



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, **AND** the purpose as set forth in statement is to develop synthesis procedures or other research not related to dosage form development



RESEARCH VS. MANUFACTURING

- 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

U.S. Department of Justice
Drug Enforcement Administration

APPLICATION FOR INDIVIDUAL MANUFACTURING QUOTA

SEE INSTRUCTIONS ON SEPARATE PAGE		No individual manufacturing quota may be issued unless a completed application form has been received, 21 CFR 1303.22		OMB Approval No. 1117-0006	
1. NAME OF BASIC CLASS OR LIST I CHEMICAL (Only one per DEA-189)		2. SCHEDULE / LIST NUMBER		3. DEA DRUG / CHEMICAL CODE NUMBER	
4. NAME AND ADDRESS OF REGISTRANT (Include No., Street, City, State and ZIP Code)				5. YEAR FOR WHICH QUOTA IS REQUESTED	
				6. DEA REGISTRATION NUMBER	
7. NAME OF CONTACT PERSON		8. TELEPHONE No. (Include extension)		9. FAX NO.	
				10. E-MAIL ADDRESS	

NOTE: All quantities are to be expressed in grams of anhydrous acid, base, or alkaloid (not as salts).

11. QUOTA HISTORY	QUOTAS PREVIOUSLY ISSUED BY DEA			QUOTA REQUESTED () grams
	2 nd PRECEDING YEAR () grams	1 st PRECEDING YEAR () grams	CURRENT YEAR () grams	
12. PRODUCTION DATA	2 nd PRECEDING YEAR	1 st PRECEDING YEAR	ESTIMATE FOR CURRENT YEAR	ESTIMATE FOR YEAR FOR WHICH QUOTA IS REQUESTED
I. INVENTORY AS OF DEC. 31				
a. Bulk Controlled Substance or List I Chemical				
b. In-process material				
c. Contained in FINISHED Dosage Forms				
TOTAL (a + b + c)				
II. DISPOSITION (SALE) / UTILIZATION				
a. Domestic				
b. Exports				
TOTAL (a + b)				
III. ACQUISITION / PRODUCTION				
a. Domestic Sources				
b. Importation				
TOTAL (a + b)				

13. IF THE PURPOSE IS TO MANUFACTURE ANOTHER SUBSTANCE(S), FURNISH THE FOLLOWING INFORMATION:

NAME OF NEW SUBSTANCE	AUTHORITY TO MARKET THIS PRODUCT	DEA CHEMICAL CODE NUMBER	AMOUNT USED FOR THIS PURPOSE			% YIELD (Historical)
			2 nd PRECEDING YEAR	1 st PRECEDING YEAR	CURRENT YEAR	

14. REMARKS

SIGNATURE OF APPLICANT	PRINT or TYPE NAME and TITLE of SIGNER	DATE
------------------------	--	------

DEA FORM 188 (May 2007)

ALL PREVIOUS EDITIONS ARE OBSOLETE.

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.dea diversion.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

CONVERSION FACTORS EXAMPLE

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.

$150 \text{ kg HCl} * 0.90 = 135 \text{ kg base}$

(they still have 5 kg (140-135) of quota left).

CALCULATION VIDEO

M a & P a

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 → Hydromorphone or
 - Ephedrine → Pseudoephedrine
- Extraction from plant material
 - Coca Leaf → Cocaine
 - Concentrated Poppy Straw → Opium

ISOMER Quotas

– Amphetamine

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

– Methamphetamine

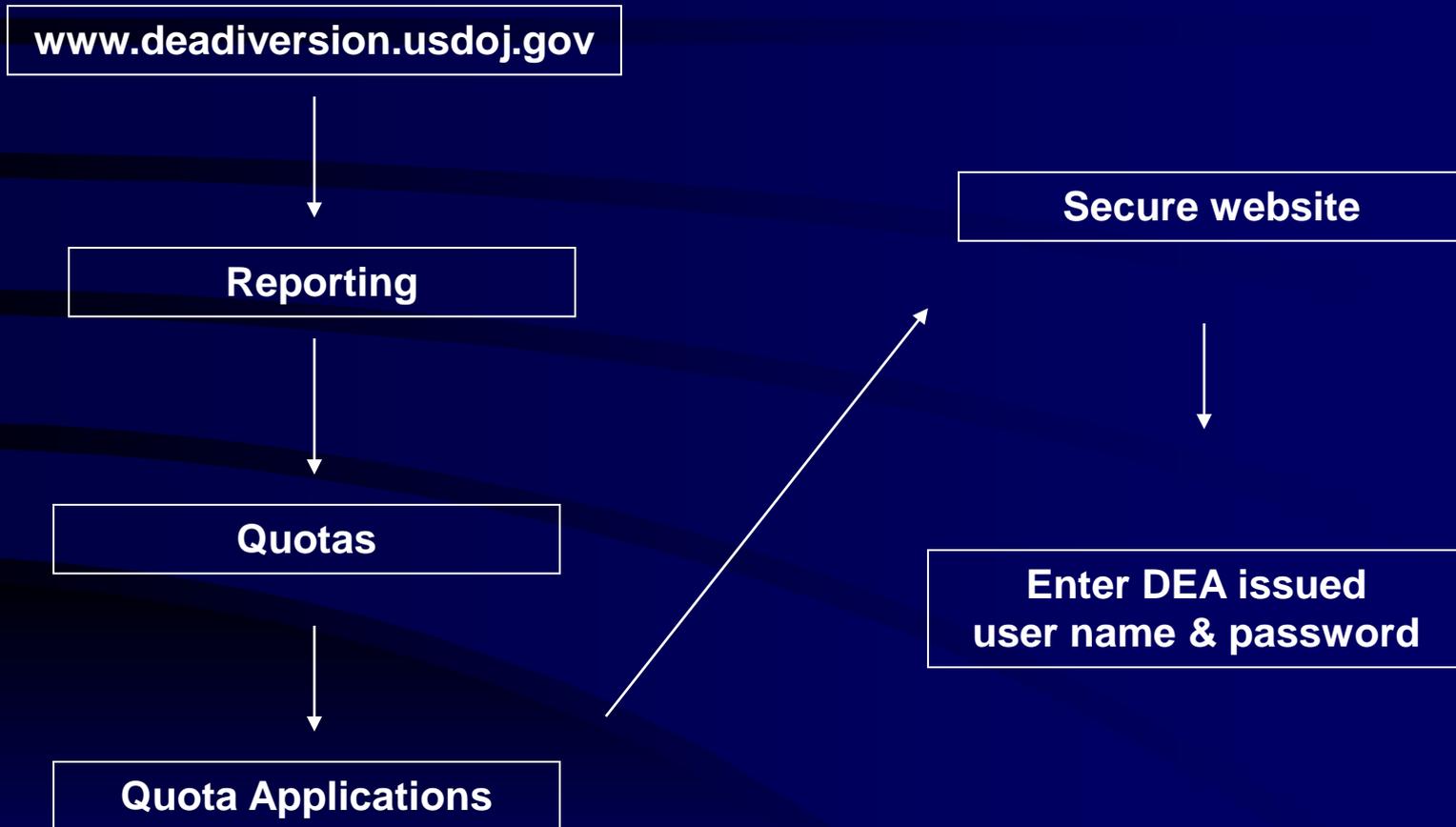
- » d-methamphetamine
- » l-methamphetamine
- » d,l-methamphetamine

– Tetrahydrocannabinols

- » Delta-9-THC
- » All Other Tetrahydrocannabinols



Accessing Quota Applications



LOGIN: www.deadiversion.usdoj.gov/quotas

Login



U.S. Department of Justice Drug Enforcement Administration
Office of Diversion Control

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.

Reset

Next

Request

Username/Password or Reset

ODE.QUOTA@USDOJ.GOV

- **Quota password same as YERS password**

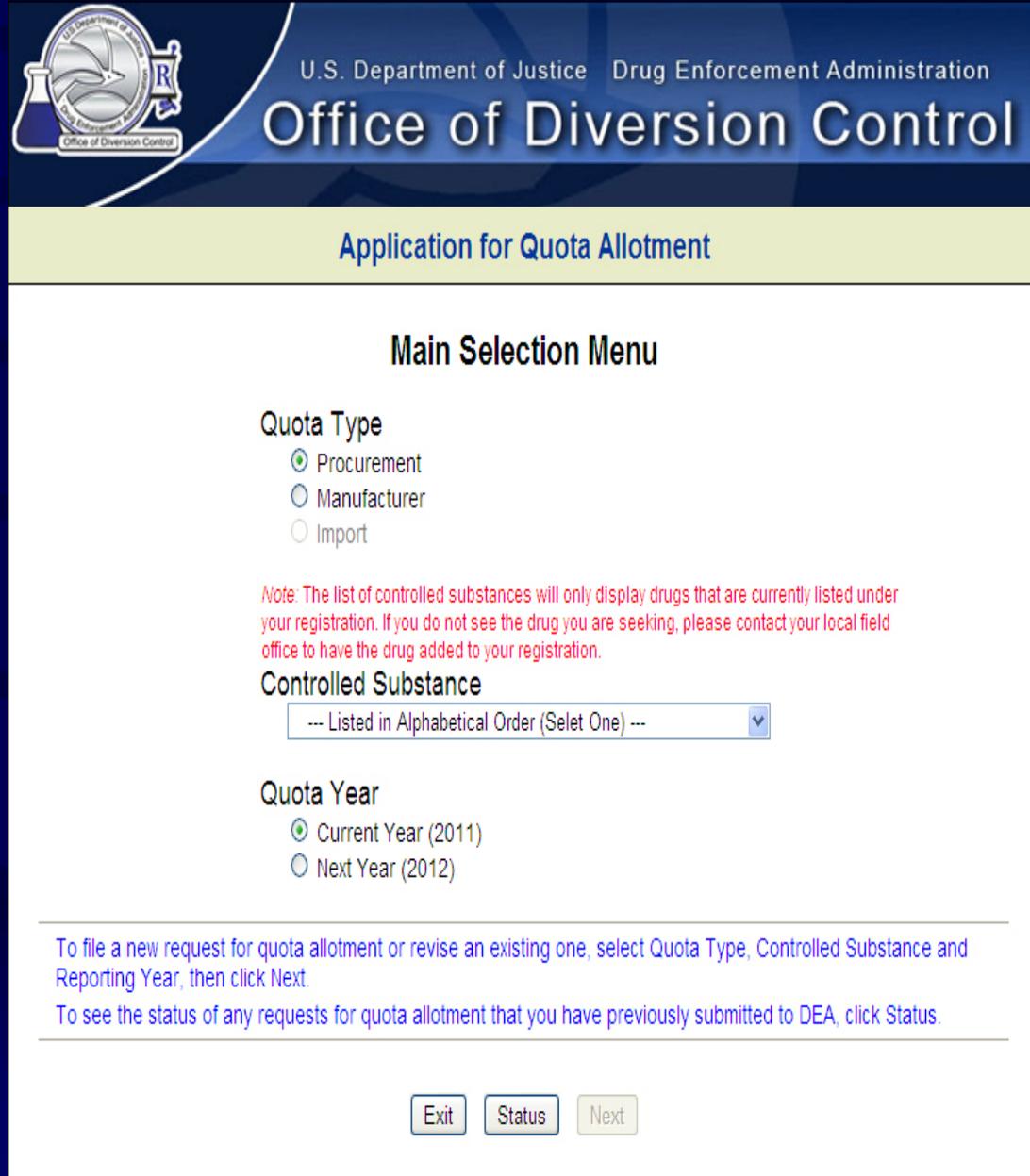
Report Selection Menu

Select Quota TYPE

- PROCUREMENT
- MANUFACTURER
- IMPORT

Select DRUG

Select Quota YEAR



The screenshot shows the 'Office of Diversion Control' website interface. At the top left is the logo of the U.S. Department of Justice, Office of Diversion Control. To the right of the logo, the text reads 'U.S. Department of Justice Drug Enforcement Administration Office of Diversion Control'. Below this is a yellow banner with the text 'Application for Quota Allotment'. The main content area is titled 'Main Selection Menu' and contains three sections: 'Quota Type' with radio buttons for 'Procurement' (selected), 'Manufacturer', and 'Import'; a red note stating '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.'; and 'Controlled Substance' with a dropdown menu currently showing '-- Listed in Alphabetical Order (Selet One) --'. Below this is the 'Quota Year' section with radio buttons for 'Current Year (2011)' (selected) and 'Next Year (2012)'. At the bottom, there are three buttons: 'Exit', 'Status', and 'Next'. A horizontal line separates the buttons from the instructions below.

U.S. Department of Justice Drug Enforcement Administration
Office of Diversion Control

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 (Selet 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.

Exit Status Next

Quota Application



U.S. Department of Justice Drug Enforcement Administration
Office of Diversion Control

Application for Quota Allotment

Year-End Estimates for Reporting Year 2011

Current Selection

Quota Type	Quota Year	Drug Code	Drug Name	Pending Quota	Approved Quota
Procurement	2011	1225(A)	PHENYLPROPANOLAMINE (FOR CONVERSION)		000

DEA Form 250 -- Box 12

Enter your estimated year-end report projections in the fields provided.
Use the TAB and SHIFT-TAB keys to tab forward and backward among the fields.
All amounts are expressed as grams of anhydrous base or alkaloid, not as salt.

Reporting Year	2009 (actual)	2010 (actual)	2011 (estimated)
Inventory (as of Dec 31)			
Bulk controlled substance (API)	0.000	0.000	<input type="text" value="0.000"/>
In-process material (in all forms)	0.000	0.000	<input type="text" value="0.000"/>
Finished dosage forms (bulk and/or packaged)	0.000	0.000	<input type="text" value="0.000"/>
Total	0.000	0.000	0.000
Dispositions			
Domestic	0.000	0.000	<input type="text" value="0.000"/>
Exports	0.000	0.000	<input type="text" value="0.000"/>
Total	0.000	0.000	0.000
Acquisitions			
Domestic	0.000	0.000	<input type="text" value="0.000"/>
Imports	0.000	0.000	<input type="text" value="0.000"/>
Total	0.000	0.000	0.000

[Click Next to advance to the next page.](#)

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)

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

BREAKDOWN
QUANTITIES

COMMERCIAL
PRODUCT
DEVELOPMENT
PACKAGING
TRANSFER



U.S. Department of Justice Drug Enforcement Administration
Office of Diversion Control

Application for Quota Allotment

Quota Request for Reporting Year 2011

Current Selection

Quota Type	Quota Year	Drug Code	Drug Name	Pending Quota	Approved Quota
Procurement	2011	1225(A)	PHENYLPROPANOLAMINE (FOR CONVERSION)		.000

Quota History (DEA 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) ---			--- Current Request ---
2008	2009	2010	2011
0.000	0.000	0.000	<input type="text"/>

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



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Application for Quota Allotment

Report Selection Menu

Current Selection

Quota Type	Quota Year	Drug Code	Drug Name	Pending Quota	Approved Quota
Procurement	2011	1225(A)	PHENYLPROPANOLAMINE (FOR CONVERSION)	2,513.000	.000

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.

Required / Optional	Current Request	Report Link
Optional		Commercial Manufacturing Converted Substances (DEA Form 250 -- Box 13)
Optional	894.000	Commercial Manufacturing Dosage Forms (DEA Form 250 -- Box 14)
Required	984.000	Product Development (DEA Form 250 -- Box 14)
Required	151.000	packaging
Required	484.000	Transfer

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

Back

Next

For Conversion

(For Conversion) QUOTAS

Identify the Drug to be made

And provide

Conversion YIELDS

Basic Class To Be Manufactured (DEA Form 250 -- Box 13)

To convert PHENYLPROPANOLAMINE (FOR CONVERSION) to another substance, select the substance from the list. If the target substance is not in the list, either contact DEA to have the substance added to your registration, or select "Users Choice" (the last entry).

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

Drug Name	Drug Code	2009 (actual)	2010 (actual)	2011 (estimated)	% Yield (estimated)

Fill in the fields above and click Submit.

Reset

Submit

Summary

Remove	Drug Name	Drug Code	2009 (actual)	2010 (actual)	2011 (estimated)	% Yield (estimated)
<input type="radio"/>	Vraxoin	0000	.000	.000	2,524.002	252.24

To remove an entry, click the Remove radio button.

Next

Commercial - Dosage Forms

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

Dosage Form Data
(DEA Form 250 -- Box 14)
Quota Requested: 894.000

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

* Name	* Mkt Auth	* Used 2009	* Used 2010	* Est. 2011
<input type="text"/>				

The * symbol denotes a required field. Number fields must be a valid number between 0 and 999,999,999.999 inclusive.

Summary

Remove	Name	Mkt Auth	Used 2009	Used 2010	Est. 2011
<input type="radio"/>	Traylopanifaphyn	Department of Agriculture	5121	1321	1231

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

Product Development

Product Development

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

Hint

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

Dosage Form Data
(DEA Form 250 -- Box 14)
Quota Requested: 984.000

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

* Name	* Strength	* Units/Batch	* # Batches	* Purpose	* Qty	* Completion Time
<input type="text"/>						

The * symbol denotes a required field. Number fields must be a valid number between 0 and 999,999,999.999 inclusive.

Summary

Remove	Name	Strength	Units/Batch	# Batches	Purpose	Qty	Completion Time
<input type="radio"/>	Calafirin	23 gm	125	521	Nausea	132	2 months

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

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, ie. 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.

Reset

Submit

Summary

Remove DEA Number

Explanation

RL0401187 Required the further analysis of product in outside independent study.

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

Next

Who transfer to?
Why?

Summary

USE Remarks Box

Include attachment for supporting documents



U.S. Department of Justice Drug Enforcement Administration
Office of Diversion Control

Application for Quota Allotment

Final Summary

Current Selection

Quota Type	Quota Year	Drug Code	Drug Name	Pending Quota	Approved Quota
Procurement	2011	1225(A)	PHENYLPROPANOLAMINE (FOR CONVERSION)	2,513.000	.000

Year-End Report Data

	2009 (actual)	2010 (actual)	2011 (estimates)
Inventory	0.000	0.000	1,272.000
Acquisitions	0.000	0.000	100.000
Dispositions	0.000	0.000	69.000

Quota Allotment Request by Category

Comm Man	Prod Dev	packaging	Transfers	Total
894.000	984.000	151.000	484.000	2,513.000

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



U.S. Department of Justice Drug Enforcement Administration
Office of Diversion Control

Application for Quota Allotment

Summary Confirmation

Current Selection

Quota Type	Quota Year	Drug Code	Drug Name	Pending Quota	Approved Quota
Procurement	2011	1225(A)	PHENYLPROPANOLAMINE (FOR CONVERSION)	2,513.000	.000

Confirmation

You have successfully submitted a Quota Allotment Request for the substance noted above. Your reference number is:

108035

You may contact DEA via email at ODE.Quota@USDOJ.gov concerning this transaction. Be sure to include the reference number in the subject line of all such correspondence.

If you find a need to amend this request, you may do so by selecting this same substance from the Main Selection Menu. At that time all data entry fields will be pre-populated with values from your latest request.

Printing Options

You are required by law to retain a copy of this Request for Quota Allotment for a period of seven years after the date of the initial request. Click the Print button below and you will be able to print or archive the resultant PDF report.

Print

Return

Exit

List 1 Import quota



U.S. Department of Justice Drug Enforcement Administration
Office of Diversion Control

Application for Quota Allotment

Worksheet-A

Current Selection

Quota Type	Quota Year	Drug Code	Drug Name	Pending Quota	Approved Quota
Import	2011	1225	PHENYLPROPANOLAMINE (FOR SALE)	6,879.000	.000

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

Current Selection

Quota Type	Quota Year	Drug Code	Drug Name	Pending Quota	Approved Quota
Import	2011	1225	PHENYLPROPANOLAMINE (FOR CONVERSION)	12.000	.000

**Worksheet-A Data
(DEA Form 488 -- Worksheet-A)**

* 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

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www.deadiversion.usdoj.gov

Drug Enforcement Administration
UN Reporting & Quota Section