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Press Conference

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CPhI – Madrid

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Pharmaceuticals Business Committee Agenda

- Regulatory activity
- Enforcement activity
- Industry activity



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Where are Unsafe APIs coming from ?

Main Source: Façade Constructions



An Example:

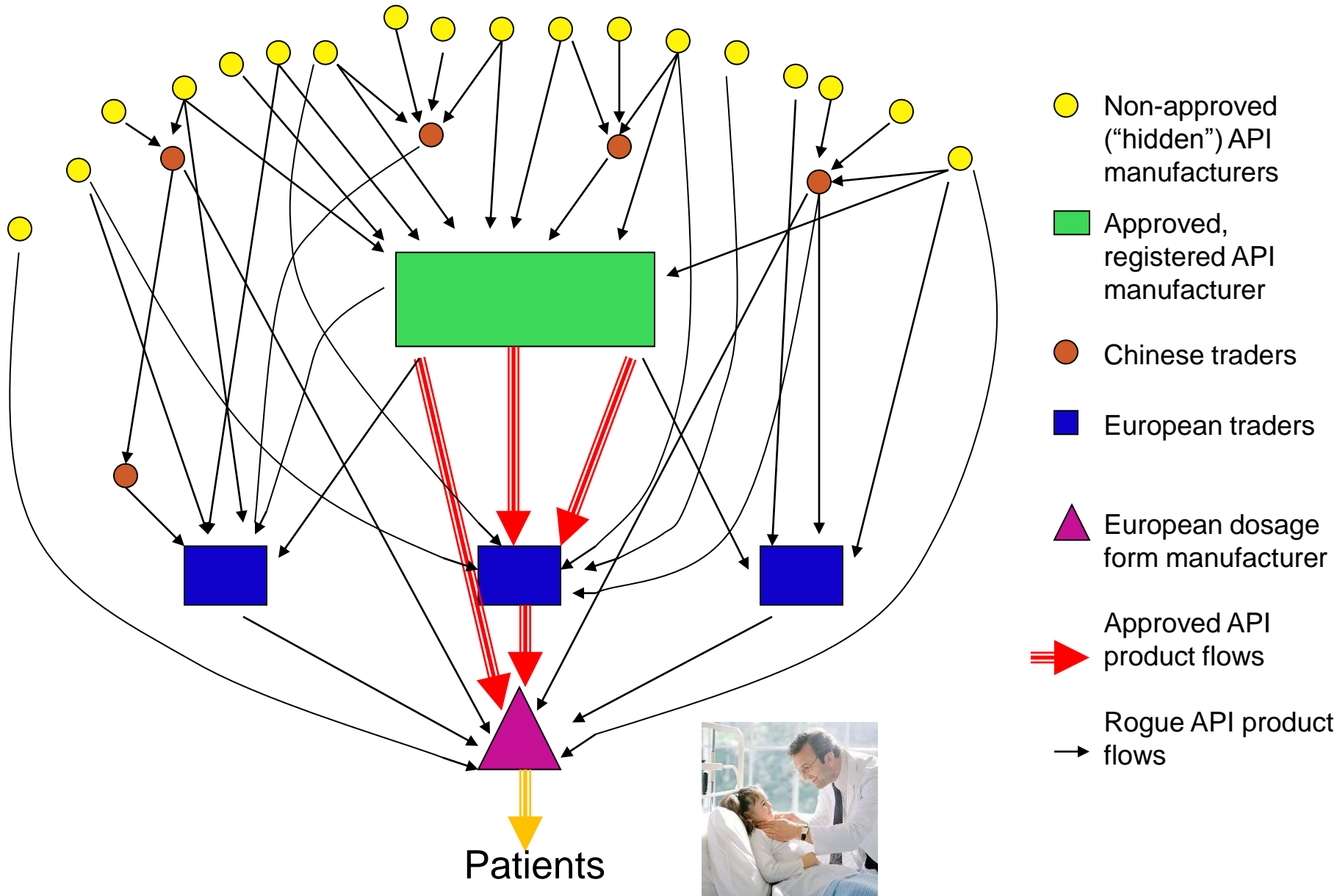
Empty drums concealing a vast warehouse of counterfeit “chemical” APIs and intermediates in an approved “pharmaceutical” API plant.

The materials were sourced from elsewhere and relabeled as if produced in-house in the approved, inspected GMP environment.

(Zhejiang, China, 2008)



Façade Constructions in China





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What is needed to solve Europe's Rogue API Problem: CEFIC's 10 Points

- 1. Mandatory API GMP Certification from European inspectorate**
- 2. Global prioritization of API inspections**
- 3. Central European Unit to coordinate API inspections worldwide**
- 4. Including focus on fraud and counterfeiting within GMP inspections**
- 5. Resolve resource problems for inspections through user fees, right prioritization and international cooperation**



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What is needed to solve Europe's Rogue API Problem: CEFIC's 10 Points

- 6. Use of analytical technologies by authorities and industry to detect counterfeit APIs (e.g. NIRS)**
- 7. IT system to help customs to stop importation of counterfeit APIs**
- 8. Introduction of tough sanctions and penalties for API counterfeiting**
- 9. Introduction of licensing system for traders and brokers**
- 10. Clarify legal liability of Qualified Persons**



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Where do we stand today?

- **EU Parliament: Written Declaration of September 2006; Signed by majority of MEPs December 2006:**

Believes that both producers and importers of active principles should submit a certificate of good manufacturing practice delivered by the European authorities following mandatory inspection at the site of production;



Are we protected ?

- Falsified medicines is more profitable than heroin and in most countries not yet legislated as a crime.**

Counterfeit medicines only addressed in the context of trademark and patent infringement	Counterfeit medicines legislated as a serious crime with intent to profit from patient's trust and impacting health	Ditto <u>and</u> the law is specific in addressing medicines made with falsified API
Canada Most of the EU Most of the rest of the World	France Germany USA	Philippines



New Legislation proposed bills

- **DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL**
 - **amending Directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source**
 - **Draft Convention of the Council of Europe on counterfeiting of medical products and similar crimes involving threats to public health**
 - **US Drug Safety Bill S.882**
- 27 countries
400 million patients
- 800 million patients
- 280 million patients



Falsified Medicinal Product EU:

Any medicinal product, including branded and generic products, which is falsified in relation to its identity (including its packaging and labelling, name, composition in respect to all components and strength), history and/or source (including the manufacturer, country of manufacturing, country of origin, marketing authorisation holder and documents and records relating to distribution channels), therefore entailing risks for public health. It may include sub-standard or falsified active ingredients or excipients, or no active ingredients or in the wrong dosage, fake packaging, or wrong handling of the medicinal products during transport or storage. This definition is not related to infringements of legislation on intellectual property rights or patent rights. (= DELIBERATE TAMPERING)



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Country API Equivalence Option; **Main Characteristics:**

- **All API manufacturers to be inspected by their own domestic authorities**
- **Standards and oversight must be equivalent to EU situation (ICH/Q7 & inspected at similar frequency)**
- **Equivalent countries: List based on evaluation by EU**
- **Non-equivalent countries: Statement with each shipment that for the involved material standards and oversight were equivalent to EU**
- **APIs exported by EU need to meet same criteria**
- **Notification system for all API imports**
- **Only Accredited Third Party Auditors acceptable**
- **Effective penalties to be imposed by Member States**
- **Effective cooperation with Member States' Customs**

Country Equivalence

- *Another Paper Tiger?*
- *Fraud Proof?*
- *Corruption Proof?*
- *Sufficient Deterrence?*
- *How About Highly Compliant In-House Foreign Operations?*
- *To be challenged as a Trade Barrier after all?*





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If these bills become law, are ratified nationally

- **Labeling an API as coming from a different source than the true one will be a counterfeit crime**
 - **Ditto with tampering with a certificate of analysis, changing manufacturing date**
- **Deliberately using an API from a source different from what is in the DMF as an authorized source may cause the medicine to be counterfeit**



Are we protected ?

- Ongoing:** Asian CEP Suspensions (now > 60)
16 CEP suspensions as a result of the latest 28 inspections (all in Asia).
- 2008:** Pilot joint Int'l API Inspection Program EU, US and Australia
Appointment of senior officials to manage international collaboration between medicine agencies
- 2009:** Shanghai No.1, Ranbaxy, Lupin WL, Sun-Caraco Seizure / Recalls, MJ Biopharm Recalls, Glochem CEP suspension => withdrawal from MAAs + naming and shaming of its customers
- = Increasing sense of urgency, but sanctions don't yet bite



Are we protected ?

- **Melamine disaster showed how a global catastrophe may develop... can also be the case with APIs**
- **New estimations of percentage of off-patent medicines in EU pharmacies that are falsified at API level (Chinese API not from the approved/labeled source) are still extremely worrying ("at least 20-30%" **see Reference below**)**

Reference: API Manufacturing-Situation in China

http://efcg.cefic.org/isoFILES/publications/items/DOWNLOAD_180.pdf



Are we protected ?

- **US Drug Safety Bill S882 in its current draft**
 - mandatory FDA API inspection worldwide 1x per 2-4 years depending on company track record.
 - web site to identify country of origin for drug, device and each active ingredient
 - civil penalties will apply if a component of the information certified are false or misleading
 - Sponsor may be subject to civil fine
 - “responsible person” may be subject to civil fine and
 - FDA already doubling its number of overseas inspections now.



Guidance for Industry

Pharmaceutical Components at Risk for Melamine Contamination

³ For the purpose of this guidance, we use the term *at-risk component* to mean those ingredients or raw materials that rely on a test for nitrogen content for their identity or purity or strength, and that contain nitrogen in amounts greater than 2.5 percent. Such a component can be derived from source material that might be contaminated with

has posted assay methods for measuring melamine contamination in foods using liquid chromatography triple quadrupole tandem mass spectrometry (LC-MS/MS) and gas chromatography/mass spectrometry (GC-MS) (see Analytical Methods for Melamine and Triazine Analogs, available at <http://www.fda.gov/AnimalVeterinary/ScienceResearch/ToolsResources/ucm135002.htm>).



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What is the Industry doing ?

- **Off-patent medicine pharma companies are auditing more frequently, sharing audits**
- **We see a flight to quality... but the intensity of competition is worrying absent enforcement**
- **More direct relationships between makers of APIs and users of APIs, more transparency less reliance on brokers and middlemen**



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What is the Industry doing ?



- **Rx-360 is a consortium being developed by volunteers from the Pharmaceutical and Biotech industry which includes their suppliers. The purpose is to enhance the security of the pharmaceutical supply chain and to assure the quality and authenticity of the products moving through the supply chain.**



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What is the Industry doing ?



An International Pharmaceutical
Supply Chain Consortium

- **The RX-360 European Launch**
- **10th November 2009**
- **GSK house Brentford Middlesex, United Kingdom.**
 - This is aimed to European based pharmaceutical companies and their suppliers, there is no conference fee, but space is limited and attendees must sign-up on the internet.
 - www.rx-360.org



The FT yesterday reported: Chirac demands tough action on fake medicines. He says: “Fake medicines have become a real market that is poised to overtake that of narcotics... An international convention ratified by the UN will provide a framework to attack criminal networks.”



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Questions ?

**This presentation can be found at
efcg.cefic.org**

Thank you.

For more information, please contact:

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Thank You

In the past 6 years

**-Brussels, Madrid, Paris, Milan, Frankfurt, Madrid-
the press has been instrumental
in getting our word across**

**We appreciate your support
and continue to count on you.**

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