Phony Drugs, Real Solutions: practical anti-counterfeiting considerations

BIO 2010 Panel and Interview findings
A panel hosted by Cambridge Consultants at BIO 2010

Counterfeit medicines and the diversion of legitimate product are serious and growing global issues for the biotechnology and pharmaceutical industries, governments and patients.

Cambridge Consultants President, Pamela McNamara, chaired a panel session at the BIO 2010 conference in Chicago which highlighted the regulatory, technical and business responses to these problems, with a lively discussion between the panellists:

- Lew Kontnik – Director of Brand Protection, Amgen
- David Kent – Vice President of Global Risk, Genzyme
- Hugh Burchett – Director of Defence & Security, Cambridge Consultants
- Andrew Emmett – Director for Science & Regulatory Affairs, BIO

In addition to the panel session Cambridge Consultants has also undertaken an interview programme. Through in-depth interviews with thought leaders from across the industry globally we have gathered comprehensive insights from pharmaceutical and biotech businesses to technology developers and industry bodies.
What impact will counterfeit products have on my business in the future?

Over the last few years the issues of counterfeit pharmaceutical and biologic products have been of growing concern to law enforcement agencies, government regulators and the pharmaceutical and biotechnology industries. The problems are increasingly driven by the financial gains and relatively low penalties compared with other forms of organised crime. This has led to a number of countries proposing legislation to counter this activity and to provide a minimum standard of protection for patients.

Motivated by patient safety concerns, the pharma and biotech industries have been addressing the issues of counterfeiting for many years. Also governments around the world are increasing regulations to tackle the problem. A number of features have already been introduced on high risk products to counter the diversion of legitimate product between markets and to combat counterfeiting, within a wider brand protection and patient protection approach.

The next few years will see substantial changes in the industries as a result of extensive lobbying efforts currently ongoing. For example, there is pressure to ban repackaging of drugs in Europe, and proposals to increase the strength of supply chain security.

However, there is no “one size fits all” solution. For all businesses, understanding what measures are appropriate to protect their brand and patients, and in the case of early stage businesses, when to implement these features, is of critical importance.

Looking further out, as the product protection changes, so will the criminal’s approach adapt; therefore, a strong system philosophy will also be important to stay one step ahead.

Counterfeit medicines – the problem

Counterfeit medicines are a serious and growing issue across the globe. Traditionally associated with developing countries and illegal online pharmacies, they are also increasingly being detected in the legitimate supply chains of industrialised countries.

The term “counterfeit medicine” is normally defined as medicine deliberately and fraudulently mislabelled with respect to identity and/or source. These can contain some or none of the Active Pharmaceutical Ingredient (API). This in itself has implications concerning the legal recourse of the manufacturer, since presence of API allows the counterfeiter to be pursued on grounds of Intellectual Property (IP) infringement.

It is very difficult to assess the size of the issue. Previous estimates include:

- “Estimated that 15% of medicines sold worldwide are fake, rising to 50% in Africa and Asia” Source: WHO 2006
- “Worldwide trade in counterfeit drugs is expected to reach $75Bn by 2010” Source: US Centre for Medicines in the Public Interest (CMPI) 2005
- US customs seizures of counterfeit pharmaceuticals increased to $11.1M in 2007, a 500% increase on 2006 Source: US Customs and Border Protection Agency 2008

It should be noted that there is much disagreement in the industry as to the size of the problem. The illicit nature of counterfeiting inherently makes assessing the economic impact difficult.

The figures from the Pharmaceutical Security Institute underline that the issue is global but with substantially more cases in Asia, supporting the World Health Organisation (WHO) findings in 2006.
The public perception is that counterfeit medicines are predominantly in the area of lifestyle drugs that treat non-life threatening conditions (e.g. erectile dysfunction and weight loss drugs); however, the UK MHRA has detected counterfeit products covering a number of chronic conditions, and cases of counterfeit medicines detected in the legitimate supply chain from clinical trials through wholesale to the Point of Dispense (PoD), with nine cases of recalled counterfeit medicine identified in the past three years having reached the patient or pharmacy.

"Pharmacists and wholesalers have identified fake drugs targeting: anti-cholesterol, anti-inflammatory, anti-platelet, anti-psychotic, erectile dysfunction, prostrate cancer, appetite suppressants, chronic asthma, alopecia” Source: UK MHRA 2009

“EU has seized 34 million fake tablets in 2 months including antibiotics, cancer treatments and Viagra” Source European Commissioner for Enterprise and Industry 2009

The Pharmaceutical Security Institute data through 2008 indicates a steady rise in counterfeit incidents relating to injectables, indicating that this now accounts for around 10% of incidents of detection of counterfeits in the legitimate supply chain globally.

Internet Pharmacies - a specific problem
The anonymity of purchasing medication through the internet is attractive for many people with sensitive conditions or reluctance to obtain a prescription; however, this carries substantial risks. Whilst legitimate internet pharmacies do exist, an in-depth analysis of over 100 websites revealed that:

- 95.6% of online pharmacies researched are operating illegally
- 90.3% of websites do not require sight of a prescription
- 86% of online “pharmacy approval” stamps are fake
- 78.8% of websites are violating brand intellectual property
- 50% of medicines supplied by online pharmacies which conceal their physical address are fake

Source: The European Alliance for Access to Safe Medicines, June 5, 2008; UK MHRA 2009

The issue of product diversion
Whilst counterfeit products are of concern, there is also the issue of diversion.

Diversion occurs when legitimate products are diverted from one market to another, where the sale price of the product is higher, or supply through illegitimate channels attracts a premium, for example for lifestyle drugs.

Aside from the illegal supply of drugs, this has an implication for a manufacturer where drugs are supplied in markets which they are not licensed, or breaching established distribution agreements with legitimate wholesalers.

Interview respondents have indicated that, in some instances, diverted products are accompanied by counterfeit products during shipping. In other instances, product diversion may be the first indication that a product is at risk of being counterfeited. As such, respondents felt that diversion of legitimate product should be taken seriously.
Diversion is of particular concern to the biotech industry, as biologics typically require very close supervision of transportation and storage in order to maintain their effectiveness. Incidences of diversion are likely to also involve transportation and storage conditions which could severely compromise the effectiveness of certain treatments.

Risk of harm to the patient

The overriding driver within pharmaceutical and biotech businesses is the delivery of safe, effective treatments to patients. This is clearly reflected in the stringent regulations and methodologies employed through the development, validation and trial of medicines.

A key threat that continues going forward is that counterfeit products, or diverted biologic products which have been through a poorly controlled supply chain, reach the consumer and cause harm.

Our research has highlighted different forms of harm to the patient from counterfeit drugs:

- Endangering their health through toxic contaminants
- Preventing treatment for chronic conditions or life threatening diseases by replacing legitimate product with a counterfeit placebo
- Preventing protection from infectious agents (e.g. counterfeit anti-malarials containing no active ingredient)
- Allowing resistance to develop through insufficient quantities of active ingredients

All respondents agreed that the manufacturer, and other stakeholders in the supply chain, therefore need the ability to detect and address this activity, whilst ensuring the flow of products to the patient is not encumbered.

For certain products the implementation of anti-counterfeit measures should also address the issue of diversion.

So what does this mean for biotech businesses?

Whilst significant attention is focussed on pharmaceuticals, diversion of legitimate biologic product through uncontrolled supply chains and the counterfeiting of injectables are significant issues for biotech businesses.

For established biotechnology companies, many will have developed approaches to mitigate these risks, often in response to real threats to their products.

Approximately 90% of the Biotechnology Industry Organisation’s (BIO) members are emerging biotechs that do not have a product on the market yet. We have found that often emerging biotech companies have not fully considered the implications of counterfeiting/diversion on their future products or implemented a strategy to protect their business.

One respondent emphasised that as counterfeit products have been detected at the clinical trials phase of development, some form of supply chain security or product authentication measures should be in place at this early stage, as this is often make or break for a developing company.

Some respondents from established companies indicated that they would not expect an acquisition target to have a complete set of anti-counterfeiting measures implemented and fully integrated in the manufacturing process, as they would prefer to implement their own methodologies on newly acquired products.

Other respondents expected that, as a minimum, acquisition targets would be aware of the implications of the threat of counterfeiting and have plans for possible product protection. Instead of making a significant investment in an anti-counterfeiting technology, a savvy resource-limited emerging biotech firm could position itself well by characterising product risk, considering possible mitigations, and carefully negotiating vendor contracts to allow for future implementation of security measures.

“For the majority of biotech businesses the only product they sell is themselves”

“Some erectile dysfunction drug counterfeits were on the market before the real product was”
Managing brand protection as part of global risk

Addressing the issue of counterfeit and diverted products is a complex task involving many stakeholders from the brand owner / manufacturer, supply chain companies, dispenser, healthcare providers, patients and law enforcement agencies.

The strategic approach adopted by a number of pharma and biotech businesses combines both technology and business process to present a system which any potential counterfeiter or diverter has to defeat.

Brand protection strategies need participation from a range of internal and external stakeholders. Internal stakeholders include materials management, product validation, quality and audit, regulatory affairs, legal team, regional management and customer service. In addition, close liaison with product and packaging development and supply chain participants (raw material manufacturers, product manufacturers and packaging suppliers) is also needed.

“Amgen incorporates security technologies on its products and implements business process to deter, detect and minimise disruption from counterfeit attacks” Lew Kontnik, Director, Brand Protection, Amgen Inc.

In many instances, the brand protection function within a company is part of a wider management of global risk encompassing incident management and crisis planning, competitive and technical intelligence, security operations, physical security and information security.

“We adopt a unified approach to risk assessments, security elements and market monitoring and investigations” David Kent, VP Global Risk, Genzyme

An essential element of brand protection strategy is the education of patients and medical professionals who may be administering the drugs and therefore act as the final check of the packaging features, or in the case of ingestibles, changes in appearance, smell, or taste of their medication.

This is against the backdrop of a need for wider education concerning the dangers behind buying drugs from internet pharmacies.

Supporting this education is the support for the introduction of new and improved regulatory standards to protect the patient as well as support for legislation to deter the criminal and close liaison with law enforcement agencies in terms of detecting, intervening and prosecuting criminals.

Fundamental to this approach is balancing the risk versus the threat to the brand which requires an assessment of a number of factors:

- Product specific risk: likelihood and severity if a specific product is counterfeited
- Counterfeiter capability: skill, opportunity and financial gain
- Strength of brand protection: How well the current or proposed security features and processes deter activity as well as defeating the capabilities of the adversary

In taking these different factors into account and balancing the risk versus the threat to the brand the brand can develop a proportional response – as shown on the diagram below.

“On the other hand, while there have been recent improvements in enforcements and regulations, there continues to be a need for a comprehensive private-public response to criminal counterfeiting focusing on education, legislation, enforcement, investigation and international collaboration.” Andrew Emmett, Managing Director for Science & Regulatory Affairs for Biotechnology Industry Organization (BIO)
How is technology used to address the problem?

Technology is an integral part of a brand protection system. In the case of medications, three different types of technologies are employed (anti-tamper, serialisation and authentication) to provide a layered protection system, and with different technologies intended to interact with the different stakeholders (brand owner, patients, the supply chain and law enforcement):

Anti-tamper, or tamper evident packaging, is the first step in a protection strategy. This can be achieved through careful packaging design with integral features such as perforated openings, or through the addition of tamper evident seals.

Anti-tamper and tamper-evident packs

✓ Enables the detection of insertion of counterfeit product into manufacturers packaging, or alteration of serialisation or authentication features

✗ However success is predicated on the real pack being difficult to counterfeit, and the users and supply chain awareness of the legitimate pack design

Serialisation is a second layer of protection, which relies on the printing of a unique serial number on each package. This number is recorded at manufacture on a database, and the package marked as being dispensed at the Point of Dispense (PoD). Any subsequent packs with the same serial number will be flagged as suspect if the number has already been dispensed.

The majority of current proposals recommend the printing of a serialisation number, the unique product code (or equivalent for biologic products), expiry date and batch number on the package. This is typically in plain text but could also be implemented using a 2D barcode or an RFID tag. Many survey respondents indicated that RFID tags are less popular due to their cost, challenges with integrating with the supply chain, potential interaction with non-solid dosage forms, and the perception that they are a more complex solution than is warranted.

Serialisation

✓ Enables the detection and prevention of mass duplication of counterfeit product and insertion into the supply chain at Point of Dispense (PoD)

✓ Supports accurate reimbursement, recall of product and removal of out-of-date product

✗ However success is predicated on the real product reaching the PoD before the counterfeit

✗ Relies on truly random generation of serial numbers to prevent prediction by counterfeiters

✗ It is important to recognise that serialisation does not equal authentication: it will not stop counterfeit product from being dispensed

Track and trace uses the same basis; however, the serial number is recorded at various points within the supply chain, either on a central server, or in the case of RFID, on the product itself. This provides the ability to trace where diverted or counterfeit product enters the supply chain, as well as tracking its location at all times.

Authentication is the third level of protection and takes many forms with a large number of different technologies employed. These technologies can generally be classified as overt, covert or forensic.

Overt features are typically employed to allow patients and medical professionals and others within the supply chain to verify that the package is authentic by eye, or by touch. Typical features would be holograms or Optically Variable Devices (OVDs), watermarks but also packaging materials. These have the same drawbacks as anti-tamper features, in that the person needs to know what a correct package looks like, and the counterfeiter can clearly see what needs to be copied.
Covert features are invisible to the naked eye and are typically employed to enable stakeholders within the supply chain to authenticate items. These features require custom reader designs which can be quite simple or complex depending on the covertness of the feature. Reader development in itself has a number of complexities over and above a standard product development. Typical covert features include taggants, inks, embedded features within holograms, and Laser Surface Authentication (LSA).

Forensic features are employed to enable a brand to determine categorically that a product is authentic, to enable the brand owner to pursue litigation or for a law enforcement agency to prosecute. Typical features included taggants or the combination of specific constituents within a product. These features are normally, but not always, read under laboratory conditions.

**Authentication**

✔ Enables the detection of counterfeit product within the supply chain through authentication of packaging or the product formulation

✔ An advantage is that different features support different end-users, supply chain and litigation, as well as deterrence

✘ It is important to recognise that authentication is only as good as ‘the reader’ (this includes the human operator)

✘ A disadvantage is that authentication is technology dependent and there is a compromise between uniqueness, reader complexity and cost

Whilst describing overt, covert and forensic authentication features, in practice a number of techniques can be combined together in a single feature, which may also support either anti-tamper or serialisation.

The selection of authentication features will be influenced by the balance of risk versus threat and the need to create ‘layered’ protection. A number of interview respondents stressed that the adoption and reading of authentication features must not reduce the safety or efficacy of the therapy. Therefore due consideration should be given to any potential interaction between the product and the technology.

Experience is being shared across the industry

The complex, global nature of counterfeiting and diversion carried out by organised criminals means that collaboration amongst different stakeholders (manufacturers, supply chain and law enforcement) is critical to address the problem.

The Pharmaceutical Security Institute (PSI) and the US National Biopharmaceutical Security Council (NBSC) are two industry bodies who share information amongst their members concerning incident data, locations and suspected organisations in order to improve the collective understanding of the threat.

This resource can be particularly important for emerging biotech and pharma businesses in order to gain the experience of the other members and allow them to put appropriate anti-counterfeiting strategies into place.

Both the PSI and NBSC also provide an industry point of contact for government regulatory agencies and law enforcement, in many cases providing information to initiate investigations and prosecutions.

Organisations such as NBSC and PSI also offer outreach and support to the general public, by way of education and increasing public awareness. They provide a means for informing consumers of counterfeit incidents and also encourage consumers to report suspicious products for investigation. These consumer reports, in turn, help companies better understand the threat to their products.
The role of regulation in combating counterfeit products

Regulations are another important aspect of addressing the issues of counterfeiting and diversion. These are central to the law enforcement, and hence the ability to prosecute criminals for their actions.

However, there are a number of complexities in drafting policy, regulations and laws which are specific to the counterfeiting and diversion issues, which provide a challenge even in industries with a long record of regulatory requirements:

- **Applicability**: An immediate complexity arises when describing counterfeits, as the existing framework does not adequately distinguish Intellectual Property considerations such as those protecting legitimate generics from illegitimate counterfeit products.

- **Flexibility**: Regulations need to be flexible such that they do not limit the ability of the manufacturers to select new technologies or methodologies to address a rapidly changing threat from the criminals. This is particularly critical given the length of time to frame new regulations and the subsequent laws to enforce the policy.

In practice, regulations provide a minimum standard to achieve a level of protection, and given previous experience in the pharmaceutical industry with RFID, there is now a drive towards regulations which are technology independent, but with standards applied to key measures, such as serialisation using GS1 standards for product coding for pharmaceuticals.

> “..unlike the format wars between BetaMax and VHS, or more recently with BluRay and HD, a pharmaceutical or biotech company can not tolerate investing in one technology, only to have the industry decide that another is the preferred one”

Policy and regulations are generally lagging behind the problem of counterfeit and diverted products, and therefore it is not surprising that laws are also relatively immature to address the problem.

The interviewees commented that stricter laws are required. Currently, in some countries, counterfeit drugs are not illegal; or are a violation of trademark laws; and in many countries the punishment associated with counterfeiting is a fine, which is small in comparison to the revenues generated by the sale of counterfeit products, and not reflecting the potential harm of counterfeit drugs.

Ensuring the issues are addressed globally

A key complexity of tackling anti-counterfeit and product diversion is that this needs to be addressed globally at a system level; otherwise the criminals will simply move to less well protected markets. This requires everything from coordination of customs and law enforcement, through to the adoption of legislation.

The European Union is currently drafting regulations for the introduction of serialisation, with a number of industry groups (European Federation of Pharmaceutical Industries and Associations (EFPIA) and European Alliance for Access to Safe Medicines (EAASM)) strongly supporting this legislation. This has not stopped certain countries within the EU (France, Belgium and Italy) from pushing ahead with their own schemes.

In the US, the FDA has recently announced its final guidance for serialisation. Although the guidance is not legally enforceable, it provides a clear direction to comply with the California e-pedigree law, which has been deferred to the 2015 – 2017 timeframe. Additionally, there is a need for strong federal guidance by the FDA on serialisation to pre-empt the potential confusion that would arise from a myriad of conflicting state regulations. Industry bodies such as PhRMA and BIO are actively contributing to these discussions.

In addition, inter-governmental initiatives continue from Interpol, the World Customs Organisation (WCO), the World Intellectual Property Organisation (WIPO) and the World Health Organisation (WHO).
So what practical steps can I take?

The panel and interviews highlighted a number of steps which businesses can take to address the issues of counterfeit and diverted products.

- **Understand the risks**: Understanding the implications of counterfeit and diverted products is key, both at a business level, but also at an individual product level. This assessment sets the business need for the measures that need to be implemented. Noting that established biotechnology companies are increasingly including this assessment prior to purchase of emerging biotech businesses.

- **Plan early**: The cost of retrofiting a business process or set of anti-counterfeit measures once a system has been implemented is significantly more expensive than building this in from the start. The detection of counterfeit ingredients and products in clinical trials underlines that this is not just an issue for approved products.

- **Build a system**: Successful solutions require involvement from a number of stakeholders both internal and external to the business and provide a process for managing the brand protection strategy, often within the management of global risk. Key is management of the supply chain, and understanding weaknesses that may exist, along with how counterfeiting and diversion can be deterred.

- **Employ technologies as a system within the system**: Technology is an important element of an anti-counterfeit and diversion system and a ‘layered’ solution is required. The brand owner carries the risk of poor system performance, not the system or technology provider, and therefore being an intelligent customer is crucial. In addition, all technologies have vulnerabilities in their design and implementation, therefore understanding if these are significant is critical, noting that regulations only provide a minimum standard for compliance.

- **Monitor with continuous improvement**: Part of the complexity of this problem is that the counterfeiter and diverter will change their tactics over time in response to improved protection of products and acquisition of new skills. The system therefore needs to support monitoring to detect this activity as well as ensuring the process is being executed correctly and the technology has been implemented well.
About Cambridge Consultants

Cambridge Consultants has been established for fifty years as a leading product development business, now employing 300 staff with sites in Cambridge UK and Cambridge MA. For over twenty years we have been developing anti-counterfeit and authentication solutions for our clients spanning pharmaceutical, biotechnology, consumer electronics and appliances and Fast Moving Consumer Goods (FMCG) markets.

Our technology independence means that we are able to design and implement layered anti-counterfeit and anti-diversion solutions using a range of technologies, appropriate to the business need and existing or new brand protection strategies.

Our expertise extends to the development of reader technology for authentication features based on our optics, RF and sensing product design experience, allied with secure systems design knowledge.

We have specific experience in the application of statistical processing techniques for data analysis and optimal signal detection resulting in more robust and covert authentication techniques.

For further information, or to discuss your comments, please contact:

Ruth Thomson (Cambridge UK)
Ruth.Thomson@CambridgeConsultants.com
Rainuka Gupta (Cambridge MA)
Rainuka.Gupta@CambridgeConsultants.com