Essential Update on Contract Manufacturing and Quality Standards

CPhI, Paris.

Guy Villax

7th of October 2014

Agenda

- Short Introduction to Hovione
- Driving Forces Shaping the Market
- CMOs – Innovators and Generics perspectives
- FDA tips on vendor qualification programs
- New Regulations
- Quality Metrics

Hovione's Product and Service Offering

Contract Manufacturing Services

Drug Substance

Particle Engineering

Drug Product

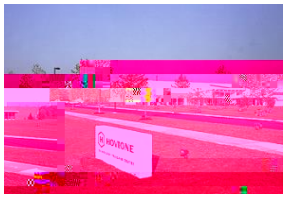
Off-Patent APIs

Proprietary Product Licensing

Global Presence Con CG [(Cn 655.3- 6(d)-fo1(PreonG Nort3-

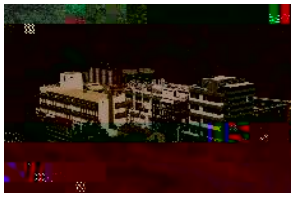
Science based, present in all segments

New Jersey, USA
Technology transfer center.
Process chemistry R&D Labs, Kilo plant and pilot plant.
Sales and marketing for North America



Loures, Portugal
430 m^3 manufacturing facilities.
Process chemistry R&D Labs, kilo and pilot plants

Macau, China
100 m^3



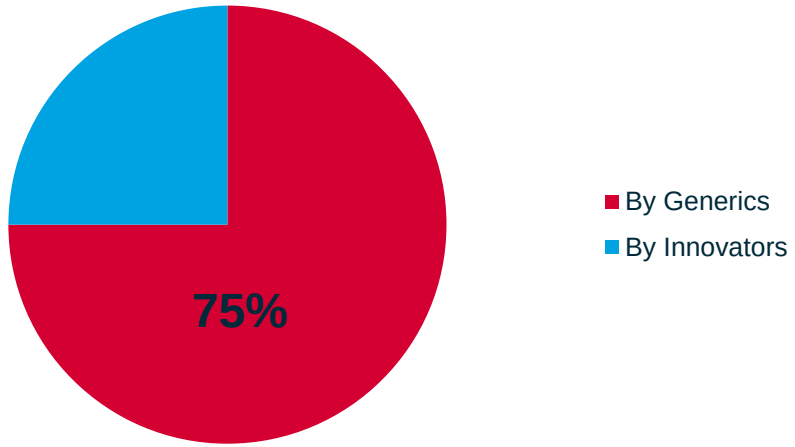
At Hovione we are making strides into the third

Driving Forces

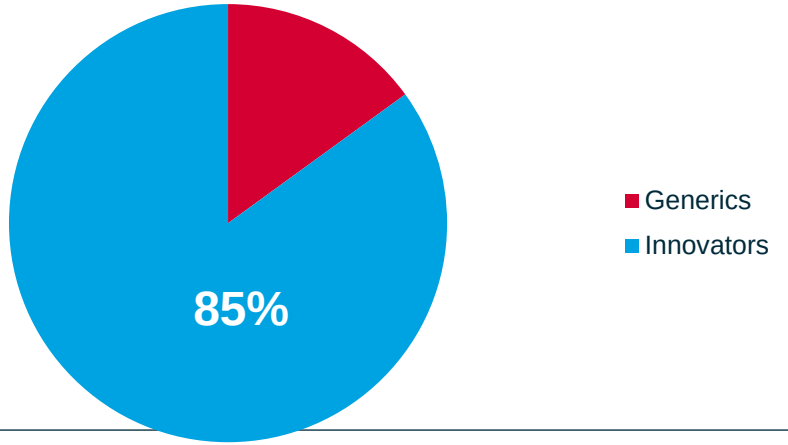
Quantity

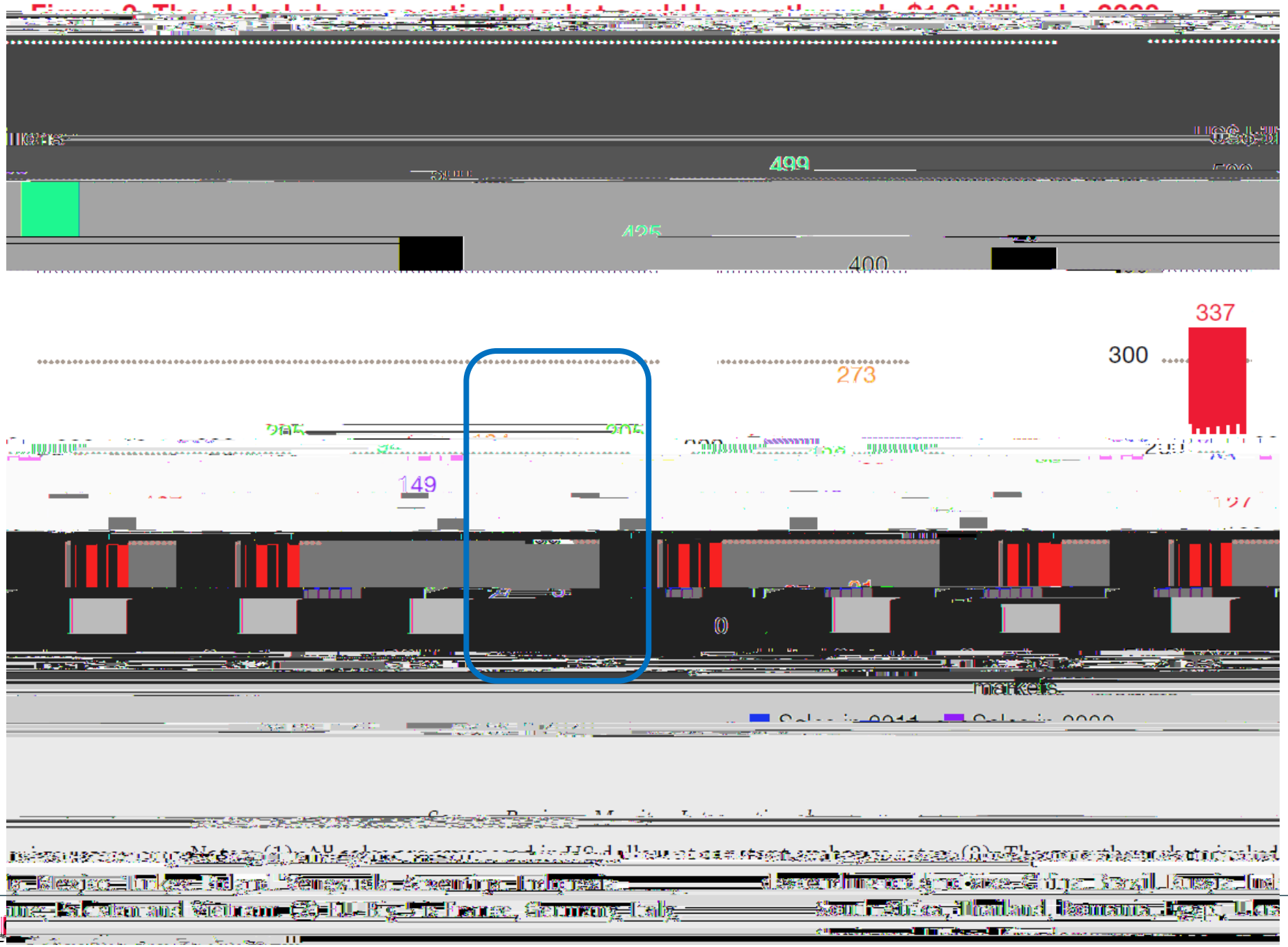
- Big Pharma: now a Minority Player
- Generics: from Pirates to Leaders
- NDAs approved: no longer blockbusters
- An ageing population
- Cost pressures

Prescriptions filled



Sales in Value




499
425
400
337
300
273
149
0

Growth yes, but somewhere else, and again in Generics

Hovione Press Conference at CPhI EMC /P 4MCID 42BDC q-0.40-0.40-0.40

Trends in the Supply Chain - Innovators

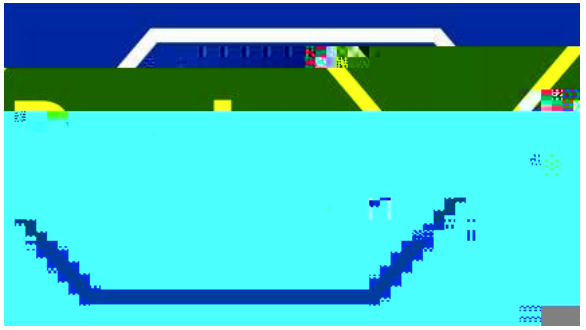
Big pharma will evolve :

Trends in the Supply Chain - Innovators

Big pharma will evolve :

Some will become more like Unilever

Some will focus on innovating only



Trends in the Supply Chain - Innovators

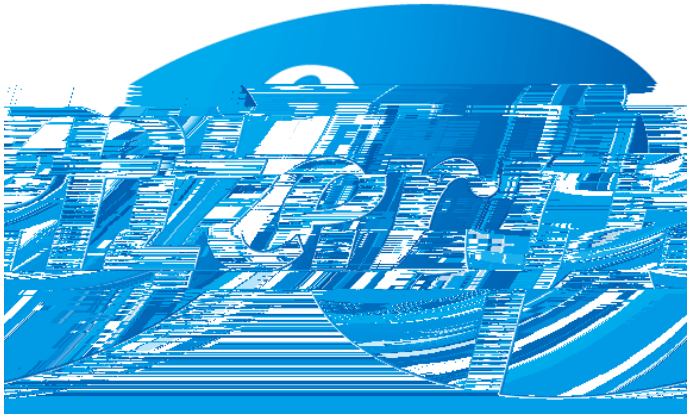
Big pharma will evolve :

Some will become more like Unilever

Some will focus on innovating only

Some will stop being of two minds

Some will get focused



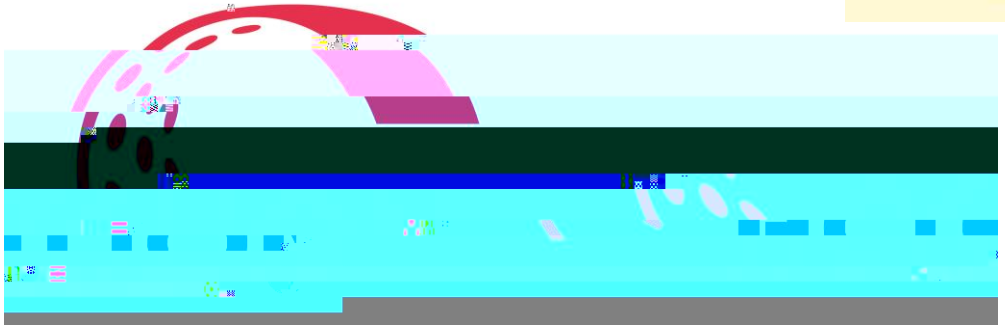
Nestlé completes acquisition of Pfizer Nutrition

zoetis

FOR ANIMALS. FOR HEALTH. FOR YOU.

Trends in the Supply Chain - Innovators

...and new companies will emerge



Rapidly escalating diversity and depth of technology and methodologies, with specific purposefulness to address:

Increasingly complex molecules, decreasingly bioavailable

Increasingly compounds are patient group specific (smaller volumes)

Deliberately specificed delivery mechanism and place

QbD, PAT, DOE, mathematical models

- CapEx is not available
- No longer possible to have it all in-house,

Trends in the Supply Chain - Innovators

... Implications of QbD to the CMC section and Regulatory Approval

CMC cant be “thrown over the wall”, the regulatory review will need dialogues

Sponsor is not just the ONE company; but a team of specialists in-house & CMOs

Reviewers and Inspectors need to work together – before and after the filing

- Adversarial confrontation must make way for a science based debate, the review and the inspection -as far as CMC is concerned- needs to be an honest challenge and an education – both ways.

Changes to the supply chain – Innovators outsource

Big Pharma has been looking for cost reductions in Asia...

Supply chain structure under intense price pressure – hence:

Fragmentation, Specialization, Consolidation

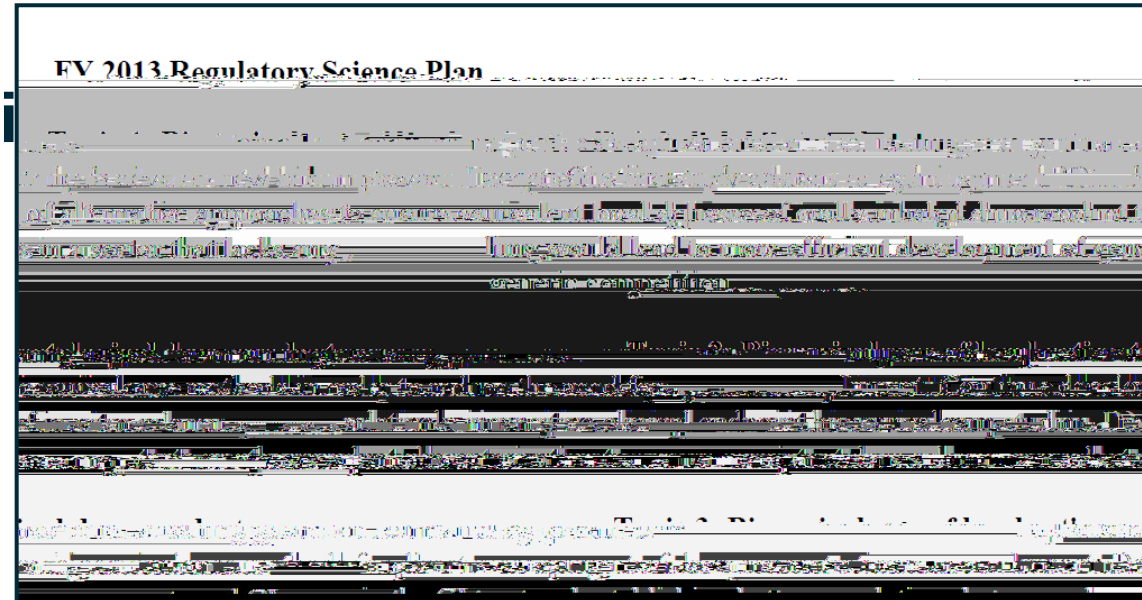
Geographical de-localization to lower cost / lower regulation / patent friendly locations :

Trends in the Supply Chai

Generics must change :

New generics (small molecules and bio-similars) are far more complex

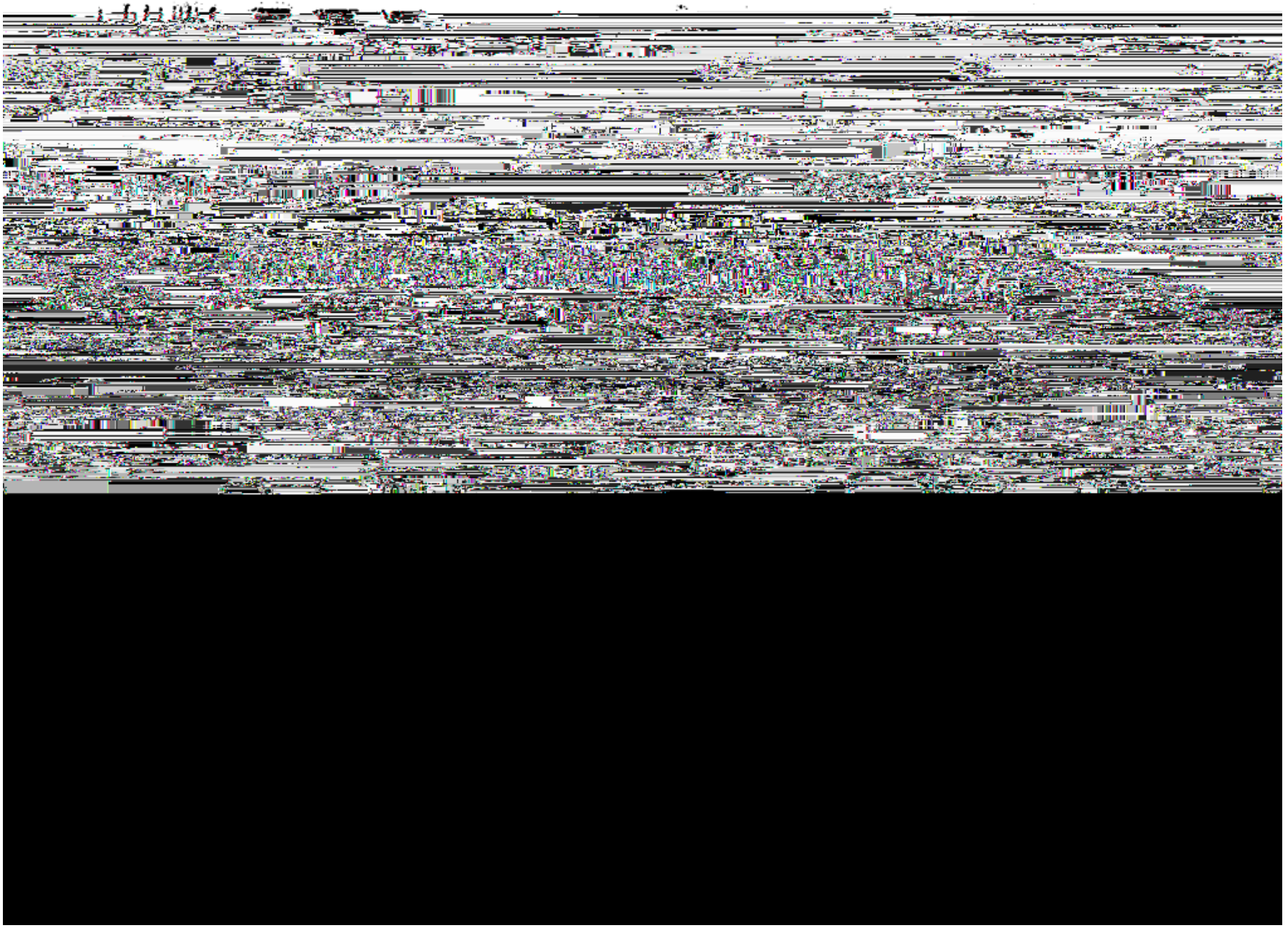
See GDUFA's regulatory science goals



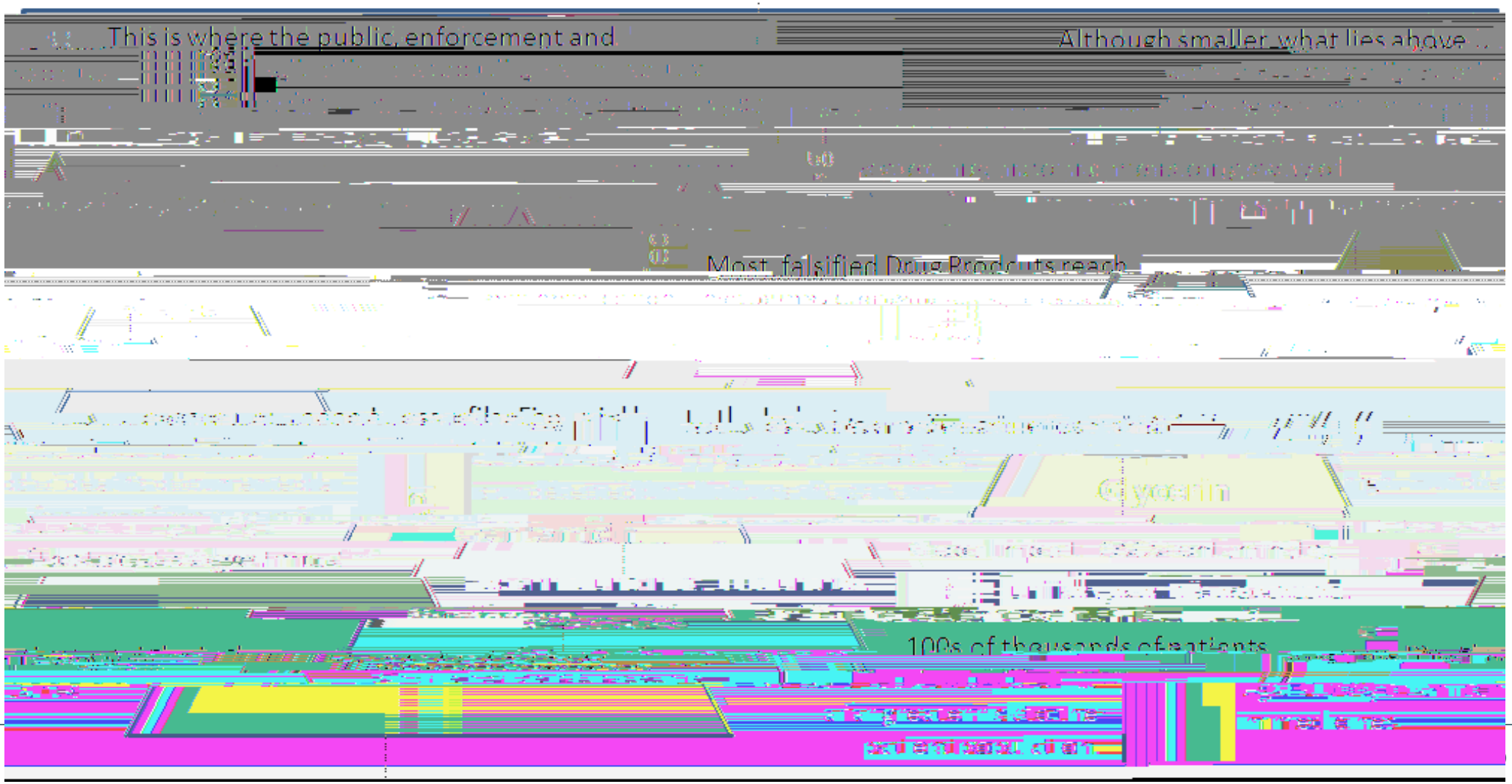
FDA is demanding that Generics start doing QbD filings and evidence process understanding

Low R&D productivity of the past decade will result in few generics to launch this decade:

- Generics' business model will be questioned ?
- Consolidation ?



Falsified Pharmaceuticals
An Iceberg



What FDA expects as a Vendor Qualification Program

- **Increasing Control in the Supply Chain of Incoming Components**
- Improving Analysis and Testing Strategies and Technologies
- Monitoring and Responding to Signals in the Market Place
- Enhancing Drug Product Distribution Supply Chain Controls and
- Use of Serilization Track and Trade and ePedigree

Monitoring and Responding to Signals in the Market Place

#	Topic	Examples of Recommendations
1	Supply communication and transparency	– Build relations with suppliers; beyond audit interactions – Single point of contact – Understand suppliers concerns with confidentiality and transparency

Enhancing Drug Product Distribution Supply Chain Controls and Use of Serilization Track and Trade and ePedigree

#			

Enhancing Drug Product Distribution Supply Chain Controls and Use of Serilization Track and Trade and ePedigree

#	Topic	Examples of Recommendations	Best Practices
1	Transportation and logistics service provider selection	–Incorporate security considerations intro Request for Proposal process and define evaluation criteria –Meet with providers –Non-disclosure agreements –Response	

Take home messages

- Give QA & Purchasing a travel budget
- Know your suppliers
- Audit your API suppliers

  this is now a legal requirement in EU and USA

  opportunity to buy audit reports via Rx-360
- Buy directly, avoid brokers and traders

Cost is not equal to Price

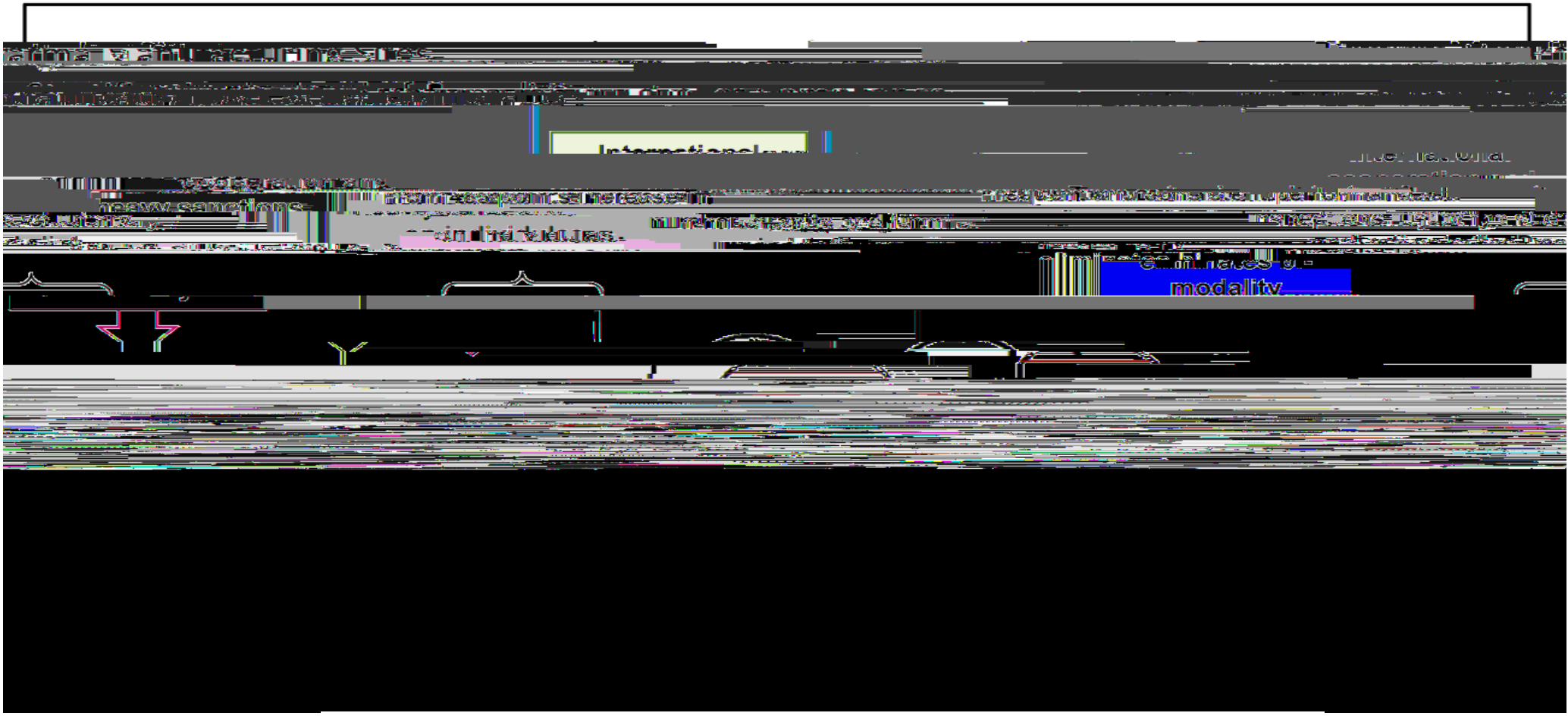
Membership:

- Over 100 organizations, including FDA.
- All actors participating in the pharma supply chain are welcome

Share information:

- On falsified pharmaceuticals
- Audit report library: Jointly sponsored audits

All actors participating in the pharma su



Costly sanctions region	Red flag region	Bulk of sites are compliant	Motivation to-do-better region	Valuable reward region

Thank you for your attention
Q&A

Guy Villax

+351 21 9829381

gvillax@hovione.com

For a copy of this presentation please visit

www.hovione.com

www.hovione.com