

What the New Bio/Pharma Business Model Means for CMOs and CROs

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Interphex
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Agenda

Outline

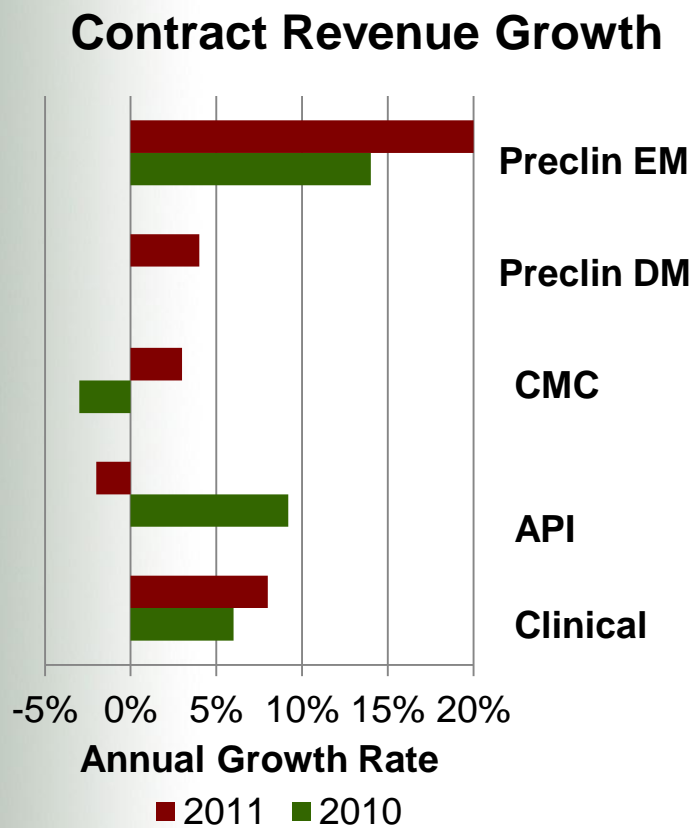
- 2011 review
- New bio/pharma business model
- Key challenges and opportunities
- Final thoughts

Key points

- Strengthening market
- New pharma priorities
- Pharma still investing in manufacturing facilities
- New pharma manufacturing needs and technologies
- Preferred provider model favors larger suppliers

2011 review

Contract services market improved

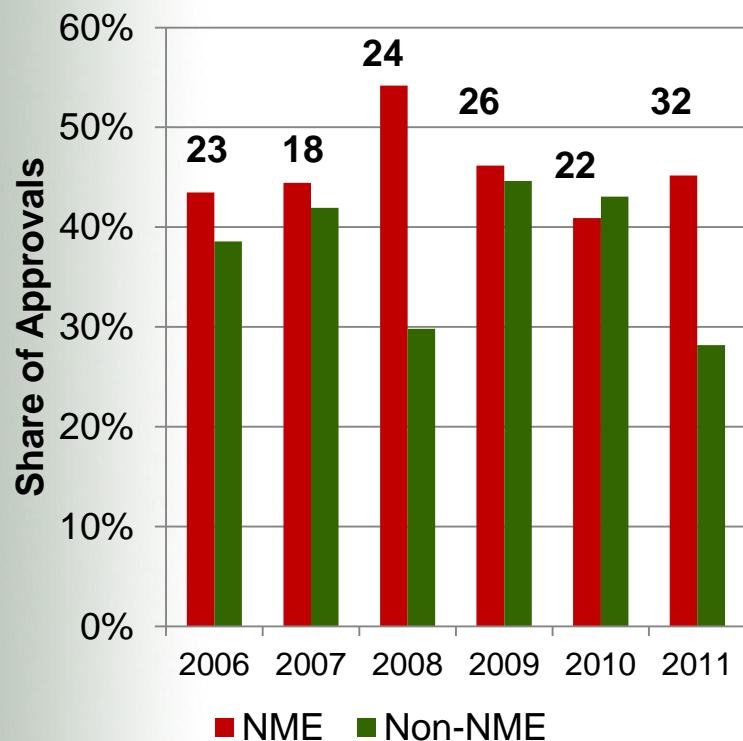


- Most of contract services industry enjoyed more growth in 2011
- Discovery services providers in Asia grew most rapidly
- API manufacturers hurt by Swiss Franc strength
 - Many private API manufacturers did well

Dose CMO overview

NME approvals up, outsourced NMEs down

NDA Approvals by FDA



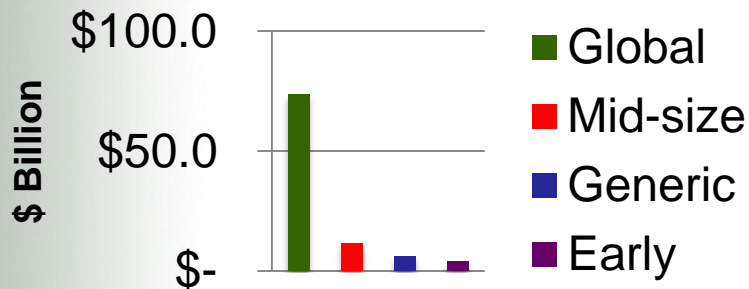
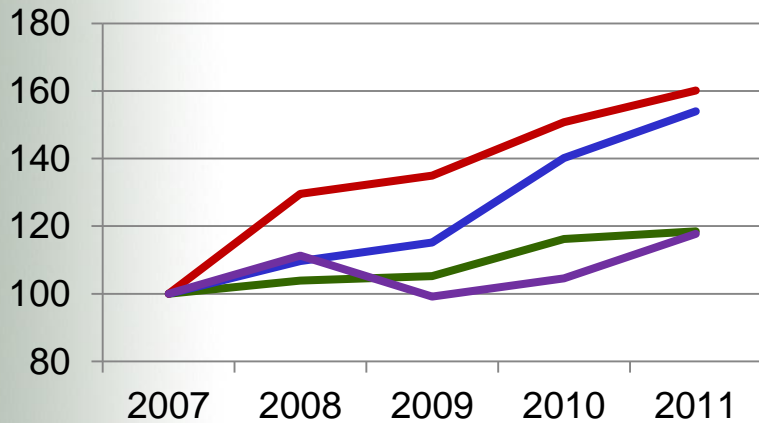
- High % of older APIs in 2011
 - 505(3) b filings
 - Branded generics, new forms
- Only 33% of injectable NMEs outsourced
 - 2006-2010 avg. = 51%
- 24 CMOs got approvals:
 - Patheon 7
 - DSM 3
 - Catalent 2

- Number above bar is number of NME approvals.
- Source: FDA data, PharmSource analysis

2011 review

R&D spending continues to climb

R&D Spending Index
2007=100

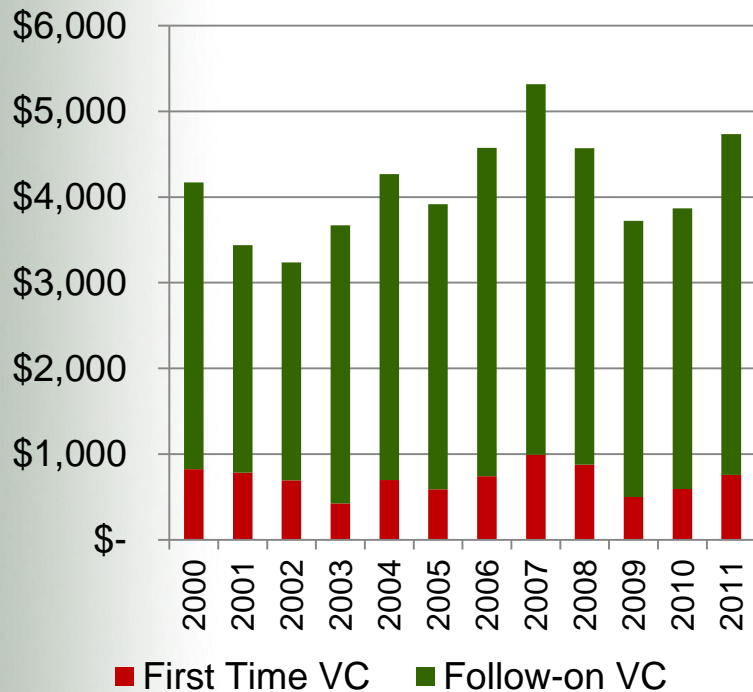


- Segments other than global bio/pharma spending more
- CMOs and CROs report rapid growth but not evenly
 - Phase 2/3 projects growing as early stage companies resurrect shelved projects
 - Preclinical/Phase 1 lags due to lack of financial support
- Global bio/pharma outsourcing more, esp. small molecule-related

R&D funding

Total VC up but early stage support weak

VC Investment in BioPharma in US

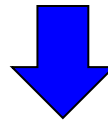


- Total venture capital has improved but established companies favored
- VCs favor companies with later phase candidates
 - Many were shelved in 2008 when funding was difficult
- Earliest stage companies are having a difficult time
- Likely to be less VC in future as investors back away

Bio/Pharma adapts to new environment

New industry environment

- Loss of blockbusters
- Price and volume resistance
- Low R&D productivity



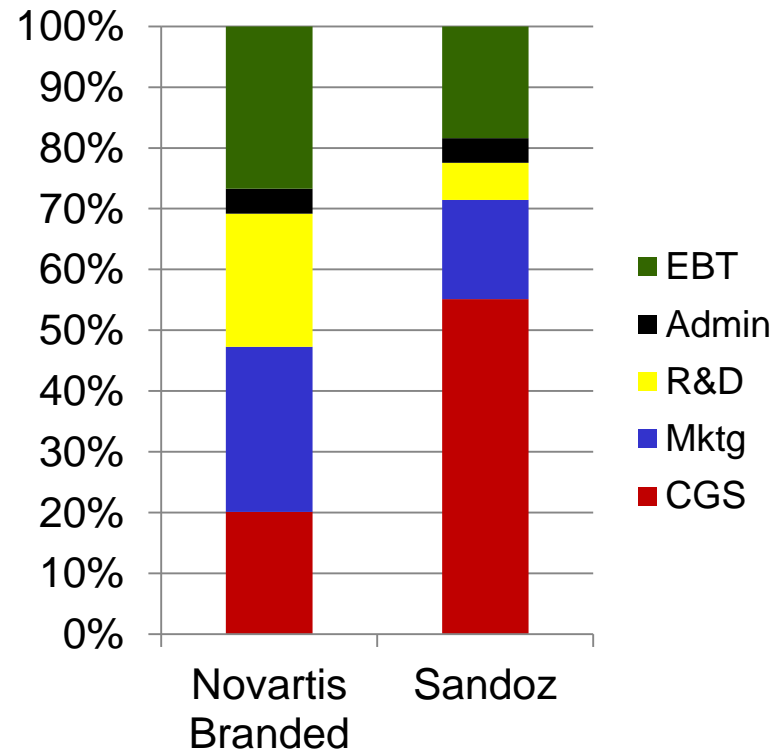
New growth opportunities	Reduce R&D Risk	Manage Costs
<ul style="list-style-type: none">• Biologics• Niche products• Emerging markets	<ul style="list-style-type: none">• Kill it early• POC focus• In-licensing• Partnering	<ul style="list-style-type: none">• Fewer therapeutic areas• Greater outsourcing

Challenges facing CR&D industry

Impact of price/volume pressure on bio/pharma

- **EU & US debt /cost crises**
 - Lower drug prices/ margins
 - Smaller volumes
 - Lack of bank capital (EU)
- **Margin squeeze hits costs**
 - Reduced R&D and marketing
 - Pressure to reduce cost of goods (CGS)
 - More outsourcing if cost-effective
- **Bio/pharma companies must preserve branded model**

Pharma Cost Structure



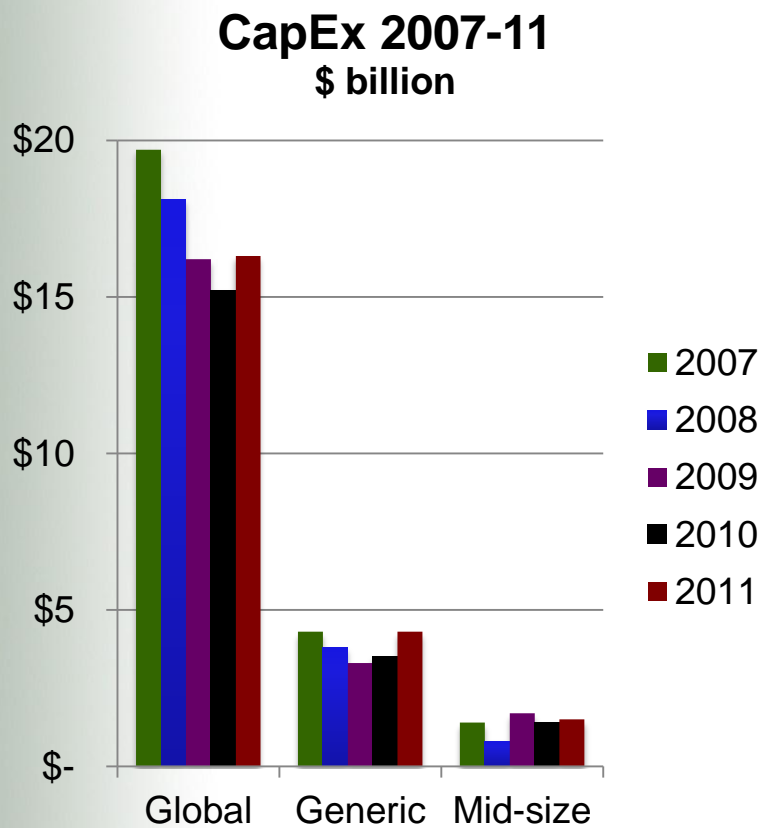
Global pharma trends

Outsourcing depends on value of know-how

Specialized Know-how	Foundational Know-how	Mature Know-how
<ul style="list-style-type: none"> Occasional need Costly to build/maintain 	<ul style="list-style-type: none"> Core to strategy Knowledge-generating 	<ul style="list-style-type: none"> Widely-available Routine Slow evolution
<ul style="list-style-type: none"> Materials engineering Cytotoxics Genetic mouse breeding 	<ul style="list-style-type: none"> Biomanufacturing Methods development Injectable formulations Protocol design 	<ul style="list-style-type: none"> Sm. mole API Solid dose Raw materials testing Trial monitoring
Propensity to outsource		
High	Low	High

Challenges facing CMO industry

Bio/pharma investing in growth targets



- Companies invest where there is growth
 - Large molecule API/dose
 - Vaccines
 - Emerging markets
- More countries granting tax-favored status to bio/pharma
 - UK
 - Ireland
 - Hungary
 - Singapore
 - Switzerland

Challenges facing CMO industry

Many projects recently announced or completed

Company	Facility	Details	Country	Investment
GSK	Dose	Expansion	Ireland	\$ 60
Merck	Dose	new vaccine facility	Ireland	\$ 270
Novartis	Dose	new facility	Russia	?
Roche	Dose	clinical supplies	Switzerland	\$ 270
GSK	Dose	facility expansion	UK	\$ 60
Genzyme	Dose-inject	Injectables	Ireland	\$ 208
Novartis	Dose-solid	OTCs	Switzerland	\$ 42
BI	Dose-solid	Hipo solid	USA	\$ 50
Roche	Dose-solid	clinical supplies	USA	?
Watson	Dose-specialty	patches and gels	USA	\$ 44

Challenges facing CMO industry

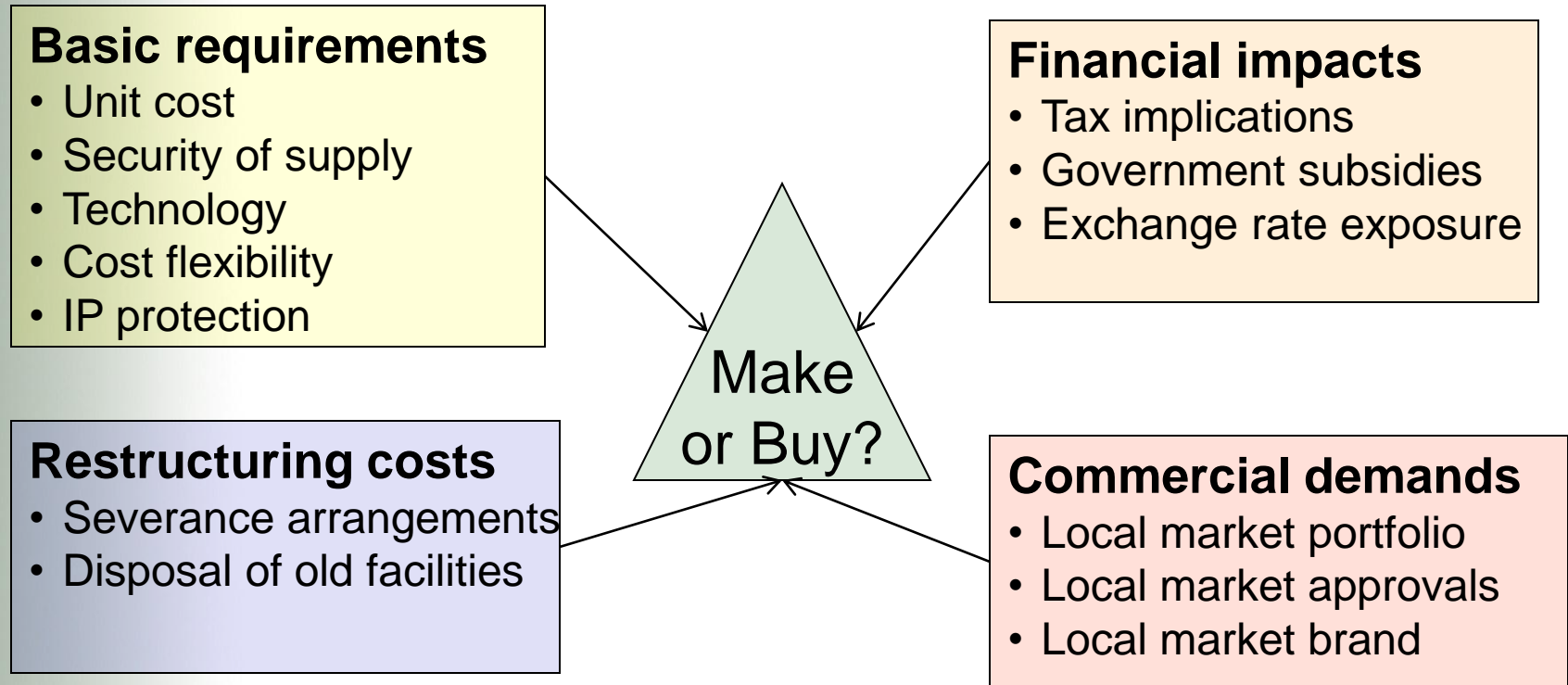
Tax incentives are difficult hurdle for CMOs

	Base Case	Tax Incentive	CGS Savings
Revenue	\$ 100	\$ 100	\$ 100
CGS	20	20	14
R&D	20	20	20
SG&A	<u>30</u>	<u>30</u>	<u>30</u>
EBT	30	30	36
Tax rate	25%	10%	25%
Net income	\$ 22.5	\$ 27.0	\$ 27.0

- Matching tax breaks requires big CGS savings
- Manufacturing costs must drop 30% to match tax savings

Challenges facing CMO industry

Global Pharma has complex manufacturing calculus



CMO model addresses only basic requirements

Challenges facing CMO industry

Lower unit volumes a threat

■ Lower volume products

- Niche products
- Orphan drugs
- Branded generics
- Emerging markets

■ Inventory management

- Lower inventories to free cash for deals

■ Long-term challenge

- Smaller CMOs compete for commercial work
- Traditional CMO cost structure a liability
 - Large scale, large batch campaigning model
- New technologies may change in-vs-out calculus

CMO industry will face new cost pressures and increased competition

Challenges facing CMO industry

New technologies challenge CMOs

■ API manufacture

- Microreactors
- Improving cell culture and fermentation yields
- Bioreactors in a bag

■ Dose manufacture

- Disposable contact parts
- Continuous processing
- Automation
- Pre-processed inputs (e.g., SCF syringes)

■ Lower capital costs

- Smaller facilities
- Simpler HVAC
- Smaller equipment

■ Lower operating costs

- Lower facility operating costs
- Less direct and indirect labor
- Faster line changeovers

■ Less working capital

- More inventory turns

CMO industry will face added competition from in-house manufacture even from smaller companies

Global pharma trends

Outsourcing favors preferred providers

Pharma	Preferred Clinical CRO Providers
Sanofi	Covance
Lilly	Covance, Quintiles, Icon, i3, Parexel
Pfizer	Icon, Parexel
GSK	PPD, Parexel
BMS	Icon, Parexel
Eisai	PPD
Otsuka	Covance
Elan	PPD
Takeda	Covance, Quintiles

- 80+% of outsourced clinical work going to preferred suppliers
- Previous experience, size and price drive choice of preferred provider
- Integrated service model winning out over functional services model

Challenges and trends facing CR&D industry

Integrated models for early development

	Services									
Business Model	Discovery Chem/Bio	Solid State chem	API Proc Dev	Preclin Tox	API CTM	Anal. Dev/Test	Dose Form	Dose CTM	Clin Pkg	
Fully integrated development	Aptuit, Wuxi, AMRI									
Integrated CMC						Biologics CMOs				
Integrated chemistry	ShangPharma, GVK					Ricerca				
Integrated dose						Patheon, Catalent				
Niche/specialty provider										

A strategic response to supplier consolidation and quick to clinic/quick to fail

Dose CMO overview

API/Dose one-stop CMOs emerging

■ Small molecule

- Siegfried
- AMRI
- Cambrex
- DSM

■ Large molecule

- Rentschler
- BI
- Laureate
- Cook Pharmica

■ Rationale

- Differentiate by offering customers single supplier
 - Reduce supply chain complexity
 - Reduce sourcing expense
- Capture more of spend

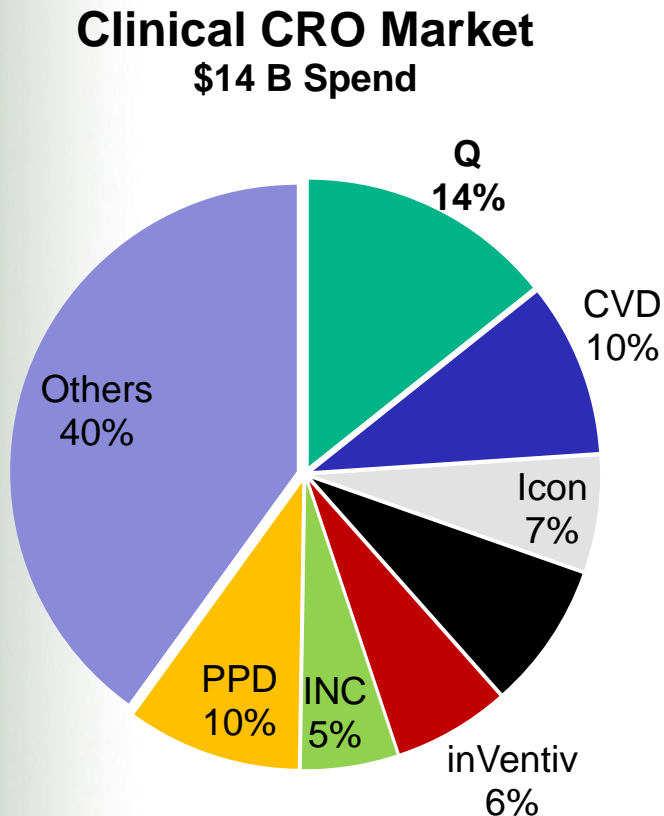
■ Will it be successful?

- Some traction in large molecule segment
- Will global bio/pharma buy it?

Potential threat to dose-only CMOs

Global pharma trends

Preferred deals force CROs to consolidate



- Major acquisitions build size
 - INC+Kendle = \$750 M
 - inVentiv + PharmaNet +i3 = \$900 M
 - But integration could be a distraction
- Market leaders build on scale
 - CVD: Data mining to make clinical site selection more efficient

Dose CMO overview

Consolidation underway, faces major hurdles

Consolidation events

- Ben Venue exit
- Nextpharma BE bankruptcy
- Patheon
 - Exits semisolids
 - Exits PR site
- CPL closed Buffalo site
- Osny absorbed by Cenexi
- Akrimax failure
- A few market leaders have differentiated themselves
 - Examples: Vetter, DPT

Consolidation drivers

- EU debt crisis
- Global pharma sourcing
- Return on capital focus

Consolidation barriers

- Low entry barriers
- High exit barriers
- Cost of moving products
- Weak differentiation
- Marginal CMO profitability
- Lack of capital

CMO consolidation could be messy,
and threaten drug supply

Final thoughts

- Industry undergoing slow consolidation
- External environment will pressure CMOs
- New manufacturing requirements and technologies are the greatest threats, not India and China
- Success strategies
 - Strong, reliable operating performance
 - Innovative business models