Quotas

UN Reporting and Quota Section (DRQ)
Diversion Control Division
Supply Chain Conference
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Houston, TX

Disclaimer

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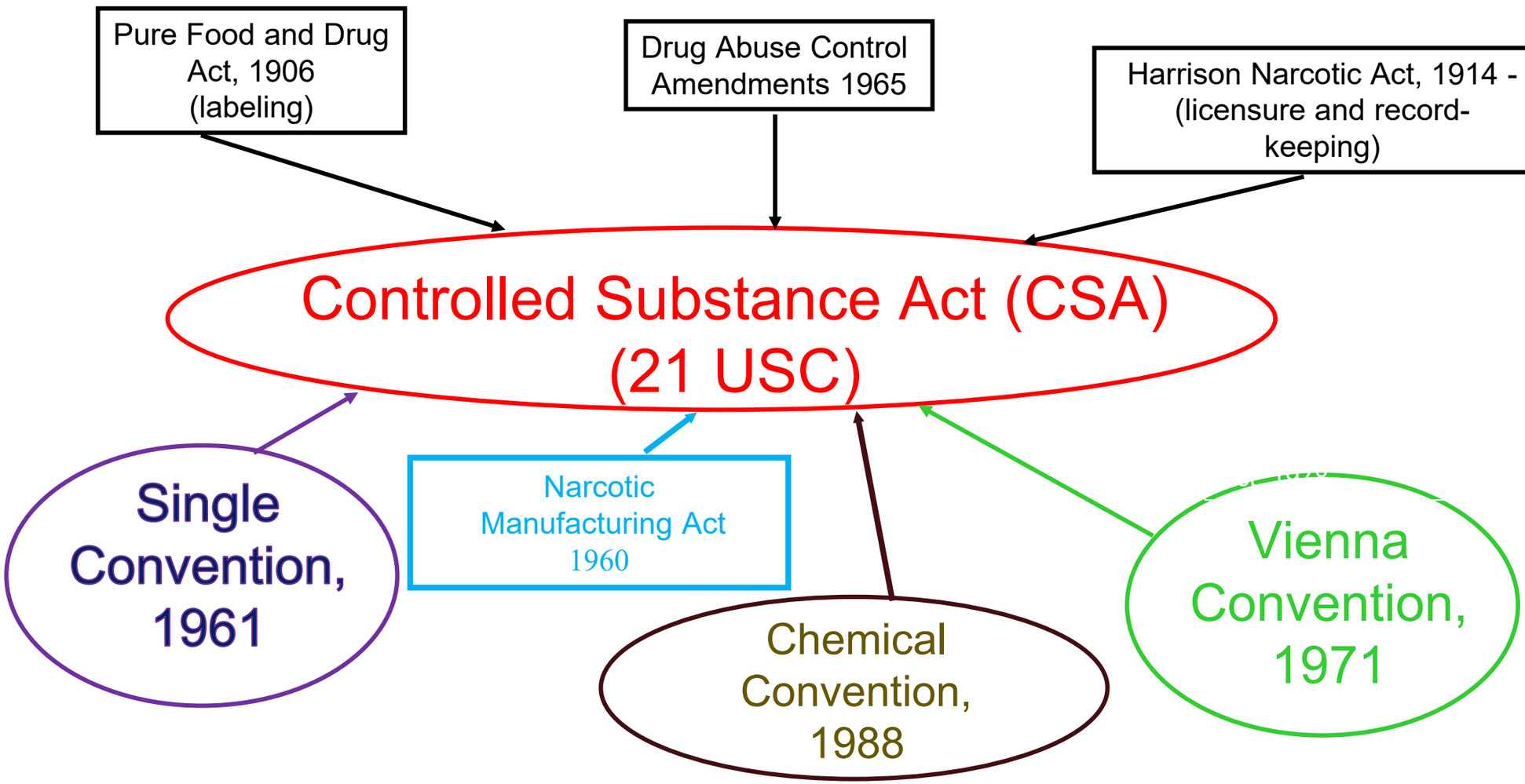
I have no financial relationship to disclose.

CSA - Historical Perspective



Levels of Drug Control under the CSA

Schedule I (CI) - NEED QUOTA (MFG)

Substances with **high** abuse potential and **no** medical utility (most restrictive): *e.g., GHB, MDMA, Marijuana, d-9-THC, Psilocybin.*

Schedule II (CII) - NEED QUOTA (MFG)

Substances with **high** abuse potential and medical utility: *e.g., Fentanyl, Hydrocodone, Morphine, Oxycodone.*

Schedule III, IV and V – no quota needed

Substances with medical utility in the U.S. and high (CIII) to progressively lower levels of abuse potential, dependence profile and regulatory controls: *e.g., NaGHB (sodium oxybate), Ketamine, Buprenorphine, Benzodiazepines.*

CMEA* List I chemicals - NEED QUOTA (MFG/IMPORT)

ephedrine (EPH), pseudoephedrine (PSE) & phenylpropanolamine (PPA)

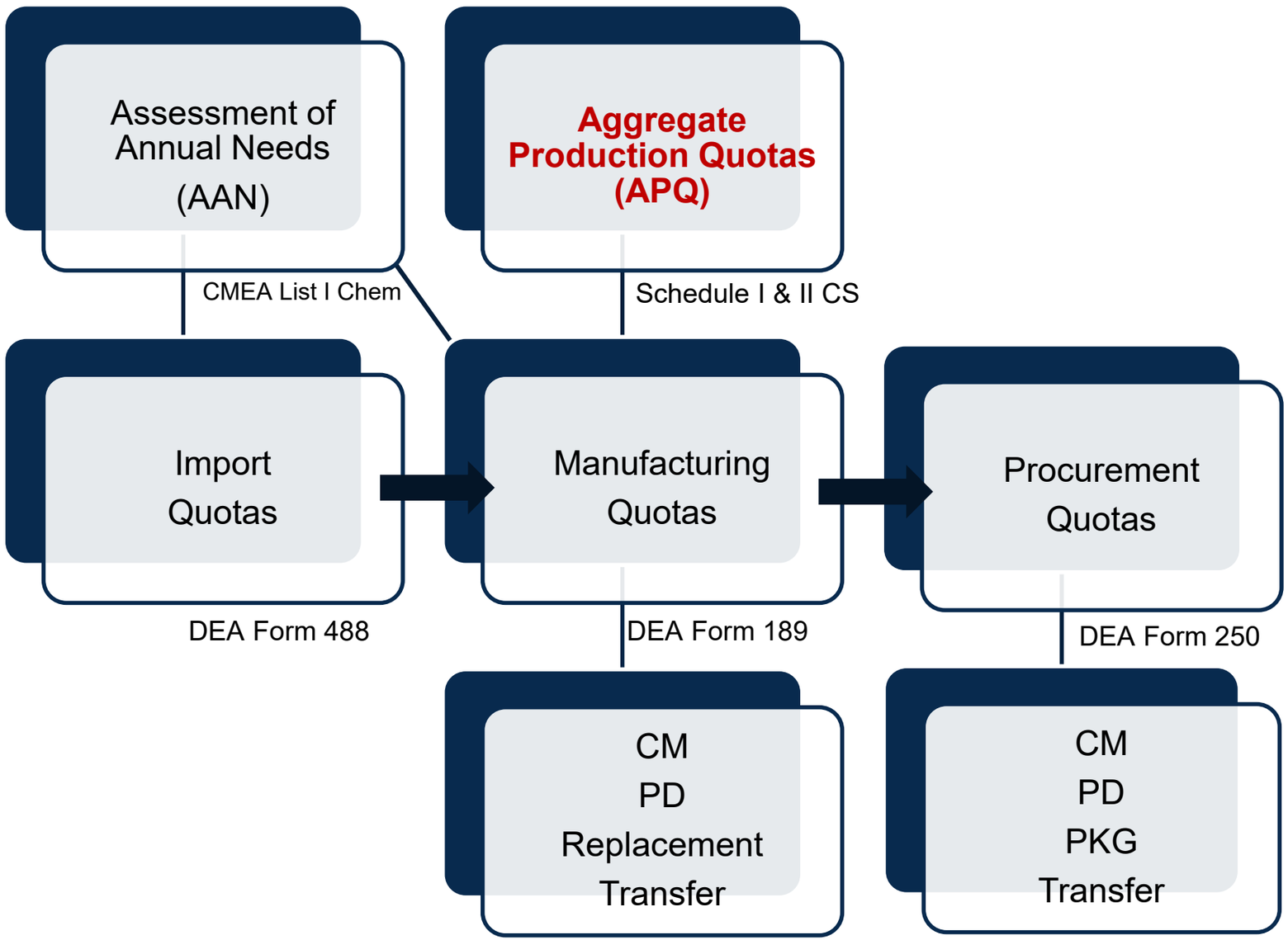
Substances used for manufacture of cough & cold medicines and vet products, but can also be used for illicit manufacture of methamphetamine & amphetamine

*Combat Methamphetamine Epidemic Act

Purpose of Quotas

- **Limit the quantity of CMEA List I chemicals imported, and CMEA List I chemicals and CI and CII manufactured and procured**
- **Restrict the above import, manufacture and procurement to DEA registered manufacturers**
- **Provide for legitimate need – medical, scientific, research, industrial, export**
- **Provide adequate inventories to support legitimate needs**

AAN vs APQ: Quotas with subcategories



Schedule I and II CS Quota Requirements
Pursuant to 21 CFR Part 1303

- **Aggregate Production Quotas (APQ)**
  (21 CFR 1303.11 and 1303.13)

- **Individual Manufacturing Quotas (MQ)**
  (21 CFR 1303.21 through 1303.27)

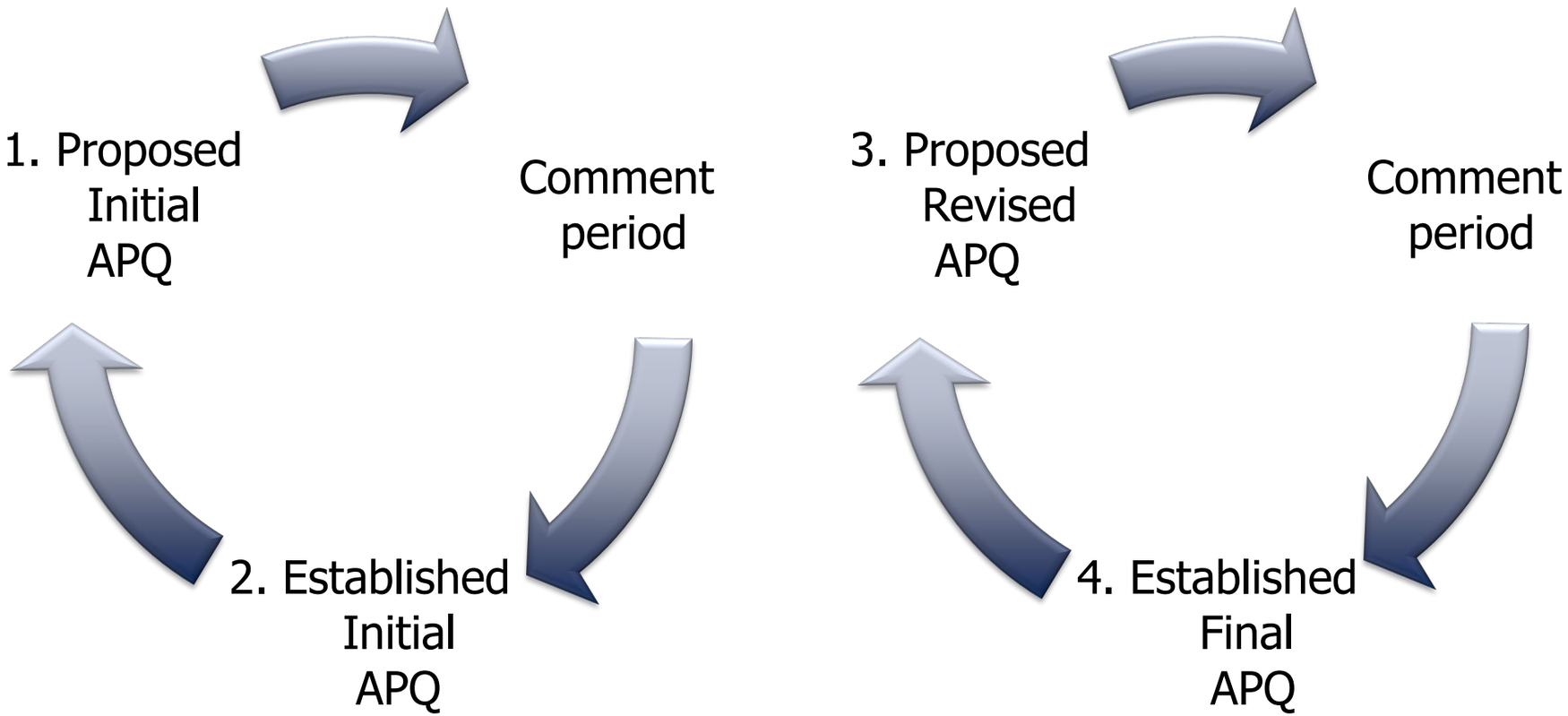
- **Procurement Quotas (PQ)**
  (21 CFR 1303.12)

- **Import Quotas (IQ)**
  None! IQ only needed for CMEA List I chemicals

Aggregate Production Quotas

- Only applies to Schedules I and II controlled substances (as the basic class i.e. anhydrous base)
- Sets the upper limit of national manufacturing
- Historically established annually with one revision
- Federal Register notices required

Aggregate Production Quotas (APQ) Federal Registers



APQ Determined By Considering

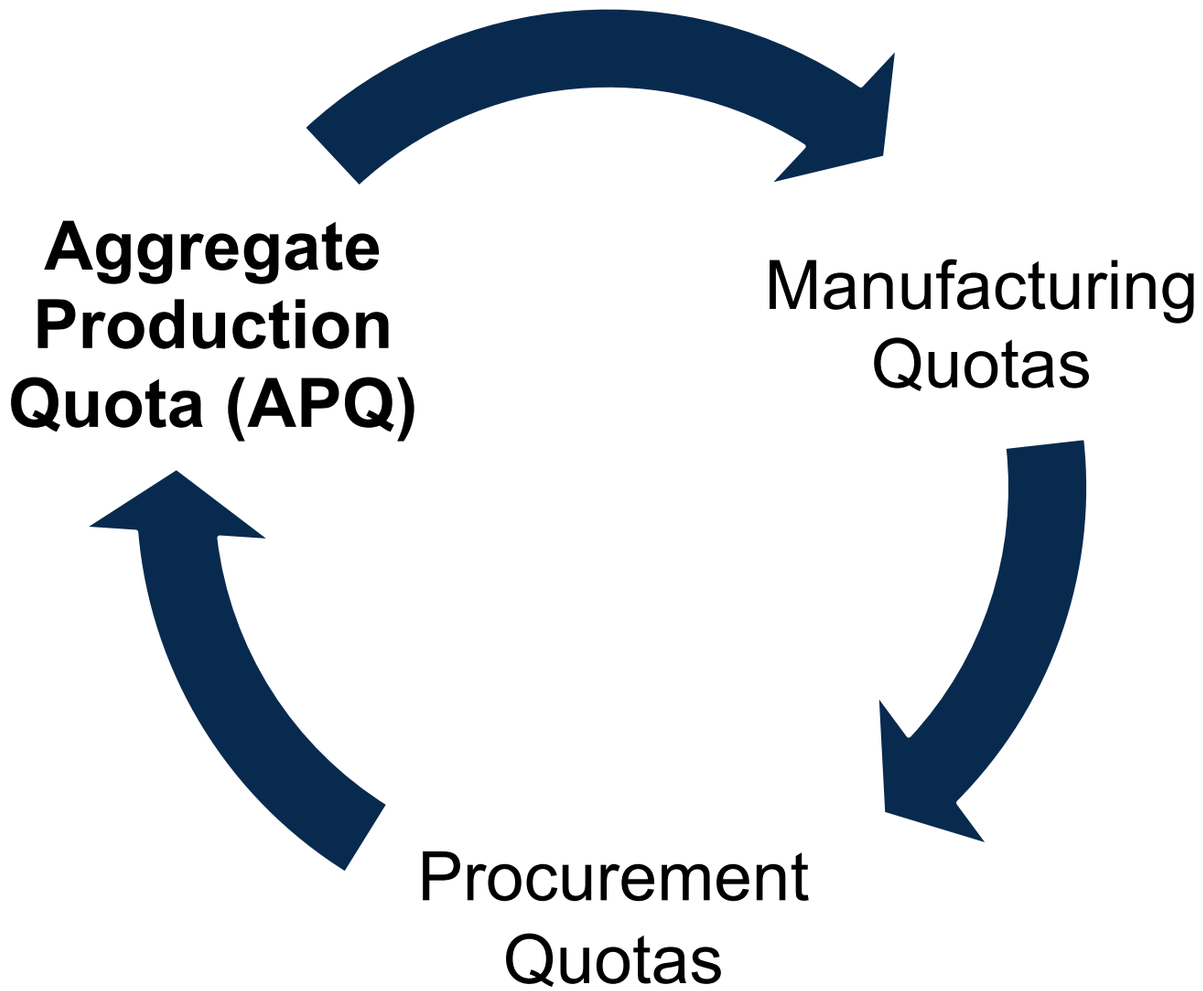
- **Data from Procurement Quotas applications**
  - Dispositions – domestic and export
  - Product development, yields, etc.
  - Inventory data

- **Data from Manufacturing Quotas**
  - Procurement quotas
  - Historical share of the market
  - Product development, yields, etc.
  - Inventory data

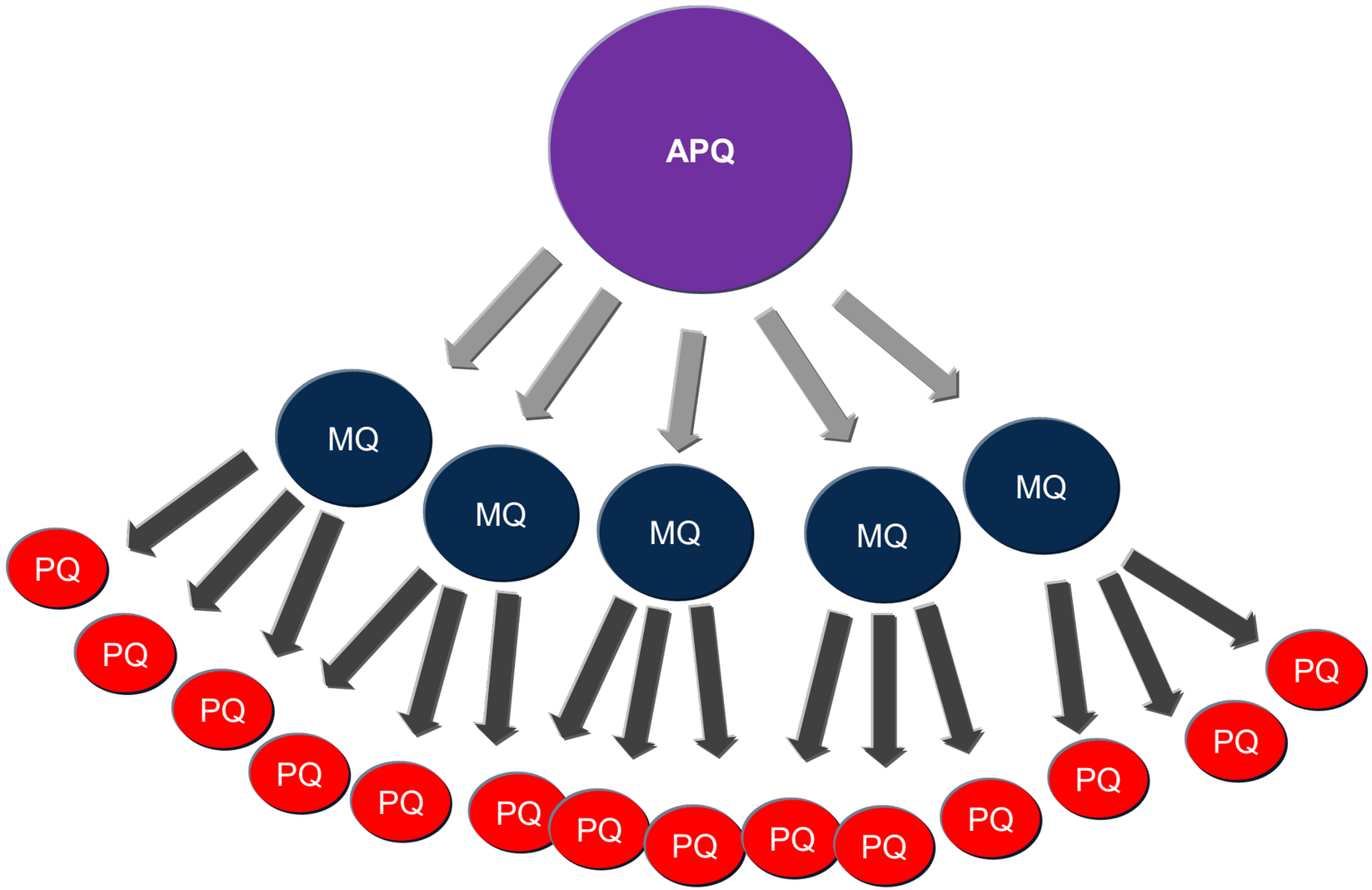
- **FDA Estimates of legitimate domestic medical need**

- **Diversion, abuse, consumption, trafficking data**
  - SUPPORT Act
  - CDC overdose data
  - State PDMP data

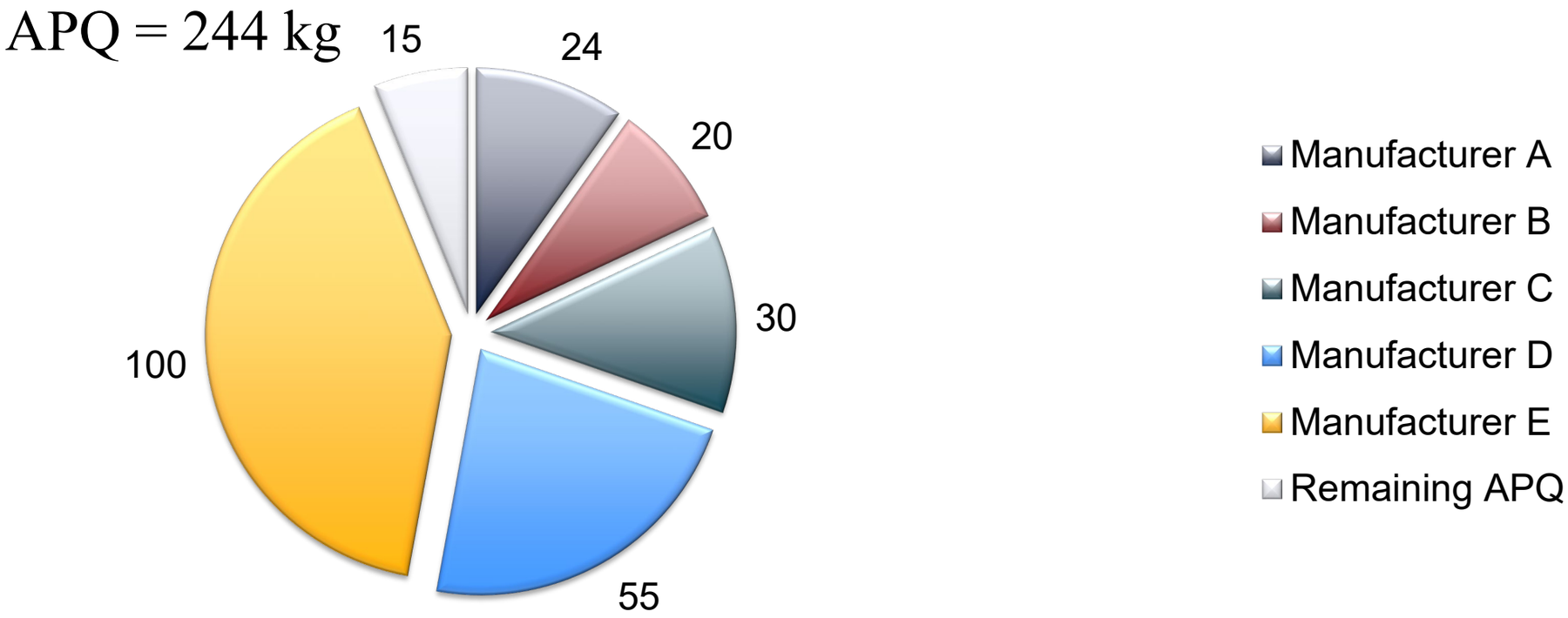
Quota – APQ Relationship



APQ – MQ – PQ



Relationship Between APQ and Manufacturing Quotas



APQ Time Machine

Basic class	Proposed 1995 quotas
Schedule I	
Acetylmethadol	2
Aminorex	2
Bufotenine	10
Cathinone	4
Difenoxin	14,000
2, 5-Dimethoxyamphetamine	15,650,000
Dimethylamphetamine	2
N-Ethylamphetamine	4
Lysergic acid diethylamide	41
Mescaline	2
4-Methoxyamphetamine	12
4-Methylaminorex	2
3-Methylfentanyl	12
Methaqualone	2
Methcathinone	9
3, 4-Methylenedioxyamphetamine	12
3, 4-Methylenedioxy-N-ethylamphetamine	2
3, 4-Methylenedioxymethamphetamine	12
Normorphine	2
Tetrahydrocannibinols	35,000
Thiophene Analog of Phencyclidine	10

1995 APQ:
21 drugs

2023 APQ:
254 drugs

APQ Time Machine

Schedule II

Alfentanil	7,000
Amobarbital	5
Amphetamine	635,000
Cocaine	550,000
Codeine (for sale)	67,312,000
Codeine (for conversion)	16,181,000
Dextropropoxyphene	124,012,000
Dihydrocodeine	202,000
Diphenoxylate	688,000
Ecgonine (for conversion)	650,000
Fentanyl	76,000
Hydrocodone	8,474,000
Hydromorphone	393,000
Levo-alpha-acetylmethadol	200,000
Levorphanol	8,000
Meperidine	8,637,000
Methadone	3,779,000
Methadone (for conversion)	364,000
Methadone Intermediate (for sale)	300,000
Methadone Intermediate (for conversion)	4,393,000
Methylphenidate	7,935,000
Morphine (for sale)	7,612,000
Morphine (for conversion)	78,105,000
Noroxymorphone (for sale)	21,000
Noroxymorphone (for conversion)	3,500,000
Opium	1,118,000
Oxycodone (for sale)	3,613,000
Oxycodone (for conversion)	6,200
Oxymorphone	2,500
Pentobarbital	15,706,000
Phencyclidine	52
Phenylacetone (for conversion)	3,528,000

1995 APQ:
36 drugs

2023 APQ:
77 drugs

Manufacturing Quotas

Bulk manufacturers of Schedules I and II controlled substances and/or CMEA List I chemicals whose methods include:

- **Extraction from plant material**
  - coca leaf, opium, concentrated poppy straw
- **Synthetic routes**
  - converting morphine into hydromorphone
  - controlled substances derived from non-controlled starting materials

Manufacturing Quotas

- **Only DEA registered manufacturers with the specific CI or CII drug codes receive MQ**
- **Establish maximum amount which the individual bulk manufacturer may *manufacture* in a calendar year**
- **Manufacturers cannot exceed manufacturing quota**
- **Establish guidelines for inventory allowances**

Manufacturing Quotas Inventory Allowance

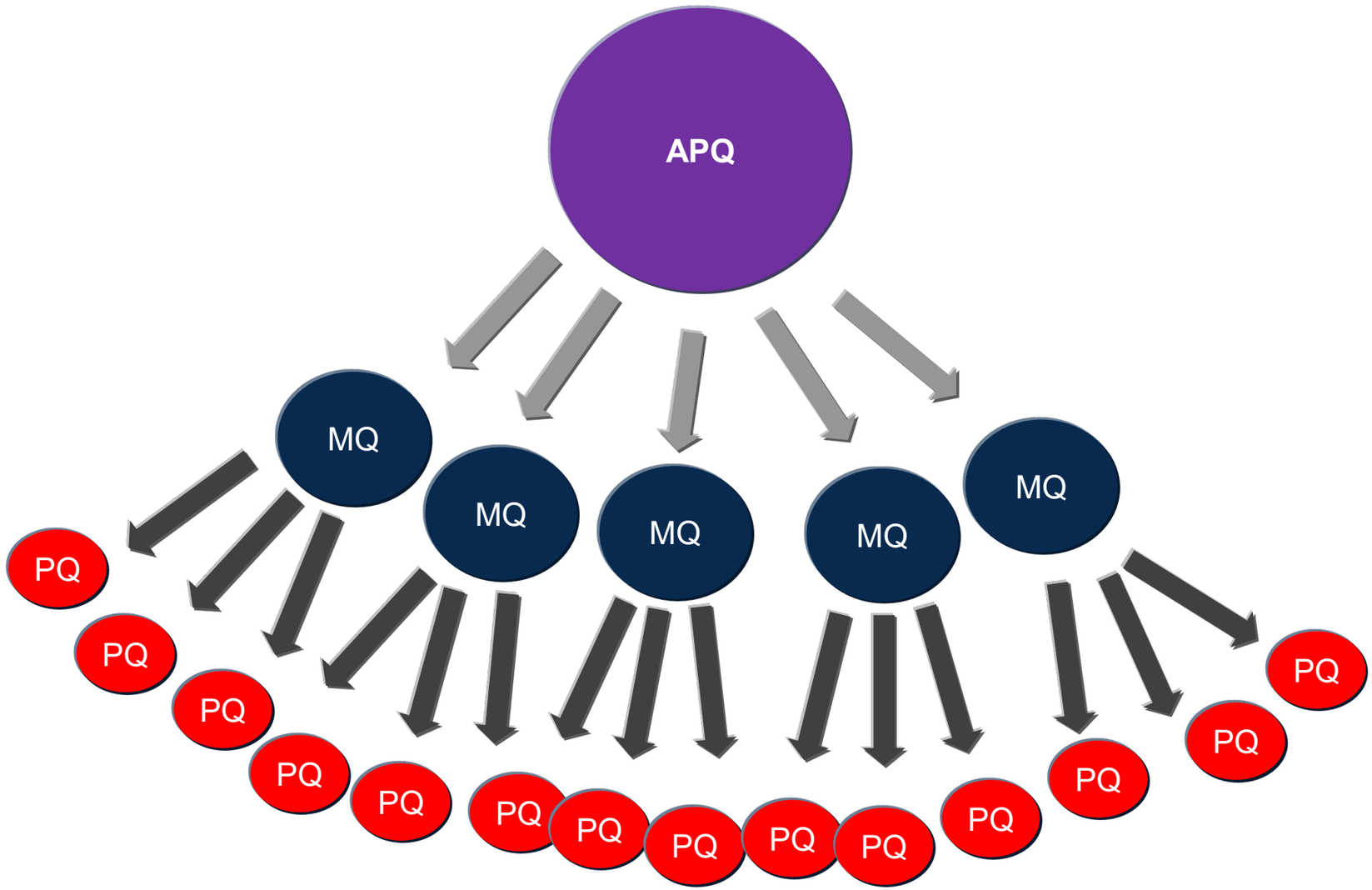
- 21 CFR 1303.24
- Normally 50% of average net disposals for current and preceding year
- During calendar year may not exceed 65% of estimated net disposal
- Exceeding 65% will suspend quota until inventory is less than 60% of net disposals

Manufacturing Quotas

Granted to DEA registrants based on:

- **Procurement Quotas**
- **Historical share of the market**
- **Inventory (saleable; bulk, in-process and finished dosage forms)**
- **Product development efforts**
- **Limited by the APQ (CI and CII), AAN (CMEA List I chemicals)**

APQ – MQ – PQ



Procurement Quotas

Manufacturers who procure a Schedule I or II controlled substances, or CMEA List I chemicals for the purposes of:

- **Converting bulk API into finished dosage forms**
- **Formulating products such as exempt chemical preparations or reference standards**
- **Packaging, repackaging, labeling or re-labeling a commercial container or dosage form**
- **Performing product development activities**

Procurement Quotas

- **Only DEA registered manufacturers with the specific CI or CII drug code can receive**
- **Establish maximum amount which the individual manufacturer may *acquire* in a calendar year**
- **Manufacturers cannot exceed procurement quota**
- **Certification of adequate quota needed to place order (21 CFR 1303.12(f))**

Procurement Quotas

Granted to DEA registrants based on:

- **Dispositions (domestic sales and exports, waste), non-saleable material (yields, QC)**
- **Acquisitions from both domestic manufacturers and importers**
- **Product development efforts**
- **Inventory**
- **Customer data**

Procurement Quota - FAQ

What if the registration number changes?

- New PQ is needed to receive transfer of inventory from old registration

- New PQ is needed to **start** activity under new registration

- Must submit new quota applications online once all necessary drug codes have been added to registration

QUOTA DOES NOT TRANSFER

Procurement Quota - FAQ

- **Analytical exempted Standards**

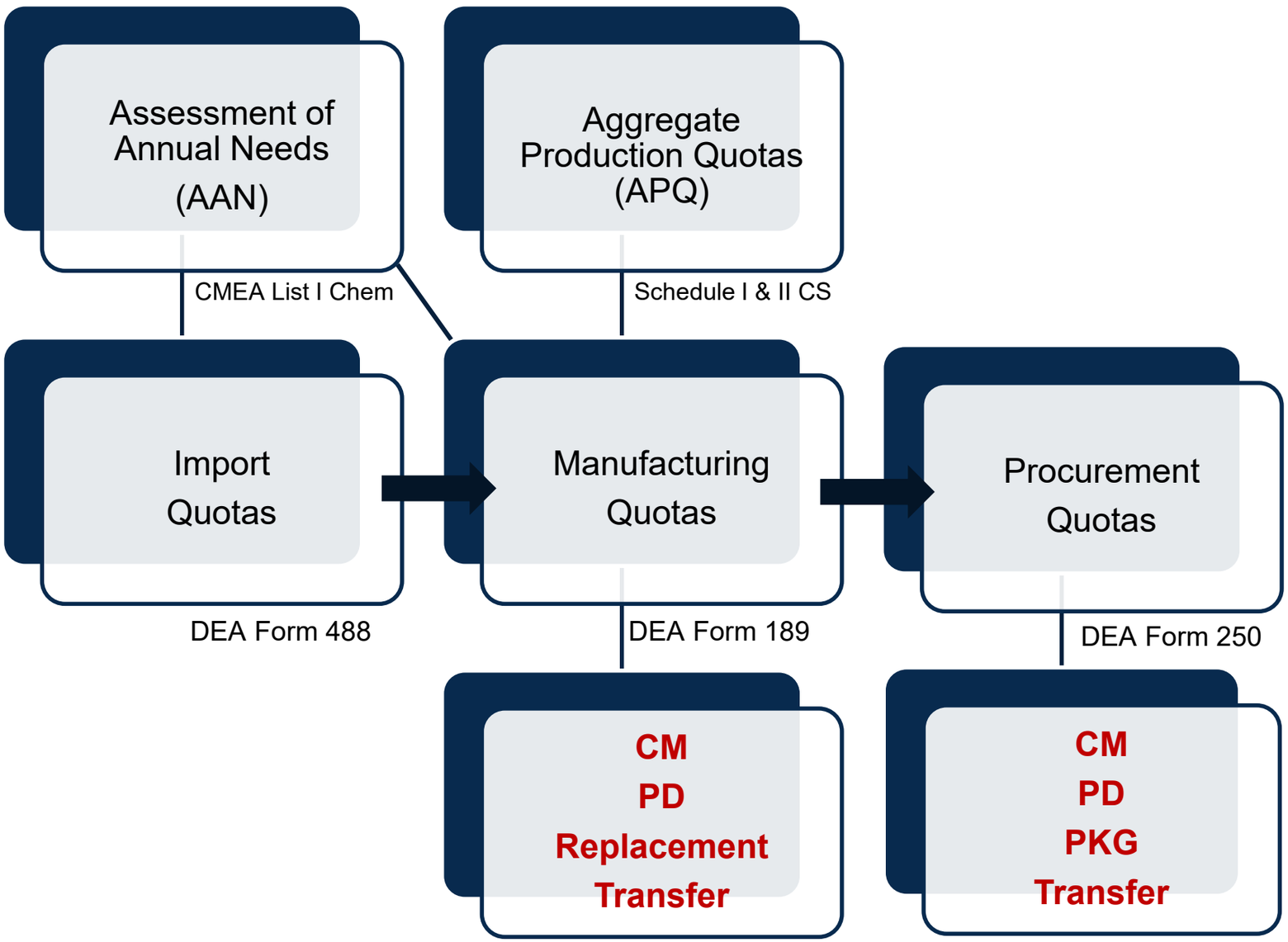
  - No quota is needed as per 21 CFR 1303.12(e)(2)

- **Research**

  - No quota needed for research registration per 21 CFR 1303.12(e)(3)

  - Be aware of what is considered research versus manufacturing

AAN vs APQ: Quotas with subcategories



What are the sub-categories of MQ/PQ Quotas?

- **CM: Commercial Manufacturing - CM**
  - Bulk, conversion to other substances (MQ)
  - Dosage form (PQ)
  - FDA approved Drug Master File (DMF), New Drug Application (NDA), Abbreviated NDA (ANDA)
  - starting material for reference standards, exempt products

- **PD: Product Development (PQ, sometimes MQ)**
  - All stages leading ***to*** FDA approval (pending DMF, NDA, or ANDA)
  - Laboratory scale
  - Scale up
  - Stability
  - Exhibit
  - **Validation**

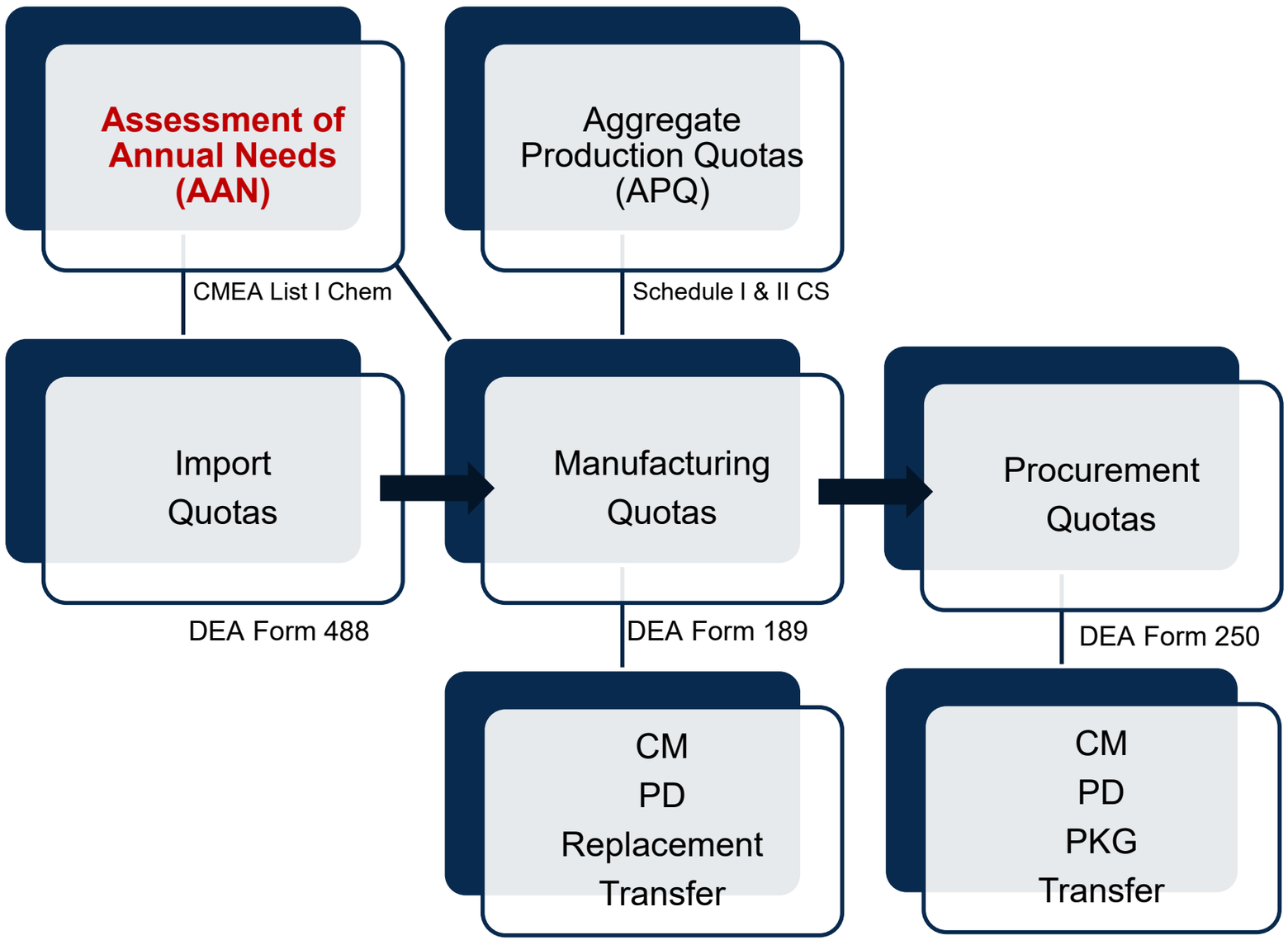
What are the sub-categories of MQ/PQ Quotas?

- **PKG: Packaging (PQ)**
  - Packaging/Repackaging
  - Labeling/Relabeling

- **Replacement (MQ)**
  - Case-by-case basis for MQ CM only

- **Transfer (MQ/PQ)**
  - Return of defective bulk API
  - Processing of product (micronization)
  - Move existing inventory from closing facilities

AAN vs APQ: Quotas with subcategories



Combat Methamphetamine Epidemic Act 2005 (CMEA)

Enacted on March 9, 2006

Ephedrine, Pseudoephedrine, and Phenylpropanolamine

- **Additional legislative and regulatory controls on the manufacture, distribution, importation, and exportation of these CMEA List I chemicals**

- **Registration now required for each physical location (manufacturer, distributor, importer or exporter)**

Quota Provisions of CMEA

- **Bulk manufacturers who synthesize EPH, PSE and PPA must obtain a manufacturing quota**

- **Manufacturers who purchase EPH, PSE and PPA must obtain a procurement quota.**
  - Dosage form manufacturers, packagers, labelers, repackagers and relabelers

- **Importers who import EPH, PSE and PPA (or products containing EPH, PSE, and PPA) must obtain an import quota**

Quota Provisions of CMEA

- **Before issuing individual quotas, DEA had to first establish the annual needs of the United States for EPH, PSE and PPA**

- **The 2008 Assessment of Annual Needs (AAN) was published in the Federal Register on December 27, 2007**

- **DRQ began issuing individual quotas on December 30, 2007 for the calendar year 2008**

CMEA List I Chemicals Quota Requirements

Pursuant to 21 CFR Part 1315

- **Assessment of Annual Needs (AAN)**
  (21 CFR 1315.11 and 1315.13)

- **Individual Manufacturing Quotas (MQ)**
  (21 CFR 1315.21 through 1315.27)

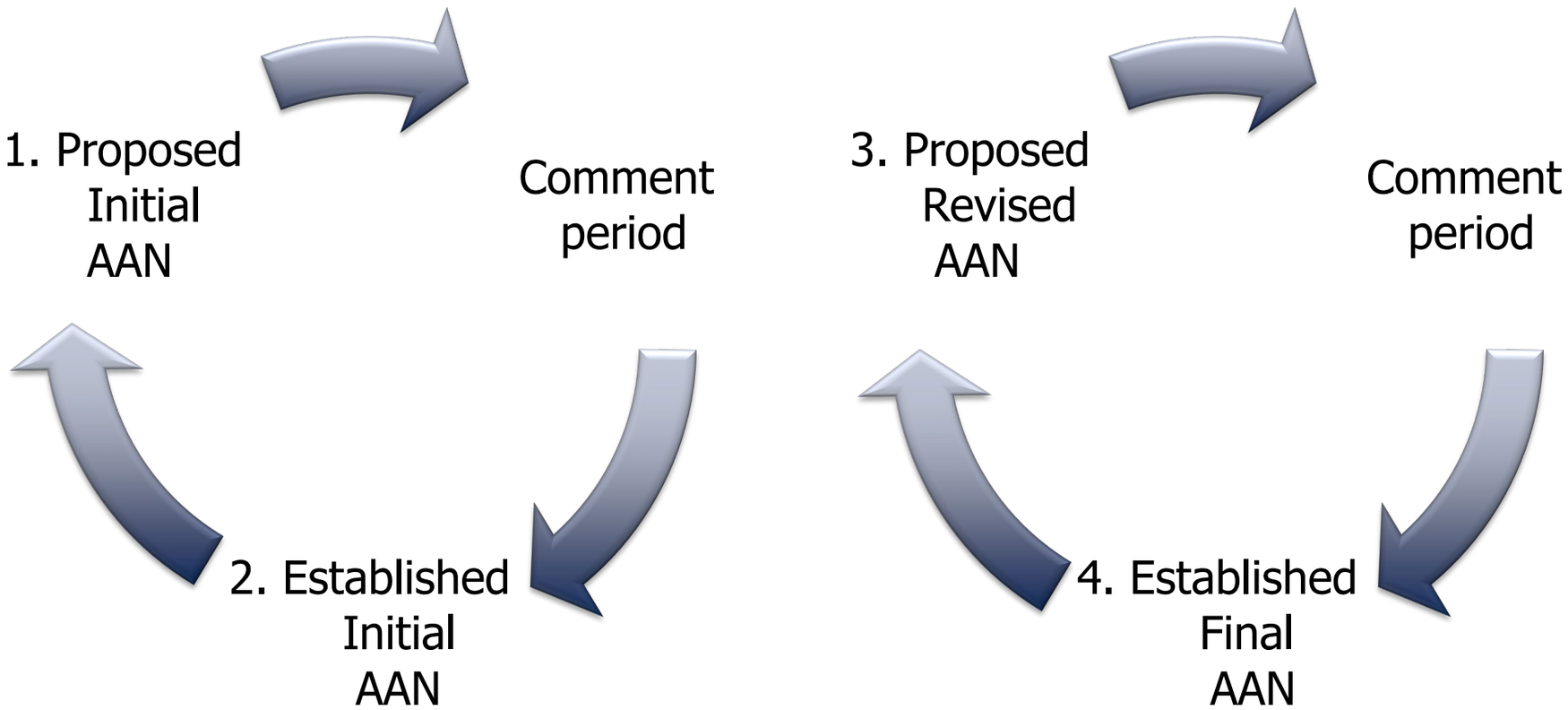
- **Procurement Quotas (PQ)**
  (21 CFR 1315.30 and 1315.32)

- **Import Quotas (IQ)**
  (21 CFR 1315.34 and 1315.36)

Assessment of Annual Needs

- **Only applies to CMEA List I chemicals**
- **Sets the upper limit of national import and manufacturing CMEA List I chemicals**
- **Established annually with one revision**
- **Federal Register notices required**

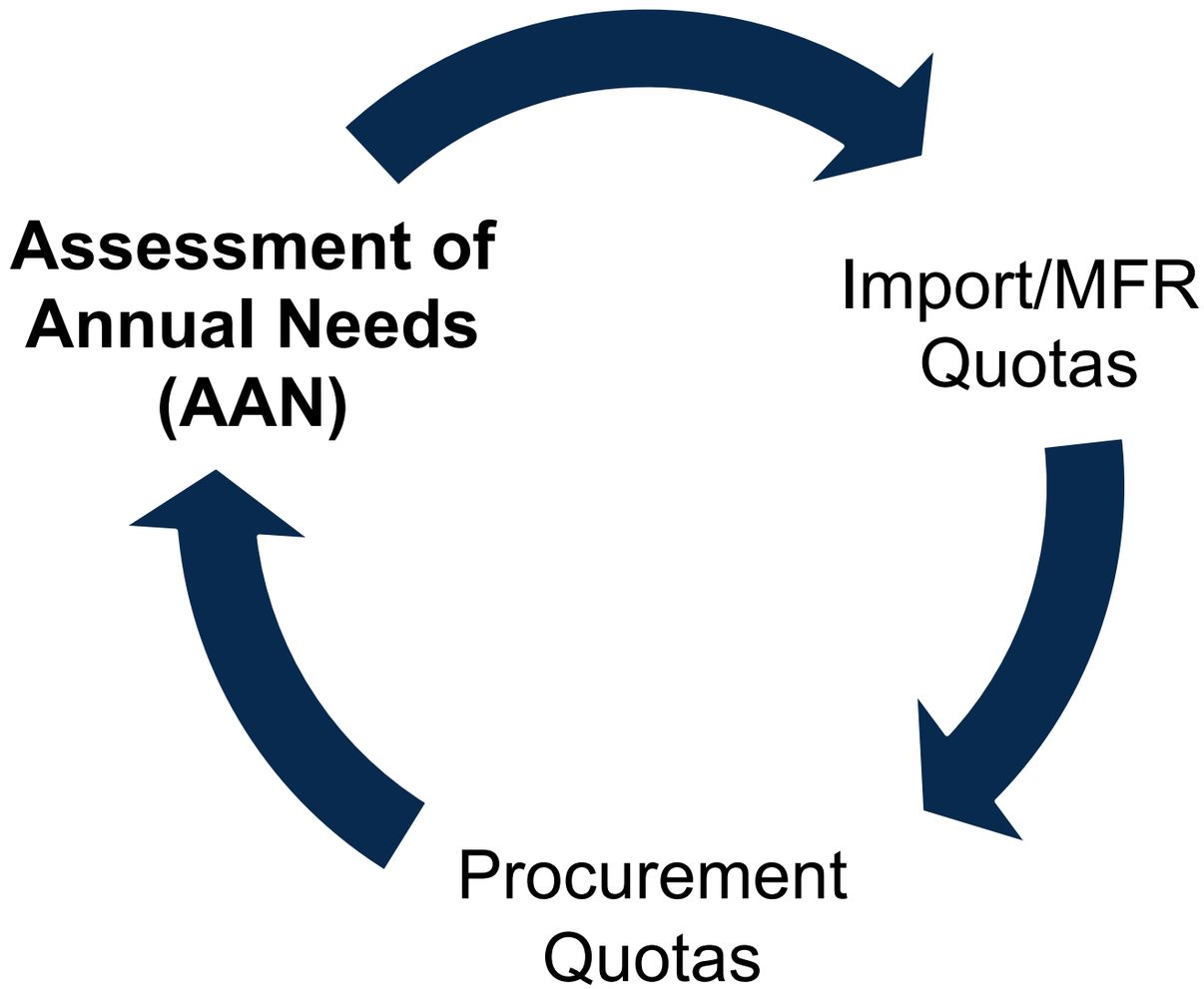
Assessment of Annual Needs (AAN) Federal Registers



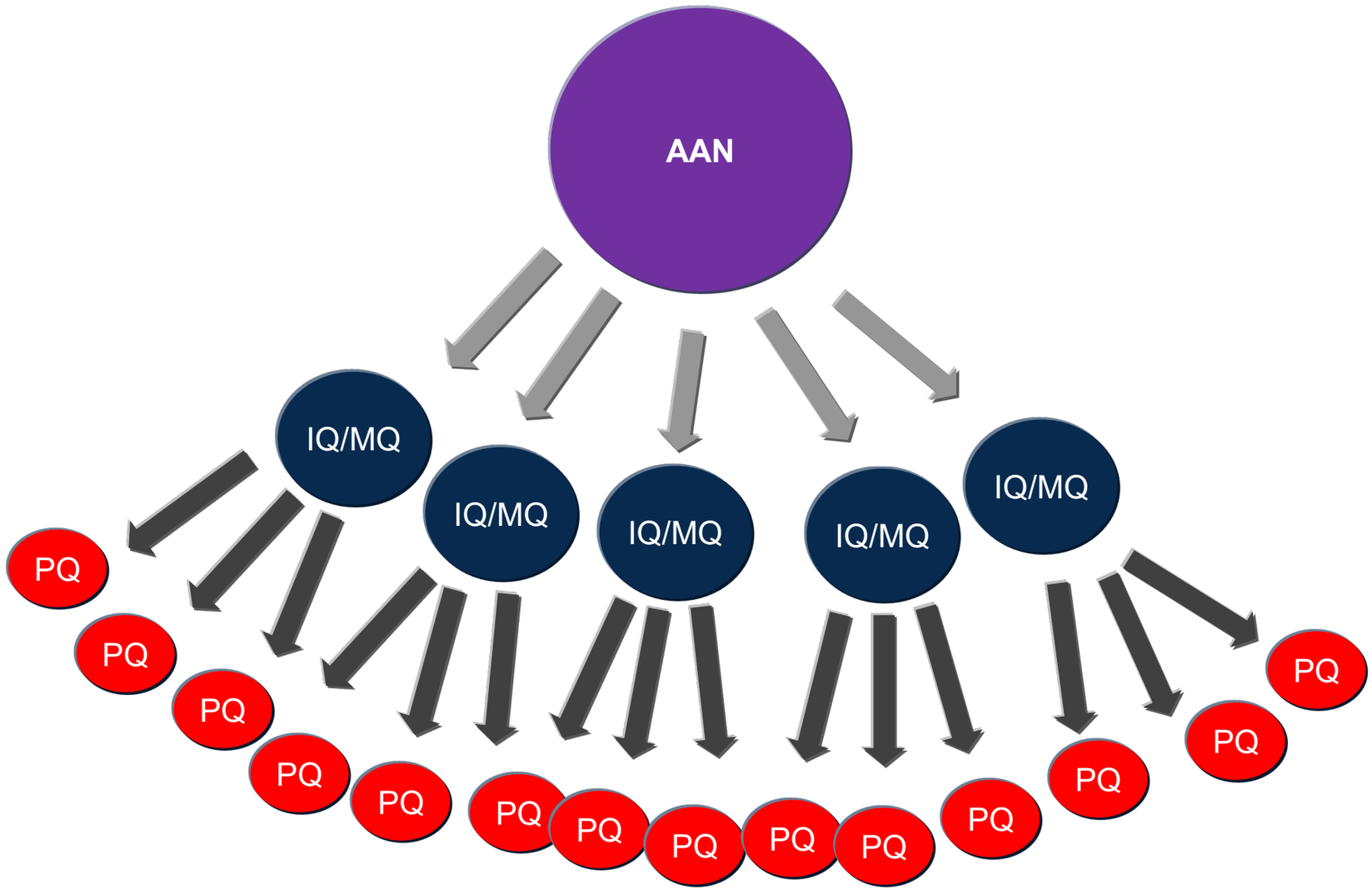
AAN Determined By Considering

- **Import, Manufacturing and Procurement Quota applications from DEA Registered manufacturers and importers**
- **The national rate of disposals (sales/utilization)**
- **Actual and estimated inventories**
- **FDA Estimates**

Quota-AAN Relationship



AAN-MQ-PQ


AAN
IQ/MQ
IQ/MQ
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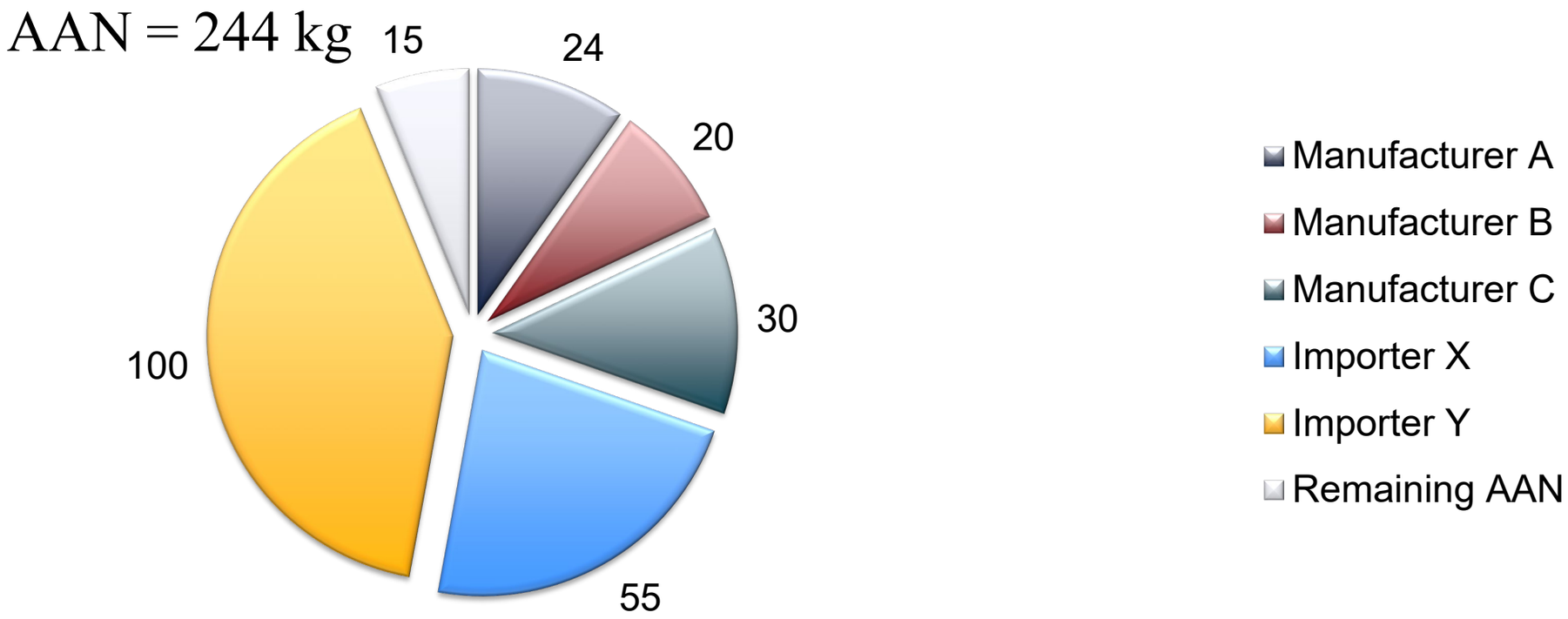
Relationship Between AAN and Import and Manufacturing Quotas



Import Quotas

- **Only DEA registered importer receive**
- **Only applies to EPH, PSE and PPA**
- **Establishes maximum amount which the individual importer can *import* in a *calendar year***
- **Importers cannot exceed import quota**

Import Quotas

Granted to DEA registrants based on:

- **Procurement and Manufacturing Quotas**
- **Sales & inventory of imported finished dosage form products**
- **Limited by the AAN (CMEA List I chemicals)**

Import Quota - FAQ

- **Can a DEA registered analytical lab import CMEA List I chemicals as a coincidental activity?**

  - No. Only DEA registered importers may import CMEA List I chemicals. Analytical labs may import controlled substances as a coincident activity only

21 CFR 1301.13(e)(1)(x)

CMEA Quota - FAQ

- **Does a manufacturer who consumes all of a CMEA List I chemical internally qualify as an “end user”?**

  - No. All DEA registered manufacturers who procure CMEA List I chemicals for a manufacturing activity must have quota, including those who do not distribute these CMEA List I chemicals

  - The absence of this information would prevent DEA from considering all relevant information required by law when establishing the AAN

Import Quota - FAQ

- **I am an importer and have a new customer. Can I supply the CMEA List I chemical to them?**

  - You may import to the extent of your firms import quota and may supply the CMEA List I chemical to your customers who can supply certification that they have quota to receive this material

  - You may request an adjustment to your firms import quota at anytime

  - You must comply with all other requirements applicable to the sale of a CMEA List I chemical, including obtaining proof of identity and of registration status.

  - You may need to update your import declaration per 21 CFR 1313.16.

Review for exercises: Who gets quota?

Importers of ephedrine, pseudoephedrine & PPA

- Includes importers of bulk and Dosage Units

Manufacturers of ephedrine, pseudoephedrine and phenylpropanolamine (PPA)

- Includes bulk manufacturers (manufacturers of API)
- Manufacturers of finished dosage units
- Packagers, repackagers, labelers & relabelers

Manufacturers of Schedule I & II Controlled Substances

- Includes bulk manufacturers (manufacturers of API)
- Manufacturers of finished dosage units
- Packagers, repackagers, labelers & relabelers

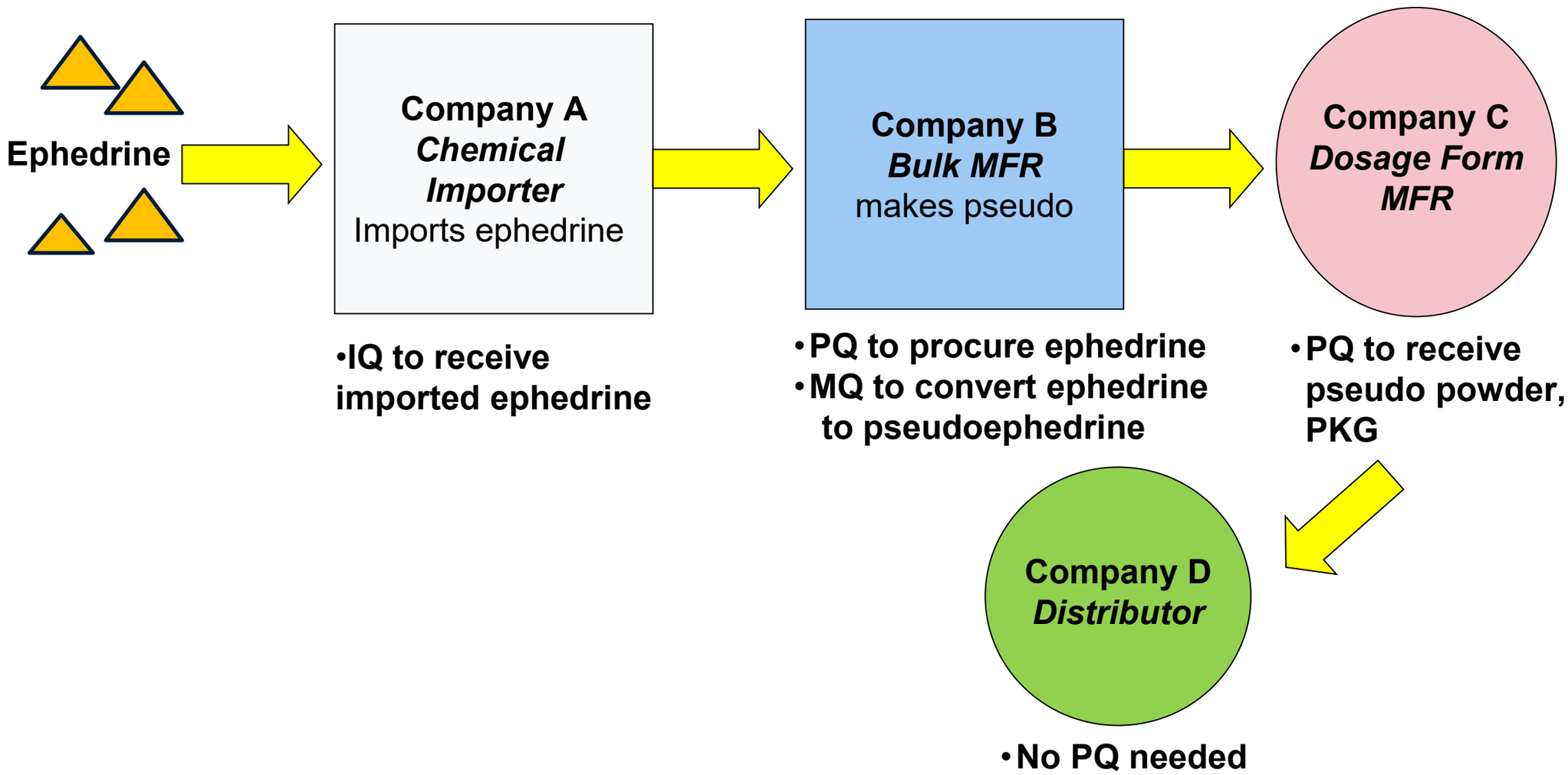
Active Pharmaceutical Ingredient (API)

Exercise 1: Who needs Quota?
Following a Product From Start To Finish

- **Company A imports bulk ephedrine for conversion into pseudoephedrine by their bulk manufacturer Company B**

- **Company B sells the pseudoephedrine to Company C which converts the bulk pseudoephedrine into dosage forms, packages and sends to Company D for distribution**

Exercise 1: Who needs Quota?
Import EPH to PSE



Exercise 1: Who needs Quota?
Answers:

- **Company A – importer**
  - Import Quota (ephedrine) is required to import the ephedrine into the U.S. under an importer registration

- **Company B - bulk manufacturer**
  - Procurement Quota (ephedrine) is required by the manufacturing registration (if different DEA Registration #) to receive the ephedrine from their importer registration
  - Manufacturing Quota (pseudoephedrine) is required to manufacture pseudoephedrine from the ephedrine

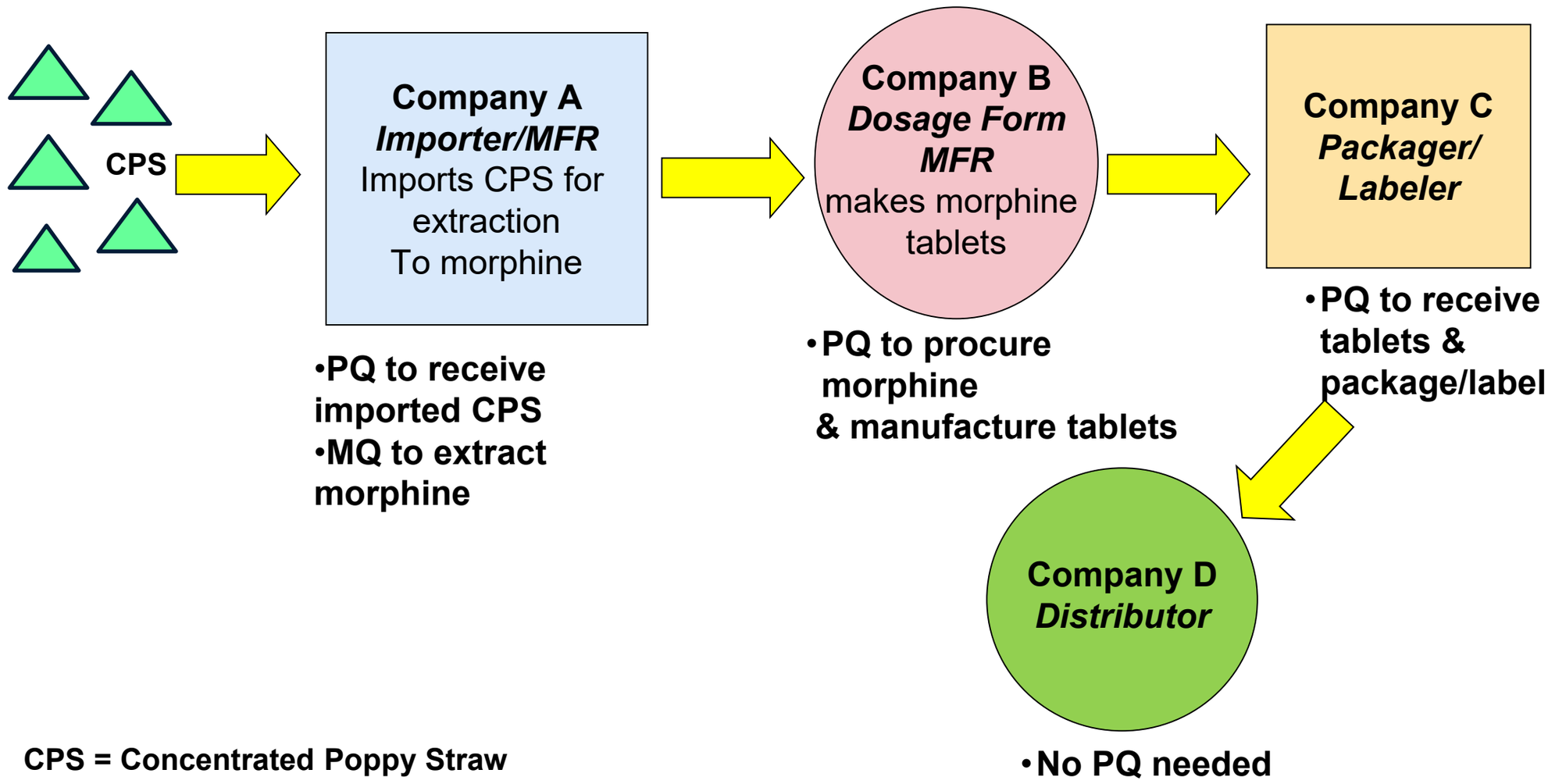
- **Company C – dosage form manufacturer**
  - Procurement Quota (pseudoephedrine) is required to procure bulk pseudoephedrine for dosage form manufacturing

- **Company D – distributor**
  - NO QUOTA NEEDED for distributors

Exercise 2: Who needs Quota?
Following a Product From Start To Finish

- Company A imports poppy straw for morphine extraction. They sell the extracted morphine to company B which converts the bulk morphine into beads and encapsulates them
- Company B sends the finished morphine capsules to their bottling and labeling company C
- Company C bottles and labels the finished dosage units and sends them to Company D for distribution

Exercise 2: Who needs Quota?
Poppy Straw to Distributor



CPS = Concentrated Poppy Straw

Exercise 2: Who needs Quota?
Answers:

- **Company A – Importer & bulk manufacturer**
  - Procurement Quota (CPS) is required to receive the imported material. (NO Import Quota required since not CMEA List I Chemical)
  - Manufacturing Quota (morphine) is required to extract morphine from the poppy straw

- **Company B – dosage form manufacturer**
  - Procurement Quota (morphine) is required to procure bulk morphine for dosage form manufacturing

- **Company C – relabeler/repackager manufacturer**
  - Procurement Quota (morphine) is required to acquire the finished dosage units for packaging and product labeling

- **Company D – distributor**
  - NO QUOTA NEEDED for distributors

Questions?

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