

Counterfeit Medicines & Pharmaceutical Crime in Europe: “Invisibility, Biohazard & System Failure”

Council of Europe Surveys & Report on Counterfeit Medicines / Pharmaceutical Crime: Findings & Recommendations

Dr Jonathan Harper BSc, MD, MBA (jrharper@axelero.hu)
Author of Council of Europe Counterfeit Medicines Report

21st Century Health Care Terrorism &
The Perils of International Drug Counterfeiting
Hyatt Regency Washington DC on Capitol Hill, Washington DC
Sept 20th 2005

Opinions presented in this presentation are those of the Report Author, and should not be directly attributed to Council of Europe

Dr Jonathan Harper

**Partial Agreement
in the Social and Public Health Field
Accord Partiel
dans le domaine social et de la santé publique**



Council of Europe Counterfeit Medicine / Pharmaceutical Crime Report

**“Harmonised Provisions for Legislative and
Administrative Procedures Applicable to Counterfeit
Medicines in the Council of Europe Member States”**

Published by Council of Europe in Sept 2005

Presentation Overview

Report Background

- **Council of Europe (CoE) Anti Counterfeit Medicine (CM) / Pharmaceutical Crime (PC) Initiative Background**
- **Council of Europe CM / PC Surveys Conducted**
- **Council of Europe CM / PC Report Topics**
- **Issues Discussed in the CoE Report**

The Problem in Europe

- **Extent of CM / PC Problem in Europe – is it a real public health & commercial threat?**
- **Case Study of Balkan Region – Kosovo & its neighbors**
- **Types of Medicinal Product Counterfeited**
- **CM practices (Finished Medicinal Products & Active Pharmaceutical Ingredients: illegal production / distribution / diversion)**
- **Factors Facilitating CM (why PC is a good business opportunity)**
- **Legislative, Regulatory, Administrative system weaknesses / gaps**

Solutions for Europe

- **Key anti CM / PC implementation factors in Europe**
- **European level Anti CM / PC implementing & coordinating body?**
- **European Implementing Tool (“Binding Instrument”)**
- **Major CoE Report Recommendations**

Conclusions (1. Problems; 2. Solutions)

Council of Europe Anti Counterfeit Medicine / Pharmaceutical Crime Initiative



Survey / Report sponsors: *CoE Committee of Experts on Pharmaceutical Questions (& its Ad Hoc Committee on Counterfeit Medicines)*

A. Goals of Surveys / Report:

- (1) provide overview of current CM situation in territory of CoE Member States
- (2) identify potential gaps in legislation & administrative procedures
- (3) propose models for best co-operation practices & info exchange between Member States' authorities and stakeholders
- (4) propose procedures for concerned authorities & stakeholders for preventing / tackling medicines counterfeiting

B. Objectives:

- (1) increased public health protection
- (2) minimization of pharmaceutical enterprise / stakeholder risks & losses related to medicines counterfeiting in the CoE Member State territory

Council of Europe Surveys Conducted



A. 2003 CoE Member State Authorities Pilot Survey

B. 2004 CoE Member State Authorities Full Survey (13 of 26 signatories to CoE Partial Agreement in the Social and Public Health Field, but only 1 from East Europe)

- Ministries of Health / Drug Regulatory Authorities
- Ministries for Interior Affairs / National Police Agencies
- Ministries of Justice (Jurisdiction, Prosecution, Civil & Penal Procedures)
- Ministries of Finance / Tax & Customs Agencies
- Ministries of Economy / Trade

C. 2004 CoE IPR Studies (inc. Criminal Law comparative study)

D. 2004 Stakeholder Survey (30 companies represented by following associations)

- (1) API Manufacturers: APIC / CEFIC
- (2) FP Manufacturers: EFPIA
- (3) Wholesalers: GIRP
- (4) Veterinary products: IFAH

NB: European generic manufacturer and broker trade organizations invited to participate in survey but no responses received

CoE CM / PC Report Topics



- **CM market** (known current & estimated future)
- **CM trade issues** (parallel trade, regulation of import / export / transit etc)
- **Pharmaceutical regulation** (situation in relation to CM (API & FP) prevention)
- **Analytical testing procedures** (for suspected CM)
- **National Inter-sectoral cooperation** (between relevant authorities)
- **International Inter-sectoral cooperation** (between relevant authorities)
- **Authority, industry & wholesaler cooperation**
- **CM detection: authorities, systems & procedures** (who, what & how)
- **Legal provisions, enforcement, sanctions, judicial & IPR procedures** (concerning unlicensed MP/ CM)
- **System adequacy** (legal / judicial / administrative systems for tackling CM)
- **Legal definitions** ('Counterfeit Medicine' & 'Pharmaceutical Crime')
- **Professional training needs** (adequacy of authority / wholesaler/ manufacturer personnel training concerning CM detection & control)
- **Conclusions & Recommendations** (by survey respondents / report author)

Issues Discussed in the CoE Report (1)

- **Rise of medicines counterfeiting** (factors behind current CM phenomenon)
- **Extent of CM problem** (counterfeiting risk according to drug type / types of counterfeiting practice identified)
- **Extent of CM impact on public health**
- **Public / Authority awareness of CM** (& impact on health system perception)
- **Trade control** (import / export / transit licensing, bonded warehouses / freezone control & cross border trade)
- **Parallel trade** (of MP & its impact on CM phenomenon)
- **Internet pharmacy, mail order & unlicensed medicines**
- **Brokers / Traders** (their role in CM supply)
- **CM Distribution chain** – legal & illegal (non regulated)
- **Medicinal Product supply chain complexity**
- **Organised crime & CM** ('CM business model')
- **Action priority accorded to anti CM**
- **Definitions of 'Counterfeit Medicine' & 'Pharmaceutical Crime'**
- **Legal provisions applicable against CM** (sanctions & penalties)

Issues Discussed in the CoE Report (2)

- **Perceived system adequacy** (legal / judicial / admin systems for CM control)
- **Active Pharmaceutical Ingredients (API) regulation** *
- **Medicines packaging & labelling regulation** (inc. printing facilities)
- **CM detection** (systems & procedures)
- **Customs control of medicinal products** **
- **Analytical testing of suspected CMs**
- **Medicinal product security & traceability systems**
- **IPR** (with relevance to CM)
- **National authority cooperation** against CM
- **International authority cooperation** against CM
- **Authority & industry cooperation** against CM
- **Anti CM Training needs** (detection & prevention)
- **Further CoE actions required** (including possible extension of surveys to East European CoE Member States)

* Annex 18 (API GMP) of EU GMP Guidelines / Directive 2004/27/EC Art. 46 & 47; Directive 2003/94/EC / GMP principles & guidelines for human MPs & IMPs / § 17 of ICH Q7a: API GMP guide

** Council Regulation (EC) 1383/2003 - Customs action against goods suspected of infringing certain intellectual property rights and the measures to be taken against goods found to have infringed such rights

How Extensive is CM Problem in Europe?



A real threat to public health & legitimate commercial activity?

- **CM problem exists practically everywhere in Europe** (not just confined to East Europe)
- **CM source / transit / destination – affects all European States** (one way or another)
- **Indications are CM is on increase in CoE territory** (? in cases reported by authorities & stakeholders)
- **Not all CoE Member State authorities think they have CM problem** (*some Member States don't think they have an ADR problem!*)
- **Under reporting likely to be significant** (compare with extent of ADR under reporting; impact of CM on public health not entirely apparent and thus reduces public health risk perception)
- **Lack of differentiation of CM from other types of product counterfeiting** (detection & enforcement often better with latter - CMs by nature harder to detect, but public health impact greater)
- **'System Failure' - Major weaknesses in European legislation, regulation and administration** (identified by overwhelming majority of survey respondents – both authority & stakeholders)

Case study of Balkan Region - Kosovo & its neighbors (1)

('Black Hole of European Pharmaceutical & Trade Regulation')



Case study of Balkan Region - Kosovo & its neighbors (2)

(‘Black Hole of European Pharmaceutical Regulation’)

Narcotic / Psychotropic / Counterfeit Medicine: Balkan Trading Pattern – ‘The Battlefield’



Case study of Balkan Region - Kosovo & its neighbors (3) (‘Black Hole of European Pharmaceutical Regulation’)

‘The pharmaceutical regulatory & organised crime wilderness’

- Post conflict transitional situation & Kosovo under UN administration
- All types of CM practice identified (including vaccines)
- Origination of identified CMs in Kosovo: local, neighboring territories + international (including EU!)
- CM / PC strongly linked with illicit narcotics & psychotropics business
- Public health impact and extent of problem (unknown, probably significant)
- Import licensing system easily subverted (+ no export / transit control)
- Actions taken: active Kosovo DRA inspectorate, good cooperation with UN police / drug crime unit + customs (but a detection problem)
- Kosovo balkan neighbors: very weak control compared to Kosovo
- Other International cooperation with Kosovo?? (practically none)

Conclusions:

1. CM is a cross border & cross authority issue (thus easy for ‘CM criminal business model’ to exploit the many legislative, regulatory and administrative gaps/loopholes)
2. Territories such as Kosovo (with limited regulatory/enforcement infrastructure) also suffer from CM problems because of weaknesses in the greater European legal / regulatory / administrative situation

Types of Medicinal Product Counterfeited



All types (irrespective of class). Medicines counterfeiting is 'open for business':

- High volume (high level of prescribing)
- High price
- Known brand
- Lifestyle / embarrassment & non-reimbursed
- Blockbusters
- All generics
- Short supply drugs
- Off label use drugs
- Parenterals (in less developed/regulated countries)

Degree of CM risk likely to depend on particular local market characteristics

Specific drug and therapeutic class examples quoted:

Developed world: branded drugs for erectile dysfunction, weight loss & cholesterol lowering agents (e.g. Procrit, HGH, Viagra, Cialis, Reductil, Epo, Epogen, Neupogen, Lipitor & Augmentin)

Developing world: antibiotics, anti-malarials, vaccines, HIV drugs

Medicine Counterfeiting Practices (1)



Highly diverse, no shortage of creativity shown by counterfeiters (in particular for Active Pharmaceutical Ingredients)

1. Finished / Intermediate medicinal products

Identical Copy	<i>Identical packaging and formulation</i>
Pure Counterfeit	<i>Look alike (altered ingredients with similar packaging) (but no/different/wrong dose API or excipient)</i>
Re-use of components	<i>e.g. refilling, re-use, replacement of components</i>
False Labeling/Packaging	<i>Product falsely labeled as being from the original manufacturer</i>
Illegal Re-labeling & Repackaging	<i>Product from original manufacturer but illegally relabeled & repackaged (includes fake pricing label)</i>
“Hybrid Counterfeit”	<i>Genuine bulk or packaging, but manipulated labels (& other CM variations)</i>
Illegal diversion & trade of medicinal products	<i>Whether or not through the Internet (e.g. primary pack diversion with secondary counterfeit)</i>
Placing a non licensed medicinal product on the market	<i>Due to weak unlicensed medicine / compassionate use import regulations</i>
False documentation	<i>e.g. granting a COS without auditing the given company, incorrect status on import documents</i>
Waste/expired product re-entering the market	<i>Relabeled as non-expired (Diversion)</i>

Medicine Counterfeiting Practices (2)



Highly diverse, no shortage of creativity shown by counterfeiters (in particular for Active Pharmaceutical Ingredients)

2. Active Pharmaceutical Ingredients (illegal production / distribution / diversion)

Procurement of API's from uncontrolled / non GMP origin	<i>By some FP authorized manufacturers, because uncontrolled API source is cheaper</i>
Re-labeling and repackaging of API's	<i>By who ?? (confidential info) Unauthorized API material may also be shipped in containers labeled with the name of a different API</i>
"Ghost API Manufacturing plant"	<i>API is sold by, but not manufactured by the 'registered producer'</i>
"Ghost supplier"	<i>MAH purchases API from different manufacturer than that specified in MA</i>
"Paper curtain"	<i>API manufacture performed through different process than the one registered in the MAA and MA authorization</i>
"Authorized facades"	<i>Manufacturer/trader with approved CoS or DMF supplies API from large number of unauthorized manufacturers</i>
"Illicit intermediate production"	<i>Unauthorized API materials from obscure sources blended with the registered API material</i>

Factors Facilitating Medicines Counterfeiting (1)



Why medicines counterfeiting is a good business opportunity

- **Lack of awareness / no perception of problem at all levels** (authorities/public)
- **Regulatory gaps** (particularly API & distribution chain regulation)
- **Weak export / transit regulations** (import regulations are generally strong except in the context of internet / mail order pharmacy)
- **Incoordination between relevant authorities both nationally & internationally** (related to absence of CM problem recognition – ‘weakest link’)
- **Regulatory body lack of resources** (particularly to follow up reports on suspected counterfeit medicines)
- **Weak administrative structures**
- **Inefficient cooperation between stakeholders**
- **Weak / uncoordinated enforcement & inappropriate penal sanctions** (but n.b. recent German drug law revision)

Factors Facilitating Medicines Counterfeiting (2)



Why medicines counterfeiting is a good business opportunity

- **Disparity in legal non availability of certain types of high value medicinal products between countries** (unlicensed medicines)
- **Rapid rise in Internet pharmacy trade** (hardly regulated at all)
- **Weak packaging & printing regulations**
- **Increasingly complex distribution chain with transactions involving many intermediaries**
- **High medicinal product prices**
- **Recent appearance on the market of “life style & embarrassment” drugs**
- **A move of organized crime into medicines counterfeiting associated with increasing sophistication in clandestine manufacture**
- **Corruption & conflicts of interest**

Legislative Weaknesses & Gaps



- **No single satisfactory coherent national legal provision against medicines counterfeiting exists in Europe**
- **Large inconsistency of 'possibly applicable' legislative provisions between CoE Member States**
- **Weak national level inter-sectoral legislative coordination - possible provisions covered by different types of law:**
 - **Medicines Law**
 - **Penal/Criminal Code/Law**
 - **Customs / Trade Law**
 - **IPR Law**
- **Absent applicable international legislative / regulatory guidelines**
- **Absent internationally accepted definitions (Counterfeit Medicine / Pharmaceutical Crime)**
- **Inadequate sanctions / penalties**

Regulatory Weaknesses & Gaps



- **APIs**
- **Export & Transit control**
- **Traders/brokers**
- **Secondary wholesalers & wholesaling retailers**
- **Parallel import (??)**
- **(Re-) Packaging / Labeling & Printing**
- **Internet pharmacy**
- **'Unlicensed medicines'**
- **Testing & reporting systems**
- **Traceability systems**

Administrative Weaknesses & Gaps (1)



‘Massive in-coordination = System failure’

- **Lack of recognition of problem (priority for action?) + inadequate systems for CM detection** (& incorporation into existing *Pharmacovigilance* systems)
- **Lack of knowledge/understanding of ‘CM criminal business model’**
- **Insufficient MoH / DRA resources** (how to allocate resources when CM problem extent not well determined?)
- **Inter-sectoral in-coordination** (e.g. between health & customs; health & law enforcement)
- **Weak authority - industry cooperation** (insufficient disclosure & reporting)
- **Weak reporting & database systems**
- **Weak inspection & enforcement** (often lack of powers to inspect & enforce)
- **Difficult product traceability & security**
- **Absence of effective supranational coordinating function**

Who to report CM cases to ? (who will take action ?)

Administrative Weaknesses & Gaps (2)



Europe: Anti - medicines counterfeiting system failure'

European Union:

- single trade market, but divergent national economies
- highly divergent health policy, health management & health financing systems
- emerging single EU pharmaceutical regulatory system (current split EMEA / national authority responsibilities)



Council of Europe:

- policy making body (in specific areas) which encompasses all European states
- only half CoE member states subscribe to a common health policy (via the CoE Partial Agreement for Public Health)

Conclusions about Europe:

- CM / PC falls in gap between health policy, pharmaceutical regulatory, trade and enforcement authority control = unclear sectoral and authority responsibility
- Existing administrative system for potential control of CM extremely complicated and unwieldy

SOLUTIONS FOR EUROPE

Anti - Counterfeit Medicine / Anti Pharmaceutical Crime: Key Implementation Ingredients

- **Political Will (trade/crime/public health priorities) – why?**
- **Implementing / coordinating body – who?**
- **Implementing tool / framework - what?**
- **Multiple implementation measures required – what?**
- **Necessary resource allocation (European level & nationally) – what / who?**

Political Will for Anti-Counterfeit Medicine / Pharmaceutical Crime in Europe Exists at Council of Europe Level

“Counterfeiting: problems and solutions”
Council Of Europe Parliamentary Recommendation
1673 (2004)

Parliamentary recommendations address all types of counterfeit product that impact on health (pharmaceuticals, spare parts, toys, personal care and household items, foodstuff, alcoholic drinks and tobacco)

CoE Counterfeit Medicine Survey / Report goals and objectives supported fully by Council of Europe Parliamentary Assembly

European Level Anti Counterfeit Medicine Implementing / Coordinating Body ?



- **Clearly required ?** (currently does not exist)
- **Avoidance of unnecessary duplication and ineffectiveness of effort**
- **Definition of responsible 'European Level Body'** (responsibility for overseeing implementation of proposed recommendations & their long term management)
- **Definition of roles of other relevant International / European / EU organizations**
- **Which organization is best placed in Europe?** (Governmental / Non Governmental?)
- **European Players:** EC, CoE, ICC, WHO, WCO, WTO, PFIPC, INCB, Europol, EMEA, other ?
- **Some (not all) possible options:** CoE EDQM/OCL Network or UN INCB?
- **UN INCB model – extensive experience with management of illicit drugs** (an international body that effectively combines drug regulation with law enforcement)

Anti CM Implementing Tool / Binding Instrument (1)



A. Type of Tool / Instrument:

- Convention, Cooperation Agreement or other?
- Highest form of legal cooperation possible
- Definition of European level & national responsibilities
- Defining scope and content of binding instrument
- Codification of applicable CoE Member State legislation / regulations

B. Important definitions

C. European level implementing / coordinating body tasks

D. Model legislative provisions (with emphasis on national authority / stakeholder tasks)

Anti CM Implementing Tool / Binding Instrument (2)



B. Important definitions that should be standardized across all CoE States

Counterfeit Medicine

- WHO definition appears to be the most widely accepted and comprehensive international CM definition

Pharmaceutical Crime (needs to incorporate following items and concepts)

- Formal classification of types of medicines counterfeiting and which are linked to a clear scale of degree of regulatory violation and appropriate penalties / sanctions
- Aggravated circumstances of counterfeiting and piracy
- Intent
- Health risk and damage
- Intellectual Property Rights (IPR)
- Falsification (product, packaging, documentation)
- Fraud
- Illegal trading
- Possession
- Other items? (to be determined)

Anti CM Implementing Tool / Binding Instrument (3)



C. European level implementing / coordinating body tasks

- Coordination with/of national authorities & commercial stakeholders
- Coordination with other relevant international authorities / NGOs
- Cooperation agreements (& their supervision)
- Public relations & communications
- CM Monitoring:
 - DB of products at high risk for counterfeiting & with high public health risk
 - DB of CM & counterfeit practices
 - DB of legitimate and black listed brokers/distributors
- RAS (integration into existing reporting systems?)
- Guidelines (e.g. Good Trade and Distribution Practice)
- Inspection SOP (inc. sampling, testing & recall strategy)
- Characterization & monitoring of pharmaceutical distribution chain
- Medicinal product traceability system
- Technology strategy for product security, traceability and product pedigree rules
- Definition of national tasks & national authority coordination procedures
- Regular forum with national authority & stakeholder representatives
- Monitoring of strategy implementation results
- Training support

Anti CM Implementing Tool / Binding Instrument (4)



D. Model legislative provisions (with national task emphasis)

- **Import / Export / Transit licensing** (emphasis on export/transit)
- **Bonded warehouses / Freezones**
- **Broker & Wholesaler licensing / regulation**
- **API & Excipient regulation & inspection**
- **Packaging & Printing regulation**
- **Internet Pharmacy regulation**
- **Unlicensed Medicine (compassionate use) regulation**
- **Industry reporting & disclosure requirements**
- **National authority reporting requirements** (between authorities & to designated European level authority)
- **Risk management procedures** (e.g. Customs procedures & CM risk analysis)
- **Inspection & Enforcement** (e.g. seize and detain powers)
- **Penal sanctions** (against pharmaceutical crime, as opposed to economic crime & with clear scale of infringements)
- **Authority resource allocation requirements** (human, financial & systems)
- **Definition of role of authorities from different sectors**
- **National authority coordination procedures**
- **Authority-industry-wholesaler coordination procedures**
- **Inspector, Police, Customs officer CM specialization**
- **Provision of CM reports to European coordinating body**

Report Major Recommendations (1)

Multiple implementation measures required

- **Define European (International) level coordinating body** (with clear definition of national/Europe level institution roles & responsibilities)
- **Define Anti medicines counterfeiting implementation framework** ('Binding Instrument' - highest legal form of cooperation possible) European / International level legislative / regulatory / administrative framework that is CM specific (define scope and content)
- **Codify existing CoE Member State relevant national legislation**
- **Target medicinal product types with both high Counterfeiting and public health risk**
- **Detailed characterisation of how CM enters market** (CM Official & Unofficial Distribution Chain & 'CM Criminal Business Model')
- **Define specific definitions** (Counterfeit medicine & Pharmaceutical crime) **& rules of interpretation concerning medicines counterfeiting**
- **Inspection and enforcement requirements** (best practice, e.g. pharmaceutical crime unit)
- **Appropriate & coordinated sanctions / penalties against CM**
- **IPR measures addressing CM**
- **Import/Export/Transit regulatory control**

Report Major Recommendations (2)



Multiple implementation measures required

- **Internet Pharmacy, medicinal product mail order & unlicensed medicines regulation** (e.g. US Verified Internet Pharmacy Practice Sites - VIPPS)
- **Distribution Chain Security / Packaging & (Re)-Labeling regulatory control**
- **Active Pharmaceutical Ingredients & Excipients regulatory control**
- **Customs & Health Authority information sharing concerning suspected CM**
- **Medicinal Product Security & traceability (pedigree tracking) systems**
- **Active Searching & Analytical Testing of suspected CM**
- **Rapid Alert System & Risk Management procedures / systems**
- **ADR reporting / Pharmacovigilance systems in the context of suspected CM**
- **National authority cross sectoral coordination improvements**
- **Coordination / cooperation tasks** (communication networks, best practices, codes, protocols, database & reporting systems, information disclosure)
- **Communication strategy** (awareness raising and knowledge / perception management of general public, health professionals, supply chain participants & authorities)
- **Educational requirements** (customs, law enforcement personnel etc)

Conclusions - (1) Problems



Multiple causality: Many reasons exist why CM is prevalent

- **Phenomenon?: Medicines counterfeiting / pharmaceutical crime: a transient phenomenon or here to stay?** (what is the evidence and how big is the problem?)
- **Biohazard: CM is criminal, life-threatening & undermines health systems** (but inadequately differentiated from other forms of economic crime)
- **Invisibility: relative invisibility of Counterfeit Medicines** (hard to detect & awareness issues)
- **System failure (Europe): CM / PM is global and complex problem** (several factors inadvertently facilitating medicines counterfeiting exist – trade, legislative, regulatory & administrative related)
- **Pharmaceutical crime sophistication** (are authorities equal to the challenge?)

Conclusions - (2) Solutions

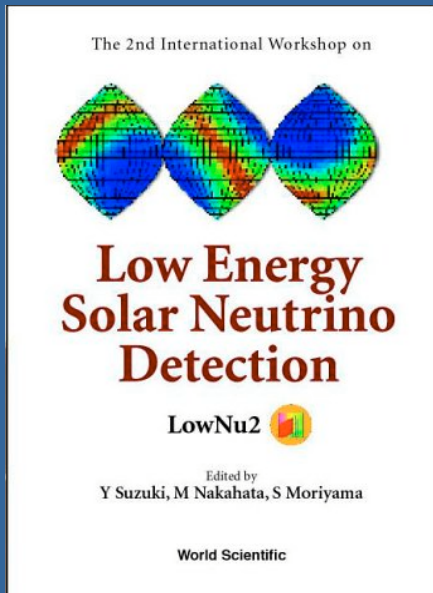
Multi-layered coordinated strategy required



- **European level multi-layered strategic approach required** (pure national approaches likely to be far less effective and coordinated)
- **Political will: Both authorities & stakeholders wish to see the CM/PC issue comprehensively tackled** (e.g. ICH Q7A full implementation, GDTP)
- **Effective cross sectoral coordination & communication** (tackling CM/PC requires effective & coordinated drug regulation, health policy, trade regulation & organized crime combat)
- **United European State approach required** (a weak link/non participation in 1 state impacts adversely on all other States)
- **European level (1) Coordinating body? & (2) 'Binding Instrument'?** (should be highest legal form of cooperation possible)
- **Anti CM / PC System implementation models? - learning from other related sectors** (e.g. control of narcotics/psychotropics & other types of counterfeit product)
- **Adequate resources for tackling CM / PC** (once & for all?)
- **CM / PC has to be explicitly differentiated from other forms of economic crime / product counterfeiting** (legislation and sanctions)

THE MESSAGE

Invisibility + Biohazard + System Failure =



Another potential '*Pharmageddon*' Scenario

Let's "*Get Real*" with Counterfeit Medicines & Pharmaceutical Crime