# Schedule I & II
# Bulk Manufacturers & Importers

## Drug Enforcement Administration
### Pharmaceutical Training Seminar

**Richmond, VA**
**April 24 – 27, 2017**

**Minneapolis, MN**
**May 8-11, 2017**

# Persons Required to Register

- Law: 21 USC 822 (a) (1)
- "Every person who manufactures or distributes any controlled substance or list I chemical …shall obtain … a registration…

# Persons Required to Register

- Law: 21 USC 822 (a) (2)
- "Every person who dispenses, or who proposes to dispense, any controlled substance, shall obtain from the Attorney General a registration…"

# Registrations

- Manufacturer
- Distributor
- Importer
- Exporter
- Pharmacy
- Practitioner
- Researcher, NTP, Analytical Lab, Teaching Institution

# Manufacturers

- Bulk Manufacturers
- Dosage Form Manufacturers
- Manufacturers Who Re-Package/Re-Label

# Specific Registrations

- Bulk Manufacturers
  CI or CII Controlled Substances

- Importers
  CI or CII Controlled Substances

# Legal Definition 21 USC 802

The term **Bulk Manufacturer** means: the production, preparation, propagation, compounding, or processing of a drug or other substance, either directly or indirectly or by extraction from substances of natural origin, or independently by means of chemical synthesis or by a combination of extraction and chemical synthesis,

# In Plain English

Produces the bulk controlled substance used for the preparation of saleable dosage units.

Synthesizer: Produces CS raw materials from basic chemicals.

Extractor: Derives a drug from an organic source. All narcotics are manufactured through extraction. Companies import raw material (Raw Opium/Cocoa Leaf) and extract the active ingredients which are the starting point for the further production of a variety of drugs.

# Importers

For purposes of this presentation, CI and CII importation applies ***only to*** Importer registrations and ***not to*** coincidental activities which are authorized for researcher and analytical laboratory registrations pursuant to 21 C.F.R. § 1301.13 (e) (1).

# “Section 303”

On October 27, 1970, Section 303 was passed into law by Congress.

303 was the number used by Congress to track the legislation.

Once passed by Congress, Section 303 was placed into 21 USC 823.

*Therefore: “Section 303 Investigations”*
*“Section 303 Registrants”*

# Legal Citations
## United States Code

- 21 USC 823(a)

  Legislates the registration of CI & CII bulk manufacturers and includes the six (6) “public interest” factors which must be examined and considered prior to granting the registration.

# The Denial of a Registration

- 21 USC 824

  Legislates the conditions under which a registration to manufacture, distribute, or dispense a controlled substance may be denied, suspended, or revoked.

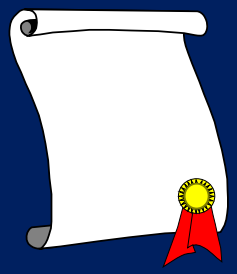
# Legal Citations
## United States Code

- 21 USC 958

Legislates the Registration and/or Denial of CI & CII Importers.

# Code of Federal Regulations

- 21 C.F.R. § 1301.33 (Manufacturers)
- 21 C.F.R. § 1301.34 (Importers)



- Establishes the regulations which govern the approval and renewal processes for CI & CII bulk manufacturer and importer applications.

# Activity which is *NOT* allowed

DEA grants Importer registrations and allows the importation of CI & CII controlled substances to "provide for the medical, scientific, or other legitimate needs **of the United States**." 21 USC 952(a)(2).

The statute does not allow an importer to import a CI or CII controlled substance for the purpose of exporting it.

Importation is authorized only for its domestic use in the United States.

# 21 USC 823
# Registration Requirements

Manufacturers of controlled substances in Schedule I and II

(a) The Attorney General shall register an applicant to manufacture controlled substances in Schedule I or II if he determines that such registration is consistent with the public interest and with United States obligations under international treaties, conventions, or protocols in effect on May 1, 1971.

In determining the public interest, the following factors shall be considered:

# 21 USC 823
# Registration Requirements

## Manufacturers of controlled substances in Schedule I and II

1) Maintenance of effective controls against diversion of particular controlled substances and any controlled substance in Schedule I or II compounded therefrom into other than legitimate medical, scientific, research, or industrial channels, by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes;

# 21 USC 823
# Registration Requirements

2) Compliance with applicable State and local law;

3) Promotion of technical advances in the art of manufacturing these substances and the development of new substances;

4) Prior conviction record of applicant under Federal and State laws relating to the manufacture, distribution, or dispensing of such substances;

# 21 USC 823
# Registration Requirements

5) Past experience in the manufacture of controlled substances, and the existence in the establishment of effective control against diversion; and

6) Such other factors as may be relevant to and consistent with the public health and safety.

# "The 303 Process"

The Section 303 Process is initiated upon receipt by DEA Headquarters of a

-New Application for Registration

-Renewal Application

-Request to Modify a Registration

# The Review Includes:

- DEA Field Investigation

- DEA HQs Analysis and Review (to include review of 303 Questionnaire)

- Publication in the Federal Register

- And any other additional information as deemed necessary (21 C.F.R. § 1301.15)

# Reviewing the Application

- The review process is required to ensure compliance with the requirements of

  21 C.F.R. §§ 1301.33 and 1301.34.

- The DEA field office does not have the authority to approve or modify a registration subject to a 303 investigation.

- In regards to a Section 303: A request to add a new drug code is considered an "application."

# Processing the Application

1) Application forms are submitted to the Registration Section at DEA headquarters.

2) The Registration Section processes the fees and reviews the application for completeness.

3) If it is a new application (as a Bulk Manufacturer or an Importer) the Registration Unit places it in a "Pending/Hold" status.

# Processing the Application (continued)

4) The application is then forwarded to the Regulatory Section for processing under the Section 303 (21 USC 823) guidelines.

5) Upon receipt of the new or renewal application from the Registration Unit, or upon the receipt of a written request to add a drug code, the Staff Coordinator/Program Analyst reviews the application. If it is a renewal application, the drug codes are compared to those for which the registrant is already authorized.

# Processing the Application (continued)

6) If the renewal application contains new drug codes, or if the application is for a new registration, the Staff Coordinator or Program Analyst will contact the firm to obtain responses to the standardized *Bulk Manufacturer Questions* or *Importer Questions*.

*The questions are incorporated at the end of this presentation.*

# Processing the Application (continued)

7) After the registrant responds to the questions, the responses, and all of the results from the investigation and analysis, are reviewed by various sections at DEA HQs.

When all sections have found no legal (public interest) reason to deny the application, a Notice of Application is prepared for signature by the Assistant Administrator, Diversion Control Division.
Once signed, the Notice is transmitted to the Office of the Federal Register for publication.

# Processing the Application (continued)

8) The CFR requires a comment period during which other bulk manufacturers of the same basic classes of controlled substances can file comments and objections to the proposed registration.

The comment period for CI & CII bulk manufacturer registrations is 60 days. For CI & CII importers it is 30 days. The comment period commences the date the Notice of Application is published in the Federal Register.

# Processing the Application (continued)

9) With the preparation of the Notice of Application, an electronic investigative tasking has already been sent to the DEA field division office responsible for the applicant/registrant.

The field office will conduct an investigation of the applicant/registrant which includes the six public interest factors in 21 USC 823 (a)(1-6).

A report must be written and submitted to the Regulatory Unit as part of the review process on the application.

# Processing the Application (continued)

10) When the comment period for the Notice of Application closes, the Staff Coordinator or Program Analyst will determine whether or not any comments or objections to the proposed registration were received.

# Processing the Application (continued)

11) If **NO** comments or objections have been received, and if the review process of the applicant's request has been completed by DEA, and found to be consistent with the public interest and with the United States obligations under international treaties, then a Notice of Registration will be prepared for the Assistant Administrator's signature. Once signed, it will be transmitted to the Office of the Federal Registrar and published.

# Completion of the Process

When the Notice of Registration is published, the Program Analyst completes the action on the application. The Program Analyst then makes any modifications which have been requested, and the application is approved or renewed.

***The registrant's updated DEA certificate is electronically generated and mailed.***

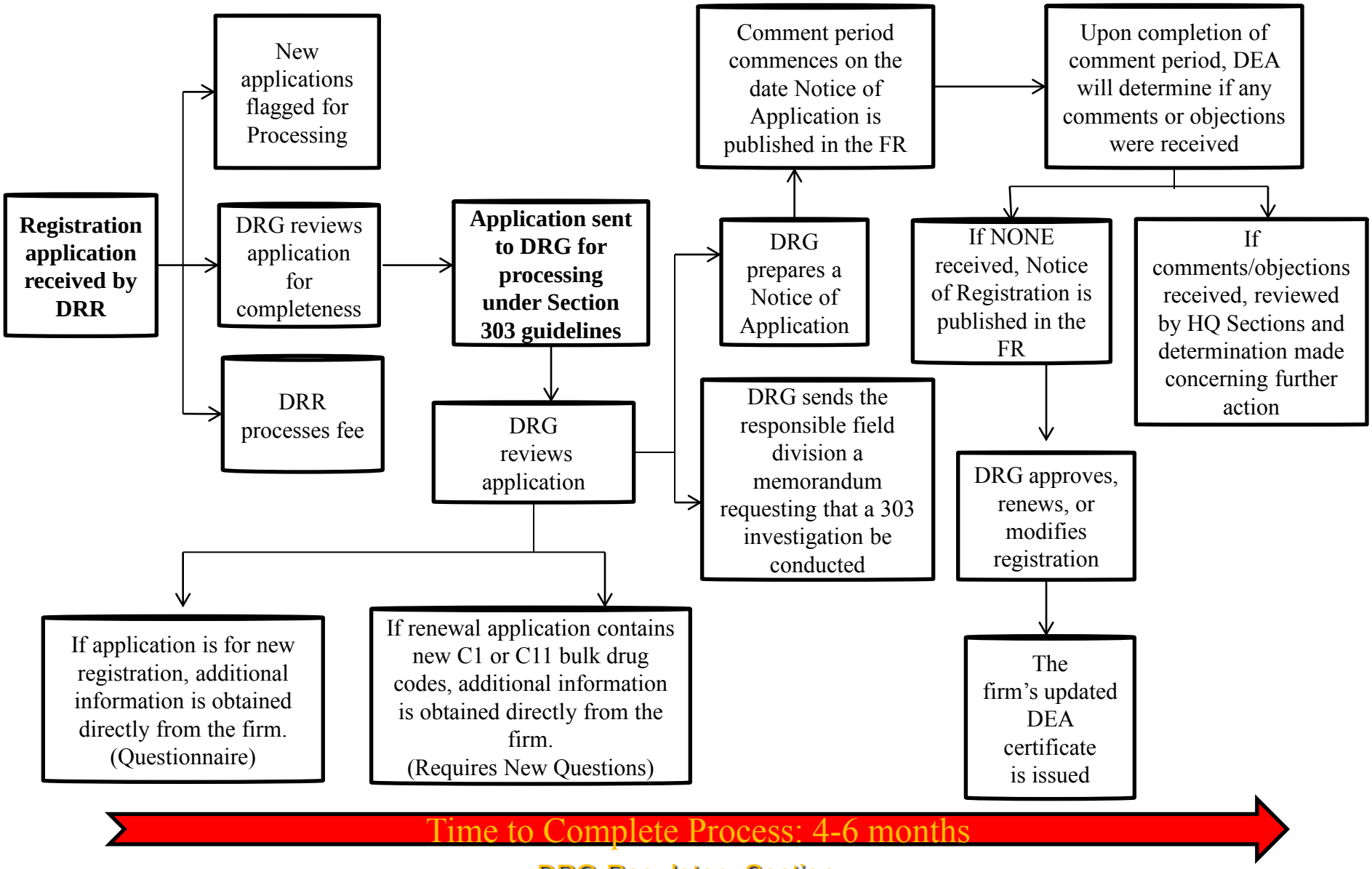
THIS IS A ***PROCESS***, NOT A ***SINGLE ACTION***. IT IS NOT UNCOMMON FOR

THIS PROCESS TO TAKE 4-6 MONTHS TO

COMPLETE.

PLEASE CONTACT THE STAFF COORDINATOR OR PROGRAM ANALYST IF YOU NEED AN UPDATE ON THE STATUS OF YOUR APPLICATION/REQUEST.

# Processing 303 Applications

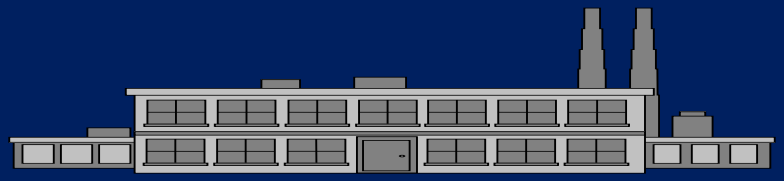



Time to Complete Process: 4-6 months

DRG-Regulatory Section
DRR-Registration Section

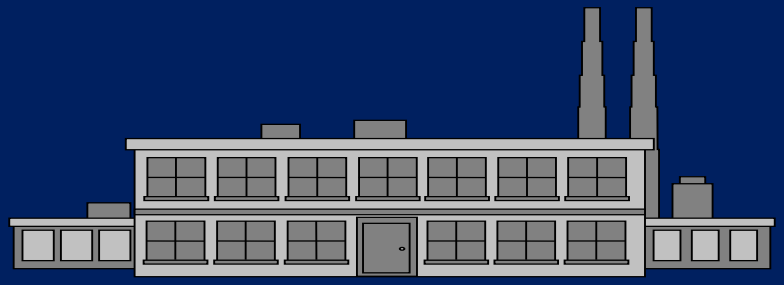
# INDUSTRY EFFORTS THAT HELP KEEP THE PROCESS MOVING

- ü Maintain copies of your application(s) and all other documents for registration and renewal.
- ü Review your applications before you submit them.
- ü Check √ (Circle) the drug codes you intend to manufacture in bulk as requested on the application. DEA will *not* presume you want the same codes that you previously requested. If the codes are not Checked (Circled), they will not be included on the FR Notice.



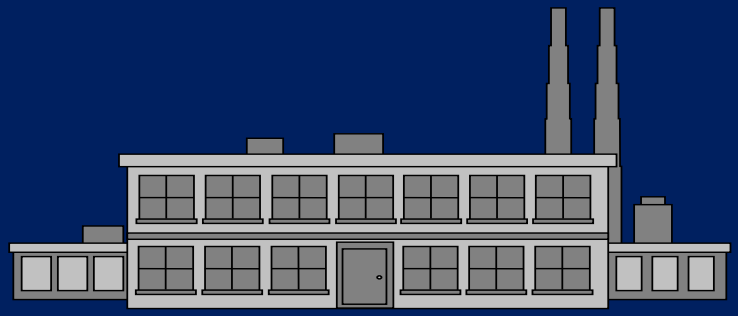
# INDUSTRY EFFORTS THAT HELP KEEP THE PROCESS MOVING

- Include all drug codes pending approval on your new or renewal application.
- Retain a copy of the Importer and Bulk Manufacturer Questionnaire.



# INDUSTRY EFFORTS THAT HELP KEEP THE PROCESS MOVING

- Submit your Application/Request ASAP
- Applications are completed on-line 120 days in advance of the expiration date.
- Be aware of the expiration date(s) on your registrations. If the expiration date is nearing (or has passed) and you have not received a renewal application, call the Registration Unit for assistance.



# INDUSTRY EFFORTS THAT HELP KEEP THE PROCESS MOVING

- If your registration has expired, and you have submitted a renewal application, you may contact the Staff Coordinator or Program Analyst and request an "extension letter" that you can provide to your suppliers and customers for verification purposes.

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES

The following questions pertain to your company's request to bulk manufacture CI and/or CII controlled substances (CS).

Please provide detailed responses to the following questions for each drug code that your company has proposed to manufacture in bulk.

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES

1) What is the purpose for the bulk manufacture of the CS?

2) Specifically describe the production process, from start to finish, for each CS.

3) What materials will be used to manufacture the CS and in what quantities?

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES (CONTINUED)

4) Please provide the name, address, method of shipment and method of delivery for each supplier from which your firm intends to procure materials for the manufacture of the CS.

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES (CONTINUED)

5) Does your company have a firm commitment from each supplier of raw material? What is the time period of this agreement and what quantity of raw material will each supplier be able to supply? **Please attach copies of commitment letters from each supplier.**

6) What quantity of each CS does your company anticipate producing in bulk?

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES (CONTINUED)

7) Who are your current and prospective customers (name/address) for each CS?

A) What product (active pharmaceutical ingredient – API, dosage units, materials for clinical research, etcetera) does your company intend to sell to each customer listed?

B) What quantity of each substance has the customer indicated it would purchase?

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES (CONTINUED)

C) For what purpose would the customers purchase the CS (i.e., dosage form development, clinical trials, drug master file submissions)? Again, please be specific as it relates to each customer and each CS identified above.

Please attach copies of letters of interest from the prospective customers.

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES (CONTINUED)

8) What are your company's future plans with regard to the manufacture of controlled substances? Please provide as much detail as possible, including time line, and discuss any plans to expand your production facility, add new equipment, conduct research and development, run initial batches, and list FDA approvals needed.

# BULK MANUFACTURER QUESTIONS CI & CII CONTROLLED SUBSTANCES (CONTINUED)

9) When does your company anticipate selling each of the CS as commercial product?

10) Do you currently have any other CS registrations from the Drug Enforcement Administration? If so, please include the DEA number (s), business activity, drug schedules, and expiration date(s) in your response.

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES

The following questions pertain to your request to import CI and/or CII controlled substances (CS).

Please provide detailed responses to the following questions for <u>each</u> CI and/or CII drug code that you (your firm) has requested authority to import.

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

1) What type of CS does your firm intend to import: bulk or dosage units?

2) What is the purpose for the importation of the CS: narcotic raw material for bulk manufacture, clinical trials, research, analytical purposes, distribution.

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

3) Why is a foreign source of supply being used instead of a domestic source?

4) What is the name, address, method of shipment and method of delivery for each supplier of CS your company proposes to import?

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

5) Does your company have a firm commitment from the supplier/suppliers of each substance proposed for importation?
   a) What is the time period of the commitment?
   b) What quantity is involved?
   c) Letters of Commitment?

6) What quantity of each CS does your company anticipate importing on an annual basis?

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

7) Who are your current and prospective customers? Please provide a list of names, addresses, and DEA numbers for each CS.

**Please attach copies of letters of intent from these customers**.

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

8) Will the controlled substances you propose to import be used to manufacture controlled substances? If so, how and in what quantity are they to be manufactured?

9) Does your company have previous experience handling CS? Please Explain.

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

10) Does your company have previous experience in the importation of CS? Please explain.

11) When does your company anticipate selling a commercial product?

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

12) Please provide a written description of what resources your company has committed to the establishment of your importation business as regards to these drug codes.

Do do you plan to or have you already made any changes to:

Physical plant

Security system

Production equipment

Recordkeeping system

What is your proposed time frame for completion of those activities?

# IMPORTER QUESTIONS
# CI & CII CONTROLLED SUBSTANCES
# (continued)

13) Do you currently have any other controlled substance registrations from the Drug Enforcement Administration? If so, please provide the registration number(s), business activity, drug schedules, and expiration date.

# Regulatory Unit (ODGR)

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