

Supplementary Information

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Mobile-Distributed Pharmaceutical Manufacturing Supply Chain Network Optimization
Under Uncertainty

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Sets

$i \in \mathbf{I}$	Set of commodities
\mathbf{I}^k	Set of active pharmaceutical ingredients (APIs)
\mathbf{I}^{rm}	Set of raw materials
\mathbf{I}^{dp}	Set of finished drug products
$n \in \mathbf{N}$	Set of all network nodes
\mathbf{N}^s	Supplier nodes
\mathbf{N}^m	API synthesis nodes (mobile units)
\mathbf{N}^t	Tableting (drug-product manufacturing) nodes
\mathbf{N}^w	Warehouse / storage nodes
\mathbf{N}^d	Distribution-center nodes
$l_1, l_2 \in \mathbf{LOCS}$	Set of candidate locations for the mobile modules
$tm \in \mathbf{TM}$	Set of transportation modes
$t \in \mathbf{T}$	Discrete time horizon
$sc \in \mathbf{SC}$	Set of scenarios

Parameters

$\eta_{i,n}$	Synthesis yield of API $i \in \mathbf{I}^k$ at module $n \in \mathbf{N}^m$
$\delta_{i,n}$	Tableting yield of drug product $i \in \mathbf{I}^{dp}$ at site $n \in \mathbf{N}^t$
$\text{scap}_{i,n}$	Supplier capacity for raw material $i \in \mathbf{I}^{rm}$ at $n \in \mathbf{N}^s$ [kg]
$\text{mcap}_{i,n}$	API production capacity of module $n \in \mathbf{N}^m$ [kg]
$\text{tcap}_{i,n}$	Tableting production capacity at $n \in \mathbf{N}^t$ [kg]
$\text{wcap}_{i,n}$	Warehouse storage capacity at $n \in \mathbf{N}^w$ [kg]
$C_{i,n}^{\text{raw}}$	Purchase cost of raw material i at supplier n [\$/kg]
$C_{i,n}^{\text{syn}}$	API synthesis operating cost at module n [\$/kg]
$C_{i,n}^{\text{tab}}$	Tableting operating cost at site n [\$/kg]
C_{tm}^{trans}	Transportation cost of mode tm [\$/((km·kg))]
C^{transMod}	Module relocation cost [\$/km]
C_w^{inv}	Inventory holding cost at warehouse w [\$/((kg·month))]
C^{short}	Penalty for unmet demand (shortage) [\$/kg]
C^{exc}	Penalty for over-served demand (excess) [\$/kg]
$C^{\text{activation}}$	Fixed activation cost per node [\$/node]
C_n^E, C_n^H, C_n^C	Unit costs of electricity, hot utility, and cold utility
$e_n^{\text{rate}}, h_n^{\text{rate}}, c_n^{\text{rate}}$	Electricity, hot- and cold-utility consumption rates per kg of production
$D_{i,n,t,sc}$	Demand for drug product i at DC n in period t , scenario sc [kg]
P_{sc}	Probability of scenario $sc \in \mathbf{SC}$
$L_{n,n'}$	Great-circle distance between nodes n and n' [km]
R	Earth radius, 6371 km
M	Big-M constant (capacity-based upper bound)
$l_0(n)$	Initial location assigned to module $n \in \mathbf{N}^m$
Lat_n	Latitude of node $n \in \mathbf{N}$, $l \in \mathbf{LOCS}$
$Long_n$	Longitude of node $n \in \mathbf{N}$, $l \in \mathbf{LOCS}$

Variables

Continuous, non-negative decision and state variables:

$F_{i,n,t,sc}^{\text{supplied}}$	Quantity of raw material i supplied at supplier n
$F_{n,n',i,t,sc}^{\text{in}}$	Inbound commodity flow of i on arc (n, n')
$F_{n,n',i,t,sc}^{\text{out}}$	Outbound commodity flow of i on arc (n, n')
$F_{i,n,t,sc}^{\text{API}}$	Quantity of API i produced at synthesis module n
$F_{i,n,t,sc}^{\text{tab}}$	Quantity of drug product i produced at tableting site n
$F_{i,n,t,sc}^{\text{storage}}$	Inventory of drug product i held at warehouse n
$F_{i,n,t,sc}^{\text{DC}}$	Quantity of drug product i delivered to distribution center n
$F_{i,n,t,sc}^{\text{short}}$	Demand shortage of drug product i at DC n
$F_{i,n,t,sc}^{\text{exc}}$	Demand excess of drug product i at DC n
E_n, Q_n^H, Q_n^C	Electricity, hot-utility, and cold-utility demand at node n
$d_{n,n',t,sc}$	Effective transportation distance on arc (n, n')
C_{sc}^{rm}	Raw-material cost in scenario sc
C_{sc}^{API}	API synthesis cost in scenario sc
C_{sc}^{tab}	Tableting cost in scenario sc
C_{sc}^{ut}	Utility cost in scenario sc
C_{sc}^{trans}	Transportation cost in scenario sc
C_{sc}^{move}	Module relocation cost in scenario sc
C_{sc}^{storage}	Inventory holding cost in scenario sc
C_{sc}^{short}	Shortage penalty cost in scenario sc
C_{sc}^{exc}	Excess penalty cost in scenario sc
C^{act}	First-stage activation cost

Binary Decision Variables

Y_n	= 1 if node n is activated
$YMA_{n,l,t,sc}$	= 1 if mobile module n is assigned to location l in period t , scenario sc
$YMM_{n,l_1,l_2,t,sc}$	= 1 if module n moves from location l_1 to l_2 between periods t and $t + 1$

Equations

Suppliers

The quantity supplied of each raw material equals the total outbound flow toward the downstream synthesis modules, bounded by the activated supplier capacity:

$$F_{i,n,t,sc}^{\text{supplied}} = \sum_{n' \in \mathbf{N}^m} F_{n,n',i,t,sc}^{\text{out}}, \quad \forall i \in \mathbf{I}^{rm}, n \in \mathbf{N}^s, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S1})$$

$$F_{i,n,t,sc}^{\text{supplied}} \leq \text{scap}_{i,n} Y_n, \quad \forall i \in \mathbf{I}^{rm}, n \in \mathbf{N}^s, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S2})$$

API synthesis

The API produced at each module is the yield-weighted sum of incoming raw-material flows, bounded by the activated module capacity. Equation (S5) additionally forces production to zero unless the module is physically present at a candidate location:

$$F_{i,n,t,sc}^{\text{API}} = \sum_{i' \in \mathbf{I}^{rm}} \eta_{i,n} F_{n',n,i',t,sc}^{\text{in}}, \quad \forall i \in \mathbf{I}^k, n \in \mathbf{N}^m, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S3})$$

$$\sum_{i \in \mathbf{I}^k} F_{i,n,t,sc}^{\text{API}} \leq \text{mcap}_{i,n} Y_n, \quad \forall n \in \mathbf{N}^m, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S4})$$

$$F_{i,n,t,sc}^{\text{API}} \leq M \sum_{l \in \mathbf{LOCS}} YMA_{n,l,t,sc}, \quad \forall i \in \mathbf{I}^k, n \in \mathbf{N}^m, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S5})$$

Tableted drug-product manufacturing

The tablet output is the yield-weighted sum of incoming API flows, bounded by the activated tableting capacity:

$$F_{i,n,t,sc}^{\text{tab}} = \sum_{i' \in \mathbf{I}^k} \delta_{i,n} F_{n',n,i',t,sc}^{\text{in}}, \quad \forall i \in \mathbf{I}^{dp}, n \in \mathbf{N}^t, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S6})$$

$$\sum_{i \in \mathbf{I}^{dp}} F_{i,n,t,sc}^{\text{tab}} \leq \text{tcap}_{i,n} Y_n, \quad \forall n \in \mathbf{N}^t, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S7})$$

Storage

The warehouse inventory balance carries stock across periods, bounded by the activated warehouse capacity:

$$F_{i,n,t,sc}^{\text{storage}} = F_{i,n,t-1,sc}^{\text{storage}} + \sum_{n' \in \mathbf{N}^t} F_{i,n',n,t,sc}^{\text{in}} - \sum_{n'' \in \mathbf{N}^d} F_{i,n,n'',t,sc}^{\text{out}}, \quad \forall i \in \mathbf{I}^{dp}, n \in \mathbf{N}^w, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S8})$$

$$F_{i,n,t,sc}^{\text{storage}} \leq \text{wcap}_{i,n} Y_n, \quad \forall i \in \mathbf{I}^{dp}, n \in \mathbf{N}^w, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S9})$$

Distribution centers and demand balance

Delivered quantity equals the inflow from connected warehouses; the demand balance closes the network through the shortage and excess variables:

$$F_{i,n,t,sc}^{\text{DC}} = \sum_{n' \in \mathbf{N}^w} F_{i,n',n,t,sc}^{\text{in}}, \quad \forall i \in \mathbf{I}^{dp}, n \in \mathbf{N}^d, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S10})$$

$$F_{i,n,t,sc}^{\text{DC}} + F_{i,n,t,sc}^{\text{short}} - F_{i,n,t,sc}^{\text{exc}} = D_{i,n,t,sc}, \quad \forall i \in \mathbf{I}^{dp}, n \in \mathbf{N}^d, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S11})$$

Logical and module-dynamics constraints

The node-activation big-M constraint forces all inflows to zero at a deactivated node:

$$F_{n,n',i,t,sc}^{\text{in}} \leq M Y_n, \quad \forall n \in \mathbf{N}, i \in \mathbf{I}, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S12})$$

Each module starts at its designated location, occupies exactly one location per period, and its inter-period movement is tracked by the directional move variables:

$$YMA_{n,l_0(n),1,sc} = 1, \quad \forall n \in \mathbf{N}^m, sc \in \mathbf{SC} \quad (\text{S13})$$

$$\sum_{l \in \mathbf{LOCS}} YMA_{n,l,t,sc} = 1, \quad \forall n \in \mathbf{N}^m, t \in \mathbf{T}, sc \in \mathbf{SC} \quad (\text{S14})$$

$$YMA_{n,l,t,sc} - YMA_{n,l,t-1,sc} = \sum_{\substack{l' \in \mathbf{LOCS} \\ l' \neq l}} YMM_{n,l',l,t-1,sc} - \sum_{\substack{l' \in \mathbf{LOCS} \\ l' \neq l}} YMM_{n,l,l',t-1,sc}, \quad (\text{S15})$$

$$\forall n \in \mathbf{N}^m, l \in \mathbf{LOCS}, t \in \mathbf{T}, sc \in \mathbf{SC}$$

Cost structure

The raw-material, API synthesis, and tableting cost components:

$$C_{sc}^{rm} = \sum_{i \in \mathbf{I}^{rm}} \sum_{n \in \mathbf{N}^s} \sum_{t \in \mathbf{T}} C_{i,n}^{raw} F_{i,n,t,sc}^{supplied} \quad (\text{S16})$$

$$C_{sc}^{API} = \sum_{i \in \mathbf{I}^k} \sum_{n \in \mathbf{N}^m} \sum_{t \in \mathbf{T}} C_{i,n}^{syn} F_{i,n,t,sc}^{API} \quad (\text{S17})$$

$$C_{sc}^{tab} = \sum_{i \in \mathbf{I}^{dp}} \sum_{n \in \mathbf{N}^t} \sum_{t \in \mathbf{T}} C_{i,n}^{tab} F_{i,n,t,sc}^{tab} \quad (\text{S18})$$

Utility demands are obtained by scaling reference demands by the realized API throughput; the utility cost aggregates the three utility streams:

$$E_n = D^{\text{RefE}} \frac{\sum_i F_{i,n,t,sc}^{API}}{F^{\text{RefS}}}, \quad Q_n^H = D^{\text{RefH}} \frac{\sum_i F_{i,n,t,sc}^{API}}{F^{\text{RefS}}}, \quad Q_n^C = D^{\text{RefC}} \frac{\sum_i F_{i,n,t,sc}^{API}}{F^{\text{RefS}}} \quad (\text{S19})$$

$$C_{sc}^{ut} = \sum_{n \in \mathbf{N}^m \cup \mathbf{N}^t} \sum_{t \in \mathbf{T}} (C_n^E E_n + C_n^H Q_n^H + C_n^C Q_n^C) \quad (\text{S20})$$

The transportation cost multiplies flow, the per-distance shipping rate, and the inter-node distance, where the distance is selected by the realized module assignment (Eq. S23) and reduces to the Haversine distance (Eq. S24) for fixed-location arcs:

$$C_{sc}^{trans} = \sum_{(n,n') \in \mathbf{E}} \sum_{i \in \mathbf{I}} \sum_{t \in \mathbf{T}} C_{tm}^{trans} F_{i,n,n',t,sc} d_{n,n',t,sc} \quad (\text{S21})$$

$$d_{n,n',t,sc} = \begin{cases} \sum_{l \in \mathbf{LOCS}} YMA_{n,l,t,sc} L_{l,n'} & n \in \mathbf{N}^m, \\ \sum_{l \in \mathbf{LOCS}} YMA_{n',l,t,sc} L_{n,l} & n' \in \mathbf{N}^m, \\ L_{n,n'}, & \text{otherwise} \end{cases} \quad (\text{S22})$$

$$L_{l_1,l_2} = 2R \arcsin \left(\sqrt{\sin^2 \left(\frac{\Delta \text{lat}_{l_1,l_2}}{2} \right) + \cos(\text{lat}_{l_1}) \cos(\text{lat}_{l_2}) \sin^2 \left(\frac{\Delta \text{lon}_{l_1,l_2}}{2} \right)} \right) \quad (\text{S23})$$

The module-relocation cost penalizes every active move per kilometer; the remaining components are inventory holding, demand-side penalties, and the first-stage activation cost:

$$C_{sc}^{move} = \sum_{n \in \mathbf{N}^m} \sum_{l_1, l_2 \in \mathbf{LOCS}} \sum_{t \in \mathbf{T}} C^{\text{transMod}} L_{l_1,l_2} YMM_{n,l_1,l_2,t,sc} \quad (\text{S24})$$

$$C_{sc}^{storage} = \sum_{i \in \mathbf{I}^{dp}} \sum_{n \in \mathbf{N}^w} \sum_{t \in \mathbf{T}} C_w^{\text{inv}} F_{i,n,t,sc}^{\text{storage}} \quad (\text{S25})$$

$$C_{sc}^{short} = \sum_{i \in \mathbf{I}^{dp}} \sum_{n \in \mathbf{N}^d} \sum_{t \in \mathbf{T}} C^{\text{short}} F_{i,n,t,sc}^{\text{short}} \quad (\text{S26})$$

$$C_{sc}^{\text{exc}} = \sum_{i \in \mathbf{I}^{dp}} \sum_{n \in \mathbf{N}^d} \sum_{t \in \mathbf{T}} C^{\text{exc}} F_{i,n,t,sc}^{\text{exc}} \quad (\text{S27})$$

$$C^{\text{act}} = C^{\text{activation}} \sum_{n \in \mathbf{N}} Y_n \quad (\text{S28})$$

Objective Function

The model minimizes the expected total operational cost across the scenario set plus the scenario-independent activation cost:

$$\min SPCost = \sum_{sc \in \mathbf{SC}} P_{sc} \left(C_{sc}^{rm} + C_{sc}^{API} + C_{sc}^{tab} + C_{sc}^{cut} + C_{sc}^{trans} + C_{sc}^{move} + C_{sc}^{storage} + C_{sc}^{short} + C_{sc}^{exc} \right) + C^{act} \quad (\text{S29})$$

Table S1: Set definitions and members.

Set	Size	Members
$\mathbf{I}^k / \mathbf{I}^{rm} / \mathbf{I}^{dp}$	1 / 1 / 1	API1 / RM1 / DP1 (single paracetamol product)
\mathbf{N}^s	2	S1, S2
\mathbf{N}^m	3	M1, M2, M3
\mathbf{N}^t	2	T1, T2
\mathbf{N}^w	2	W1, W2
\mathbf{N}^d	5	DC1, DC2, DC3, DC4, DC5
LOCS	3	LOC1, LOC2, LOC3
T	6	$t = 1, \dots, 6$ (months)
SC	5	SC1–SC5
tm	1	TM1

Parameter Values

The following tables list the numerical values used in the case study: a compact U.S. Midwest network for a single drug product, paracetamol, with two suppliers, three mobile API synthesis modules over three candidate locations, two tableting sites, two warehouses, and five distribution centers, over a six-month horizon with five demand scenarios.

Table S2: Yield parameters.

Parameter	Value	Units
η_{API1} (synthesis yield)	0.97	–
δ_{DP1} (tableting yield)	0.95	–

Table S3: Capacity parameters.

Parameter	Node	Value	Units
Supplier capacity scap	S1 / S2	10 000 / 12 000	kg
Module API capacity mcap	M1 / M2 / M3	4 000 / 4 500 / 5 000	kg
Tableting capacity tcap	T1 / T2	100 000 / 100 000	kg
Warehouse capacity wcap	W1 / W2	1 000 000 / 1 200 000	kg

Table S4: Cost parameters.

Parameter	Node / mode	Value	Units
Raw-material cost C^{raw}	S1 / S2	10 / 14	\$/kg
API synthesis cost C^{syn}	M1 / M2 / M3	60 / 50 / 40	\$/kg
Tableting cost C^{tab}	T1 / T2	25 / 20	\$/kg
Transportation cost C^{trans}	TM1	0.6	\$/(\text{km}\cdot\text{kg})
Module relocation cost C^{transMod}	–	4	\$/km
Inventory holding cost C^{inv}	W1 / W2	2.0 / 1.8	\$/(\text{kg}\cdot\text{month})
Shortage penalty C^{short}	–	10 000	\$/kg
Excess penalty C^{exc}	–	1 000	\$/kg
Node activation cost $C^{\text{activation}}$	–	200 000	\$/node
Electricity unit cost C^E	–	0.10	\$/kWh
Hot-utility unit cost C^H	–	0.020	\$/MJ
Cold-utility unit cost C^C	–	0.015	\$/MJ

Table S5: Utility consumption rates. Electricity in kWh per kg of production; hot/cold utilities in kJ per kg of production.

Node	Electricity [kWh/kg]	Hot utility [kJ/kg]	Cold utility [kJ/kg]
M1	25	10 000	8 000
M2	22	9 000	7 500
M3	20	8 000	7 000
T1	2.5	2 500	1 500
T2	2.0	2 200	1 200

Table S6: Node geographic coordinates and candidate locations. The three candidate locations LOC1–LOC3 coincide with the initial positions of modules M1–M3, respectively.

Node	Type	City	Latitude	Longitude
S1	Supplier	Chicago, IL	41.8781	–87.6298
S2	Supplier	Detroit, MI	42.3314	–83.0458
M1 / LOC1	Module / candidate	Indianapolis, IN	39.7684	–86.1581
M2 / LOC2	Module / candidate	Des Moines, IA	41.5868	–93.6250
M3 / LOC3	Module / candidate	Springfield, IL	39.7817	–89.6501
T1	Tableting	Louisville, KY	38.2527	–85.7585
T2	Tableting	Fayetteville, AR	36.0822	–94.1718
W1	Warehouse	Nashville, TN	36.1627	–86.7816
W2	Warehouse	Kansas City, MO	39.0997	–94.5786
DC1	Dist. center	Memphis, TN	35.1495	–90.0490
DC2	Dist. center	Omaha, NE	41.2565	–95.9345
DC3	Dist. center	Minneapolis, MN	44.9778	–93.2650
DC4	Dist. center	Wichita, KS	37.6872	–97.3301
DC5	Dist. center	Grand Rapids, MI	42.9634	–85.6681

Table S7: Demand parameters. The demand at each DC in period t and scenario sc is $D_{i,n,t,sc} = \text{base}_n \cdot m_{sc}$, where base_n is the base monthly demand and m_{sc} the scenario demand multiplier (Table S8).

Distribution center	Base demand [kg/month]
DC1	500
DC2	2 000
DC3	1 000
DC4	800
DC5	500

Table S8: Demand scenarios generated from a Monte Carlo analysis of historical Medicare Part D fill data (sigma-based discretization, $K = 5$). The cost factors multiply the raw-material, transportation, and energy cost terms of the corresponding scenario; in this instance the supplier-availability and production-capacity factors remain at 1.0 for all scenarios.

Scenario	Level	Prob.	Demand	Cost factors		
				P_{sc}	mult. m_{sc}	RawMat
SC1	Very low	0.10	0.815	1.000	1.000	1.000
SC2	Low	0.23	0.912	1.000	1.000	1.000
SC3	Normal	0.34	0.995	1.000	1.000	1.000
SC4	High	0.23	1.077	1.023	1.015	1.012
SC5	Very high	0.10	1.174	1.052	1.035	1.026