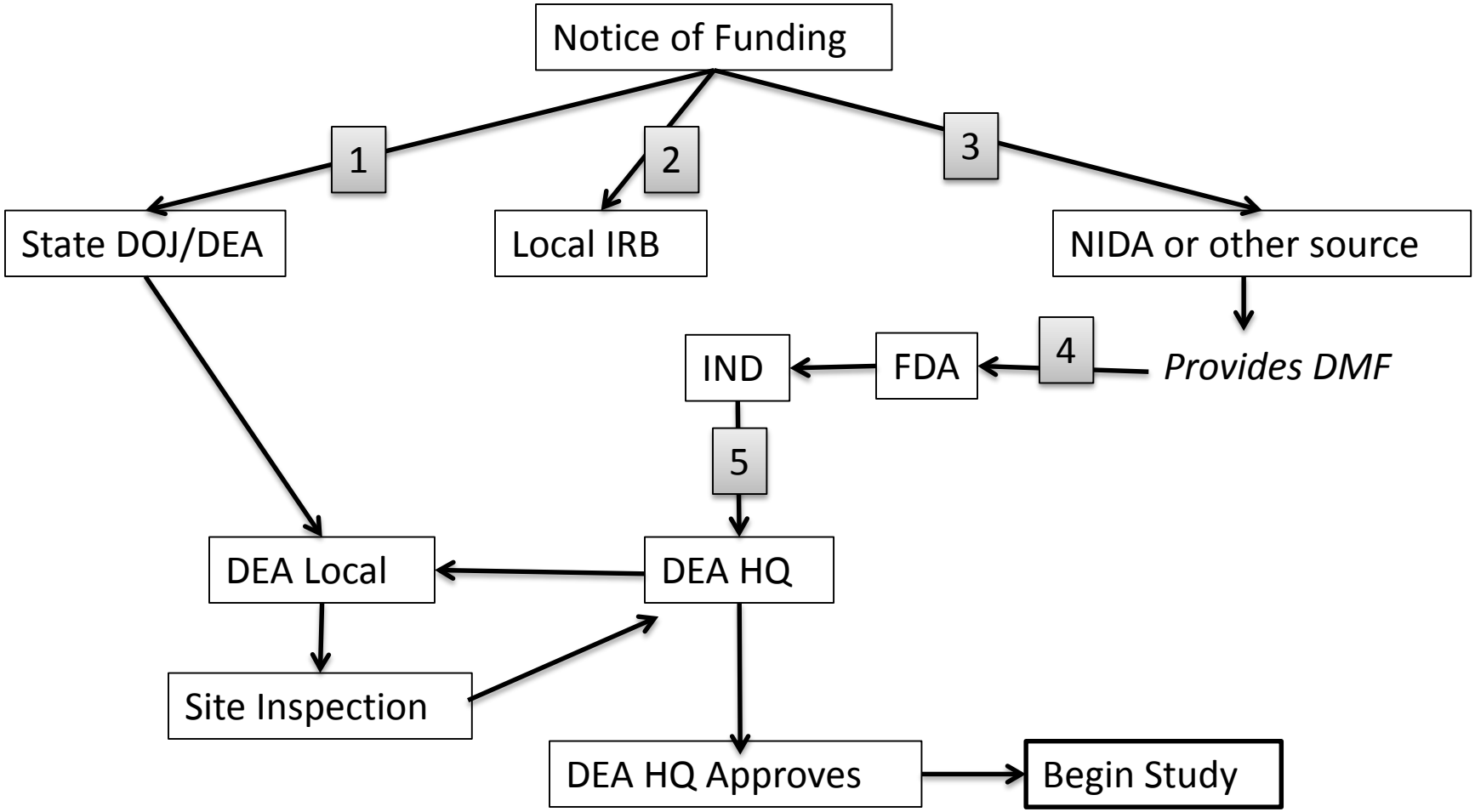

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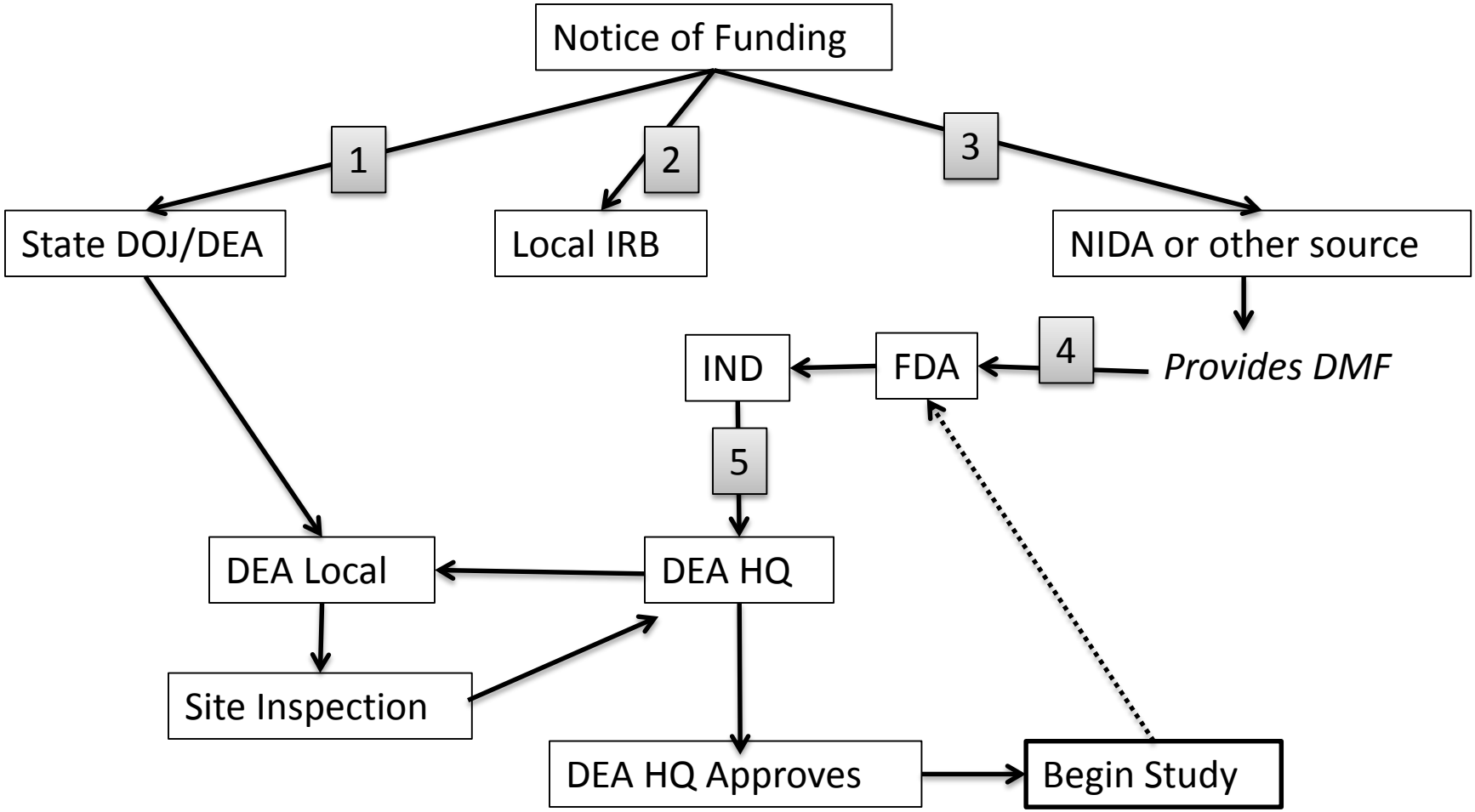

Questions?

Contact for Research Questions from this Webinar

Please email questions to:

VHABLRD-CSRD@va.gov

Additional Resources

- DMF List & Search:
  https://www.pharmacompass.com/us-drug-master-files-dmfs

  https://www.fda.gov/drugs/developmentapprovalprocess/formssubmissionrequirements/drugmasterfilesdmfs/default.htm

- NIDA Drug Supply Program:
  https://www.drugabuse.gov/researchers/research-resources/nida-drug-supply-program

- FDA IND Application Information:
  https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/investigationalnewdrugindapplication/default.htm

- DEA Schedule 1 Registration:
  https://www.deadiversion.usdoj.gov/drugreg/reg_apps/225/225_instruct.htm

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  - National Center for PTSD (NCPTSD) Executive Division