



Applied Cannabis Research within VA: An Overview & Successful Example

Clinical Science Research & Development Service

Terri Gleason, PhD
Director, CSR&D

Mallory J E Loflin, PhD
Research Scientist, VASDHCS

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VA



U.S. Department of Veterans Affairs

Veterans Health Administration
Office of Research & Development

Introduction



Mallory J E Loflin, PhD
Research Scientist, VASDHCS



Terri Gleason, PhD
Director, CSR&D

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.

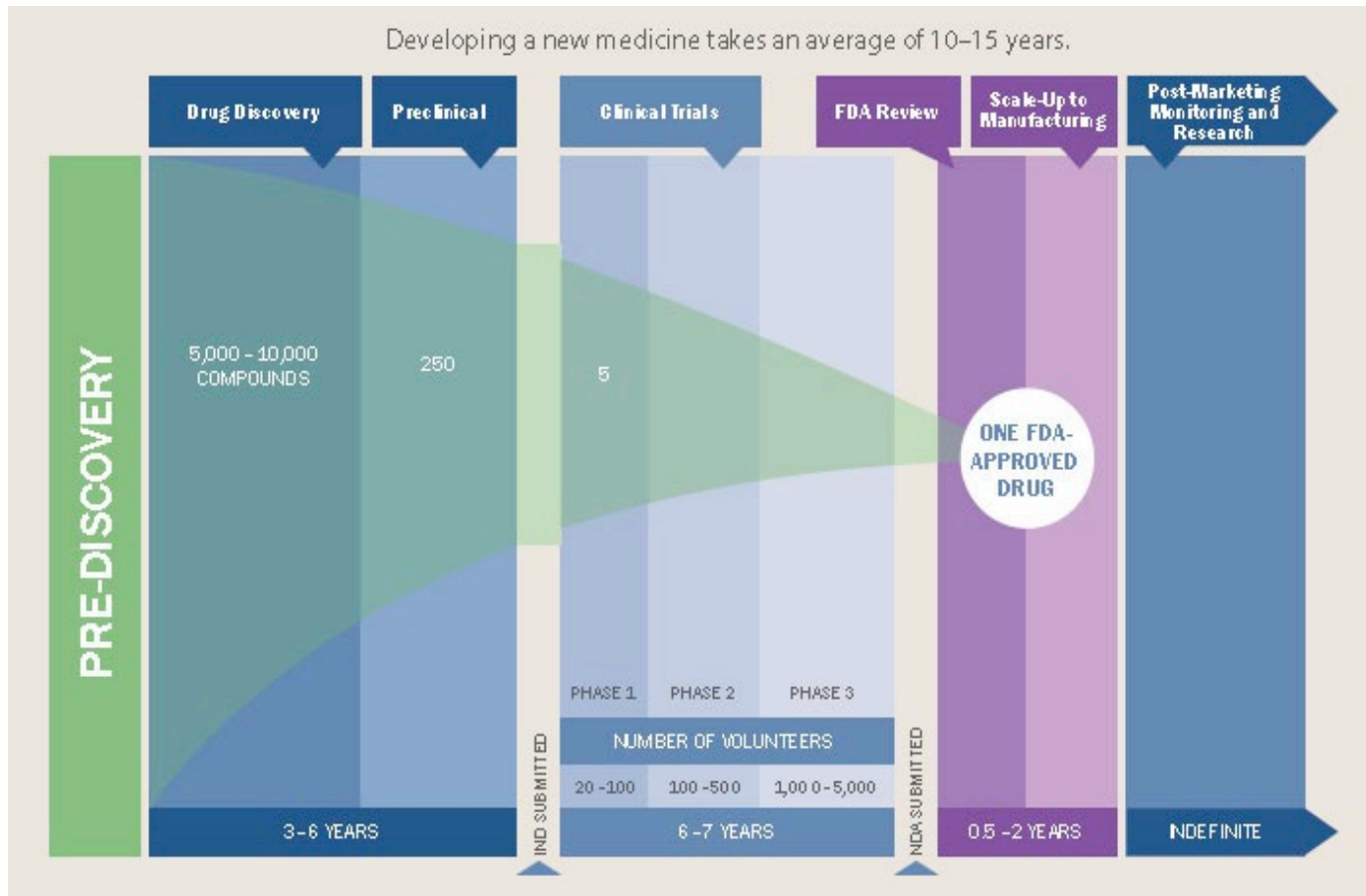
NIDA Drug Supply Program Director, Dr Rik Kline at rkline@nida.nih.gov



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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 of THC

Other Options?

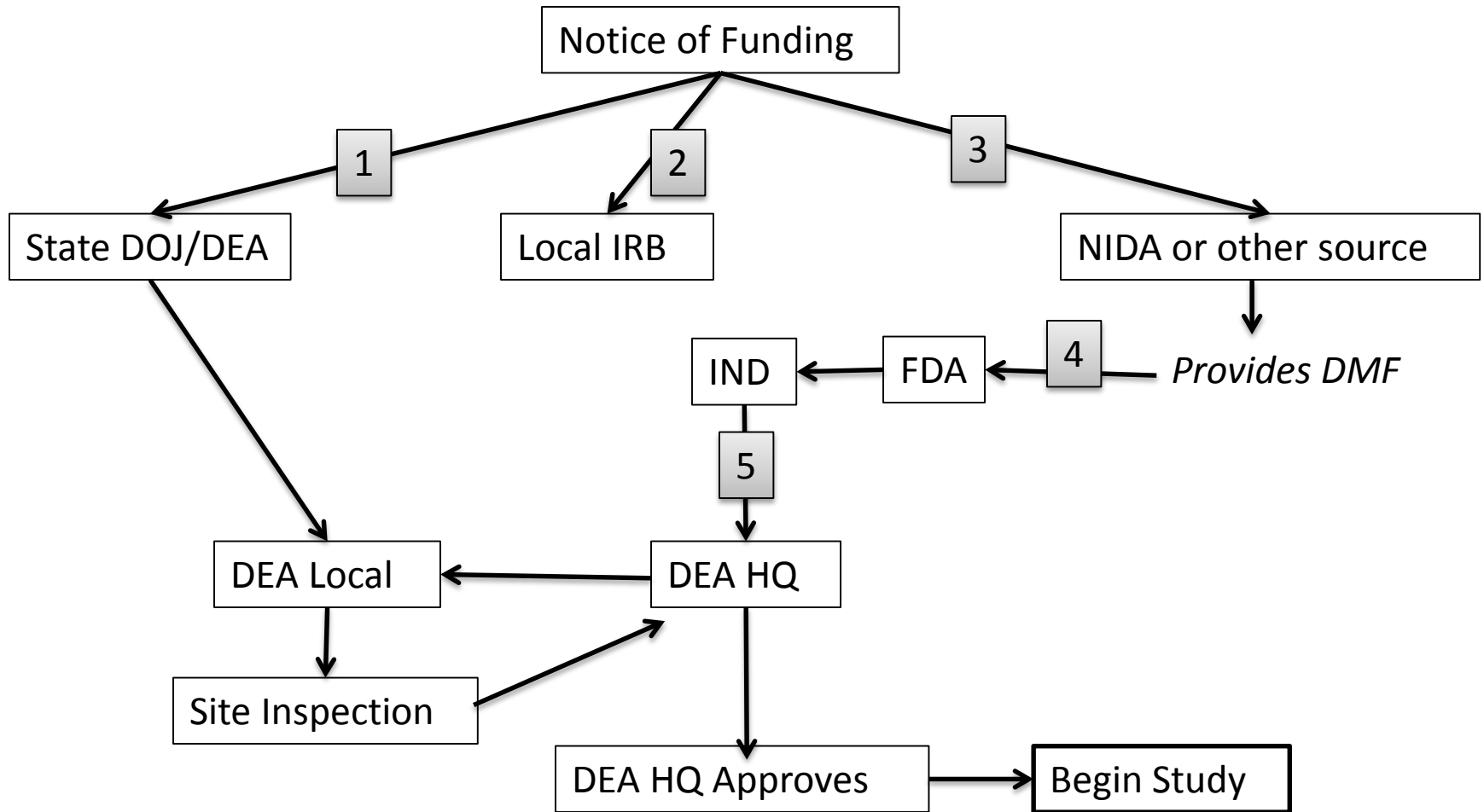
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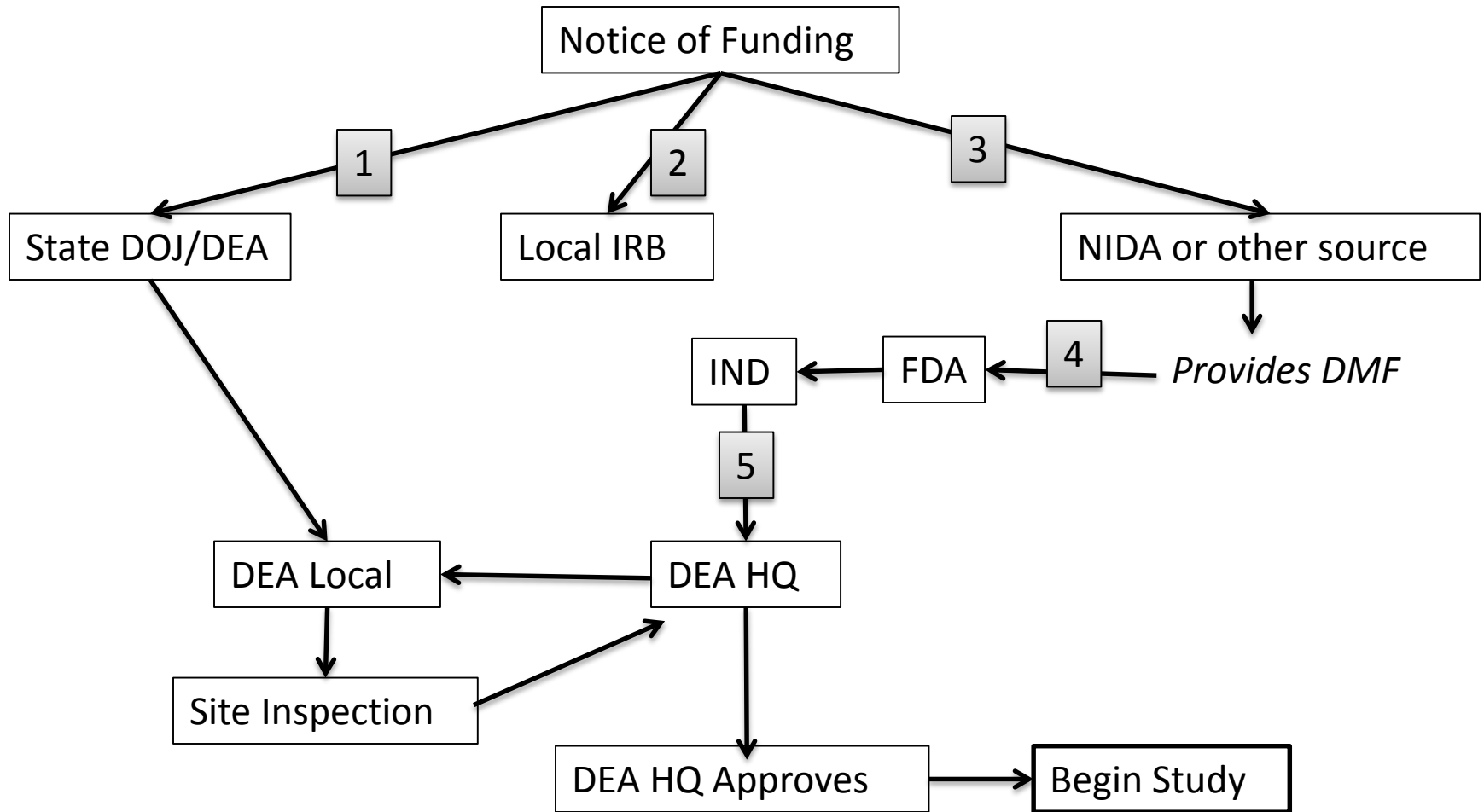
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Process of Approval ~ 6-12 mo.




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

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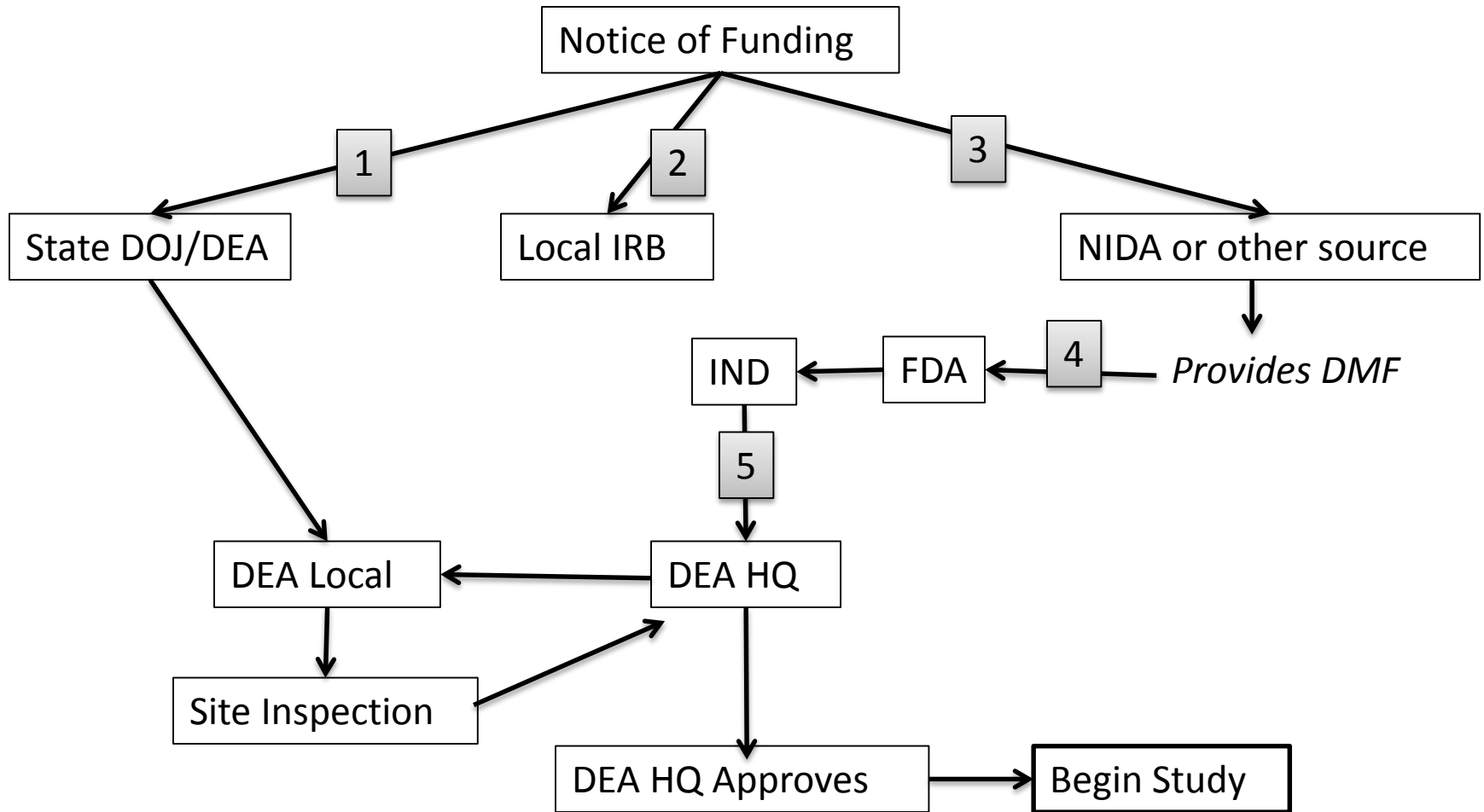
[Annual Progress Report Requirement](#)

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[Annual Report to the Governor & Legislature of](#)

Process of Approval ~ 6-12 mo.



DEA Schedule-1 Registration

The screenshot displays the official website of the U.S. Department of Justice, Drug Enforcement Administration, Diversion Control Division. The header includes the agency name and a search bar. A navigation menu features links for HOME, REGISTRATION, REPORTING, RESOURCES, and ABOUT US. The main content area is titled "DEA Form 225 - New Application for Registration" and includes a breadcrumb trail: "REGISTRATION > Applications > DEA Form 225 - New Application for Registration". Below the title, there are sections for "INSTRUCTIONS" and "SECTION 1. APPLICANT IDENTIFICATION". The instructions section provides details on who can apply and offers options to complete the form online or download a PDF for postal service. A sidebar on the right offers a "Get Email Updates" option and a list of related links: Applications, Tools, Resources, CMEA Required Training & Self-Certification, and Quota Applications. The background of the page features a collage of medical professionals in a clinical setting.

U.S. DEPARTMENT OF JUSTICE ★ DRUG ENFORCEMENT ADMINISTRATION
DIVERSION CONTROL DIVISION

HOME REGISTRATION REPORTING RESOURCES ABOUT US

REGISTRATION > Applications > DEA Form 225 - New Application for Registration

DEA Form 225 - New Application for Registration

INSTRUCTIONS

This form is for new applicants. Any person who does not currently possess a DEA registration to conduct business with controlled substances in the following categories may access the application form. The categories of applicant who can apply using this form are manufacturers, distributors, researchers, canine handlers, analytical laboratories, importers, and exporters.

Complete DEA Form 225 Online (If possible, you are encouraged to use the online forms system to apply for your registration.)

Download DEA Form 225 (PDF) to apply via U.S. Postal Service.

Before you enter the form, you may wish to print the instruction pages (recommended) which will assist in completing the form. After completing the form, print, sign and mail to DEA.

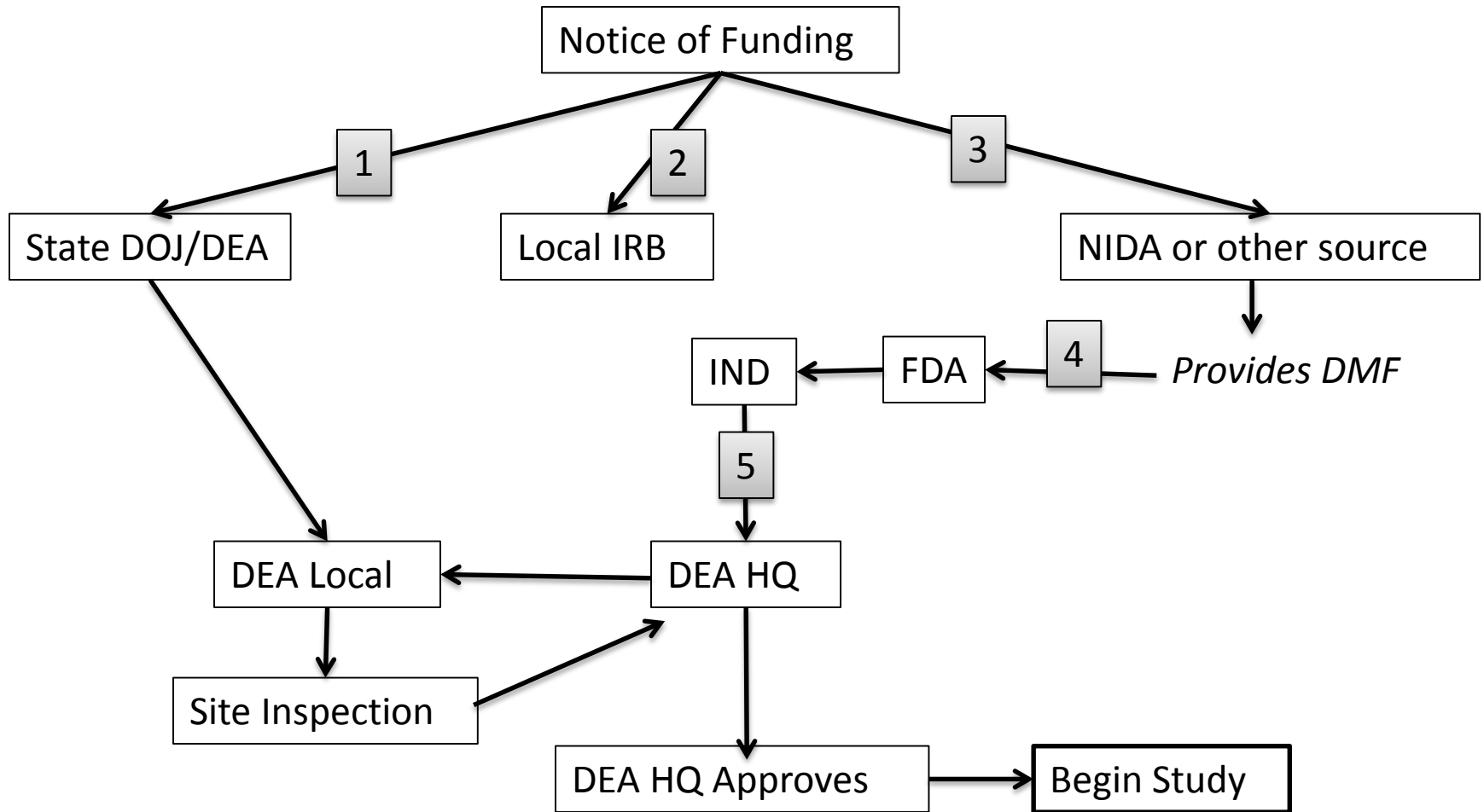
INSTRUCTIONS

SECTION 1. APPLICANT IDENTIFICATION

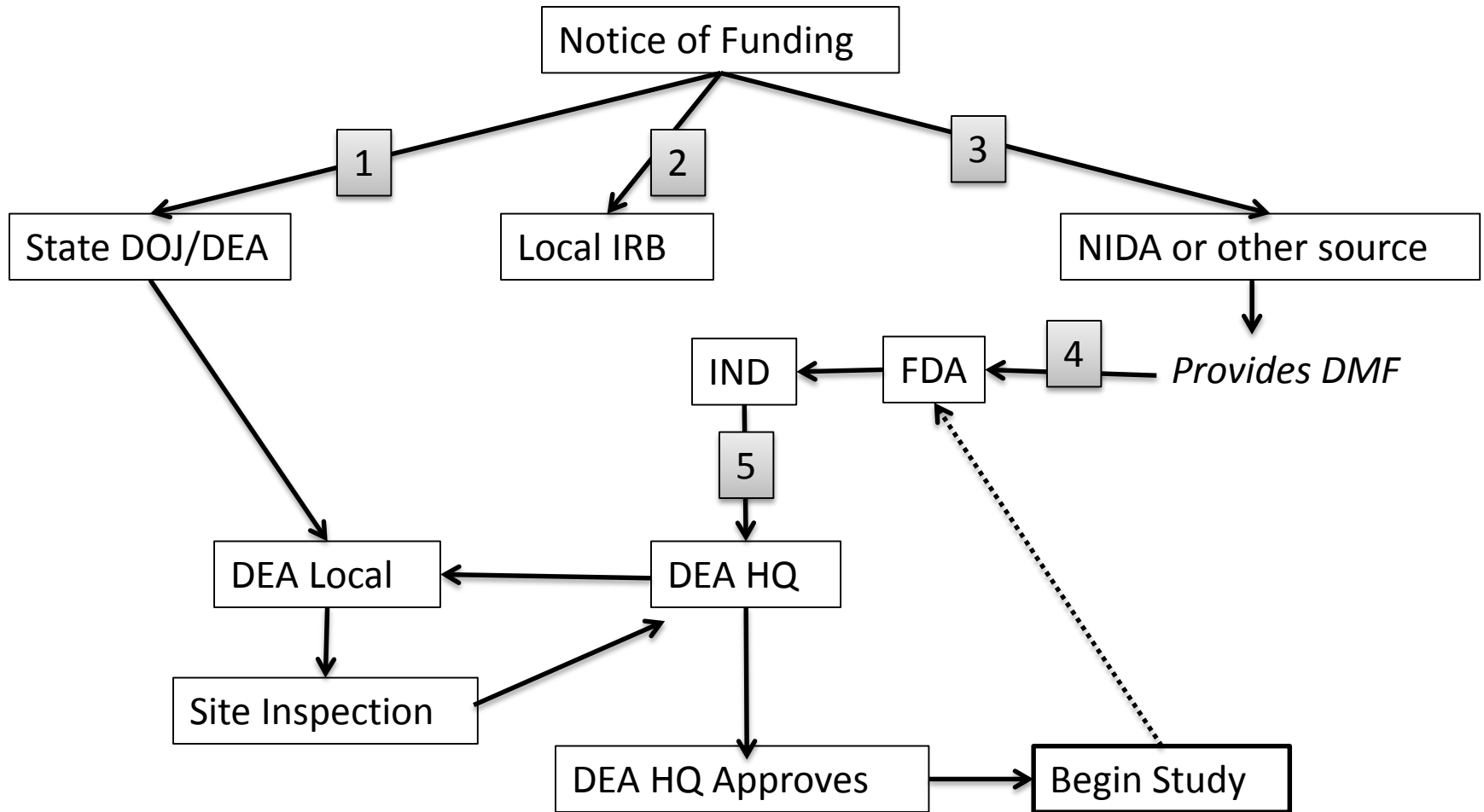
Get Email Updates: [Envelope Icon]

- Applications
- Tools
- Resources
- CMEA Required Training & Self-Certification
- Quota Applications

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Questions?

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Contact for Research Questions from this Webinar

Please email questions to:

VHABLRD-CSRD@va.gov



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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.deaiverison.usdoj.gov/drugreg/reg_apps/225/225_instruct.htm

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