Research vs Manufacturing
OCTOBER 31, 1995
(60 FR 55310)
POLICY STATEMENT: CLARIFICATION OF COINCIDENT ACTIVITIES FOR RESEARCHERS
Research Activity

Researchers:

✓ Must be registered with DEA
✓ Manufacture small amounts (21 CFR 1301.18)
✓ Protocol filed with DEA
✓ May distribute to other registered researchers
✓ For chemical analysis, instructional activity
✓ NOT for Dosage Form Development
✓ NOT FOR COMMERCIAL SALE
Manufacturing Activities

- Purpose is to satisfy regulatory requirements such as FDA submissions or good manufacturing practice
- Establishing manufacturing processes and procedures (pilot, scale up, reformulation studies etc.)
- Development including bioavailability, formulation, stability and validation studies
Research Activities

Small amounts may be manufactured if the quantities are set forth in statement filed with the application for registration, \textbf{AND} the purpose as set forth in statement is to develop synthesis procedures or other research not related to dosage form development.
Research and Manufacturing are designated as independent activities for which separate registrations are required with DEA.

21 CFR 1301.13 (e) (1) describes specific coincident activities for which separate registrations are not required.

Research is not intended for commercial sale.
QUOTA Applications

Minh T. Dang
United Nations Reporting & Quota Section
Office of Diversion Control
Drug Enforcement Administration
Quota Types

PROCUREMENT
- DEA Form 250
- Dosage form MFG
- Packagers
- Labelers
- Repackager
- Relabelers

MANUFACTURING
- DEA Form 189
- Bulk Manufacturers

IMPORT
- DEA 488 & Form A
- Chemical Importers
Quota Applications are now online

- **Procurement** – DEA 250
- **Manufacturing** – DEA 189
- **Import** – DEA 488 & Form A

www.deadiversion.usdoj.gov/quotas
Benefits of online application

- Registration verified as active and current
- Correct drug code is listed on registration
- Historical data preloaded into forms
- Program performs calculations
- Confirmation of submission
- Ability to attach supporting documentation
Online Resources

• Online Quota Applications
• User Guides
• Year End Reports
• List of Controlled Substances
• Conversion Factors
• FR Notices
• Seminars
• Email Links for Q&A

Can all be found at

www.deadiversion.usdoj.gov/quotas
Applications

- **Procurement Quotas**
  - DEA Form 250 (April 1)

- **Manufacturing Quotas**
  - DEA Form 189 (May 1)

- **Import Quotas**
  - DEA Form 488 (April 1)
    - Worksheet A (list of customers)
Additional Reports

All manufacturers/Chemical Importers

- Year End Report (YERS) due January 31
  - www.deadiversion.usdoj.gov/quotas

- Web-based system (YERs)

- CMEA – Importers of PE, E, PPA
Conversion Factors

All request for quotas quantities are to be expressed as the **free drug** (free base/free acid). All quotas are issued as the **free drug**.

- Normalizes all quantities to one drug class
- Eliminates need for multiple request by supplier/customer
- Ensures consistency
- Conversion Factors are available at [www.deadiversion.usdoj.gov/quotas](http://www.deadiversion.usdoj.gov/quotas)
- DEA issues quotas in terms of anhydrous acid or base
- DEA uses a 2-digit figure
Conversion Factors

- **Conversion Factor**: Ratio of the molecular weight of the base to the molecular weight of the corresponding salt. **EXAMPLE**
  - Pseudoephedrine HCL: CF 0.82
  - Pseudoephedrine Tannate: CF 0.089
  - Pseudoephedrine Sulfate: CF 0.77

- **Salt to base**: Multiply the quantity of salt by the conversion factor

- **Base to salt**: Divide the quantity of base by the conversion factor

[www.deadiversion.usdoj.gov/quotas](http://www.deadiversion.usdoj.gov/quotas)
A company procured 150 kg of bulk oxycodone HCl for dosage form manufacturing. Their Procurement quota for oxycodone is 140 kg. Did they exceed their quota?

The conversion factor for oxycodone HCl is 0.90.

**Answer:** No.

150 kg HCl * 0.90 = 135 kg base

(they still have 5 kg (140-135) of quota left).
Ma & Pa Kettle Math Lesson
**For Sale vs For Conversion**

If you do not change the basic drug class apply *(for sale)* quota. If you change basic drug class apply for *(for conversion)* quota:

**Examples of *(for conversion)***

- **Synthetic routes**
  - Morphine $\rightarrow$ Hydromorphone or
  - Ephedrine $\rightarrow$ Pseudoephedrine

- **Extraction from plant material**
  - Coca Leaf $\rightarrow$ Cocaine
  - Concentrated Poppy Straw $\rightarrow$ Opium
ISOMER Quotas

- Amphetamine
  » d-amphetamine
  » l-amphetamine
  » d,l-amphetamine

- Methamphetamine
  » d-methamphetamine
  » l-methamphetamine
  » d,l-methamphetamine

- Tetrahydrocannabinols
  » Delta-9-THC
  » All Other Tetrahydrocannabinols
Accessing Quota Applications

www.deadiversion.usdoj.gov

Reporting

Quotas

Quota Applications

Login: www.deadiversion.usdoj.gov/quotas

Secure website

Enter DEA issued user name & password
Login

Request
Username/Password or Reset
ODE.QUOTA@USDOJ.GOV

• Quota password same as YERS password

Application for Quota Allotment

User Login

• If you are a corporate user, enter your user name, password and DEA Number.
• If you are a corporate administrator, enter your user name and password, and the DEA Number of the registrant for which you will be managing user accounts.
• If you are a DEA administrator, enter your user name and password, and the DEA Number of the registrant for which you will be managing user accounts.

DEA Number:
Username:
Password:
Change Password:

To change your password, check the Change Password checkbox.
To reset the form's text values to their original state, click Reset.
To submit the form, click Next.
Report Selection Menu

Select Quota TYPE
• PROCUREMENT
• MANUFACTURER
• IMPORT

Select DRUG

Select Quota YEAR

Application for Quota Allotment

Main Selection Menu

Quota Type
- Procurement
- Manufacturer
- Import

Note: The list of controlled substances will only display drugs that are currently listed under your registration. If you do not see the drug you are seeking, please contact your local field office to have the drug added to your registration.

Controlled Substance
--- Listed in Alphabetical Order (Select One) ---

Quota Year
- Current Year (2011)
- Next Year (2012)

To file a new request for quota allotment or revise an existing one, select Quota Type, Controlled Substance and Reporting Year, then click Next.
To see the status of any requests for quota allotment that you have previously submitted to DEA, click Status.
Quota Application

Enter Current Years Production EST

INVENTORY

DISPOSITIONS (Sales/Utilization)

ACQUISITIONS

Previous years will automatically be populated (from YERS).

Make sure your YERS are accurate (Jan 31)

<table>
<thead>
<tr>
<th>Reporting Year</th>
<th>2009 (actual)</th>
<th>2010 (actual)</th>
<th>2011 (estimated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inventory (as of Dec 31)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Bulk controlled substance (API)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>In-process material (in all forms)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Finished dosage forms (bulk and/or packaged)</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Total</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Dispositions</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Domestic</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Exports</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Total</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Acquisitions</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Domestic</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Imports</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Total</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

[Click Next to advance to the next page]
Quota Allotment Categories

- Commercial Manufacturing
  - Conversion to other substances
  - Dosage form
- Product Development
  - All stages leading to FDA approval
- Packaging (labeling)
- Transfer
  - Returns
  - New owner (new registration)
Quota Allotment Categories

Application for Quota Allotment

Quota Request for Reporting Year 2011

Current Selection

<table>
<thead>
<tr>
<th>Quota Type</th>
<th>Quota Year Drug Code</th>
<th>Drug Name</th>
<th>Pending Quota Approved Quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procurement</td>
<td>2011</td>
<td>1225(A)</td>
<td>PHENYLPROPANOLAMINE (FOR CONVERSION)</td>
</tr>
</tbody>
</table>

Quota History
(IDA Form 250 -- Box 11)

Enter the total value for your quota allotment request in the field provided.
All amounts are expressed as grams of anhydrous base or alkaloid, not as salt.

--- History (Approved) ---

<table>
<thead>
<tr>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>--- Current Request ---</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

Quota Allotment Request by Category

Sub-divide your total quota request by category.
You must provide a value for at least one category, and the sum of the categories must equal the total quota request.
Use the TAB and SHIFT-TAB keys to tab forward and backward among the fields.

- [ ] Commercial Manufacturing
- [ ] Product Development
- [ ] Replacement
- [ ] Transfer
- [ ] Total

Click Next to advance to the next page.
Quota Allotment Categories

BREAKDOWN QUANTITIES

• COMMERCIAL
• PRODUCT DEVELOPMENT
• PACKAGING
• TRANSFER

Application for Quota Allotment

Report Selection Menu

Current Selection

<table>
<thead>
<tr>
<th>Quota Type</th>
<th>Quota Year</th>
<th>Drug Code</th>
<th>Drug Name</th>
<th>Pending Quota</th>
<th>Approved Quota</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procurement</td>
<td>2011</td>
<td>1225(A)</td>
<td>PHENYLPROPANOILAMINE (FOR CONVERSION)</td>
<td>2,513,000</td>
<td>.000</td>
</tr>
</tbody>
</table>

Sub-Reports Selection

In order to complete your application for quota allotment, you will need to provide additional information using the sub-reports below. To fill out a sub-report, click the Report Link to advance to the corresponding report form. If the color of the sub-report link is gray, it means there are reports on file that you may review by clicking the link to view the sub-report's Summary section. You will not be able to advance to the next page until all required sub-reports have been completed.

<table>
<thead>
<tr>
<th>Required / Optional</th>
<th>Current Request</th>
<th>Report Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optional</td>
<td>694,000</td>
<td>Commercial Manufacturing Converted Substances (DEA Form 250 -- Box 13)</td>
</tr>
<tr>
<td>Optional</td>
<td>884,000</td>
<td>Commercial Manufacturing Dosage Forms (DEA Form 250 -- Box 14)</td>
</tr>
<tr>
<td>Required</td>
<td>151,000</td>
<td>Product Development (DEA Form 250 -- Box 14)</td>
</tr>
<tr>
<td>Required</td>
<td>483,000</td>
<td>packaging</td>
</tr>
<tr>
<td>Required</td>
<td>3,141,000</td>
<td>Transfer</td>
</tr>
</tbody>
</table>

If you have completed all required sub-reports, click Next to continue.
For Conversion

(For Conversion) QUOTAS

Identify the Drug to be made

And provide

Conversion YIELDS
COMMERCIAL USE

• Product name
• Authority to MKT
  - List NDA number
  - List ANDA number
  - Cite FDA monograph
  - DESI

HINT

If Quantities Inconsistent with Historical Utilization

• Provide justification
  - As Comment or Attachment
Product Development

- Name
- Strength
- Units/Batch
- Purpose
- Quantity
- Completion

Hint
- Be Specific-Purpose
  - Pilot/Scale-up/Registration
- Provide justification as comment/attachment
Transfer

Transfer Data
Quota Requested: 151.000

If you intend to transfer PHENYLPROPANOLAMINE (FOR CONVERSION), fill out the fields below and click Submit. You may create as many individual Transfer forms as necessary.

* DEA Number
* Explanation

Please provide details of transfers, i.e. what will be transferred, the purpose of the transfer, etc.

The * symbol denotes a required field. Number fields must be a valid number between 0 and 999,999,999,999 inclusive.

Summary

<table>
<thead>
<tr>
<th>Remove</th>
<th>DEA Number</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RL0401187</td>
<td>Required the further analysis of product in outside independent study.</td>
</tr>
</tbody>
</table>

To remove an entry, click the Remove radio button. Click Next to return to the Report Selection Menu.

Next
Summary

USE Remarks Box

Include attachment for supporting documents

---

**Application for Quota Allotment**

**Final Summary**

<table>
<thead>
<tr>
<th>Quota Type</th>
<th>Quota Year</th>
<th>Drug Code</th>
<th>Drug Name</th>
<th>Pending Quota</th>
<th>Approved Quota</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procurement</td>
<td>2011</td>
<td>1225(A)</td>
<td>PHENYLPROPANOLAMINE (FOR CONVERSION)</td>
<td>2,513,000</td>
<td>.000</td>
</tr>
</tbody>
</table>

**Year-End Report Data**

<table>
<thead>
<tr>
<th>2009 (actual)</th>
<th>2010 (actual)</th>
<th>2011 (estimates)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inventory</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Acquisitions</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Dispositions</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**Quota Allotment Request by Category**

<table>
<thead>
<tr>
<th>Category</th>
<th>Comm Man</th>
<th>Prod Dev</th>
<th>Transfers</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>packaging</td>
<td>894,000</td>
<td>984,000</td>
<td>151,000</td>
<td>2,513,000</td>
</tr>
</tbody>
</table>

Remarks

Click Submit to transmit your data to DEA. Click Return to go back to the Year-End Estimates page to modify any part of this request.
Confirmation

Additional information documents/inquiries may be emailed to:

ODE.QUOTA@USDOJ.GOV

Include in subject line

Confirm # / company name / subject
1234 / Pharmaceutical Inc. / PQ Increase
List 1 Import quota

Application for Quota Allotment

Worksheet-A

Current Selection

<table>
<thead>
<tr>
<th>Quota Type</th>
<th>Quota Year</th>
<th>Drug Code</th>
<th>Drug Name</th>
<th>Pending Quota</th>
<th>Approved Quota</th>
</tr>
</thead>
<tbody>
<tr>
<td>Import</td>
<td>2011</td>
<td>1225</td>
<td>PHENYLPROPANOLAMINE (FOR SALE)</td>
<td>6,879,000</td>
<td>.000</td>
</tr>
</tbody>
</table>

Instructions
(DEA Form 488 -- Worksheet-A)

The Worksheet-A form is for you to document the subsequent disposition (sale) or utilization of PHENYLPROPANOLAMINE (FOR SALE). You may submit individual Worksheet-A forms using this web site. To do so, click the Next button below.
Alternatively, you may submit a Worksheet-A in Excel format via email. To email a Worksheet-A, first complete this request for an import quota, at the conclusion of which you will be given a reference number. Then prepare a Worksheet-A in Excel format and email it to ODE.Quota@usdoj.gov. Include the reference number in the subject line of the email. Click the radio button below to indicate that Worksheet-A submission by email.

○ Worksheet-A Email Submission

Reset  Return  Next
List 1 Import quota

IMPORT QUOTA
Eph, PSE, PPA
Similar to PQ/MQ Application

Must complete Worksheet A
• List of customers and amounts for year

Worksheet-A

<table>
<thead>
<tr>
<th>Quota Type</th>
<th>Quota Year</th>
<th>Drug Code</th>
<th>Drug Name</th>
<th>Pending Quota</th>
<th>Approved Quota</th>
</tr>
</thead>
<tbody>
<tr>
<td>Import</td>
<td>2011</td>
<td>1225</td>
<td>PHENYLPROPANOLAMINE (FOR CONVERSION)</td>
<td>12,000</td>
<td>0.00</td>
</tr>
</tbody>
</table>

DEA Number: ____________________________ Name of Company: ____________________________
Address: ____________________________
Phone: ____________________________ Fax: ____________________________ Email: ____________________________
Contact Person: ____________________________
Quantity to be sold (as grams of anhydrous base): ____________________________
Provide documentation for Quantity to be sold (purchase orders, supply agreements, etc.): ____________________________
Intended Use: ☐ Sale / Product Launch ☐ Product Development / Research ☐ Other (explain)

The ∗ symbol denotes a required field. Number fields must be a valid number between 0 and 999,999,999,999 inclusive.

Fill in the fields above and click Submit.
Quota Letters

- DEA issues quotas via written correspondence

- Letters are now also sent electronically (e-mail)
  - all correspondences are sent to address/POC on registration

- Itemized:
  - Product development
  - Packaging
  - Commercial

The Federal Register establishing the APQ/AAN must be published before initial quotas are issued
Quota Adjustments

- May request increase quota at any time
- Enter full amount of years requirement
- MULTIPLE DENIALS - HABITUAL FILERS
- Include justification for increase
  – WHY increase?
- Include year to date sales as free base
- Make sure ARCOS is up to date and is accurate
- Make sure YERS has been reported by Jan 31
- E, PSE, PPA – include YTD sales by customer name amount & DEA #
Helpful Information Continued

- Amount of material used per batch
- Number of dosage units per batch
- Dosage unit concentrations
- Number of batches and purpose
- Expected losses or yields
- Amounts needed for testing or retains
Helpful Information

Continued

- Product development requirements
- New product or launch
- Summary of destroyed material
- Other factors
Bulk Manufacturers

Summarize:

- Customers (include registration number)
- Sales to date (YTD)
- Forecasted sales for remainder of the year
- Exportation to date
- Forecast exports for remainder of the year
Helpful Information

- Domestic sales to-date and forecasts (kg as base)
- Exports to-date and forecasts (kg as base)
- Purchase orders, letters of intent, and other supporting documentation
Frequently Asked Questions

Importation of schedules I and II controlled substances

- No quota needed to import controlled substances
- Quota is needed to transfer material from import registration to manufacturer registration
- Quota is required to import three List I Chemicals (pseudoephedrine, ephedrine and PPA)
Frequently Asked Questions (continued)

- Contract Manufacturing
  - quota is required
- Small quantities
  - quota is required
Frequently Asked Questions (continued)

- Registration number change
  - Quota is required to receive inventory from the old registration
  - Quota is needed to continue manufacturing activities under new registration
  - Must submit new DEA form 250s and 189s with original signatures
  - QUOTAS DO NOT TRANSFER
Questions

Minh.T.Dang@USDOJ.GOV

www.deadiversion.usdoj.gov

Drug Enforcement Administration
UN Reporting & Quota Section