Emerging Issues in Europe

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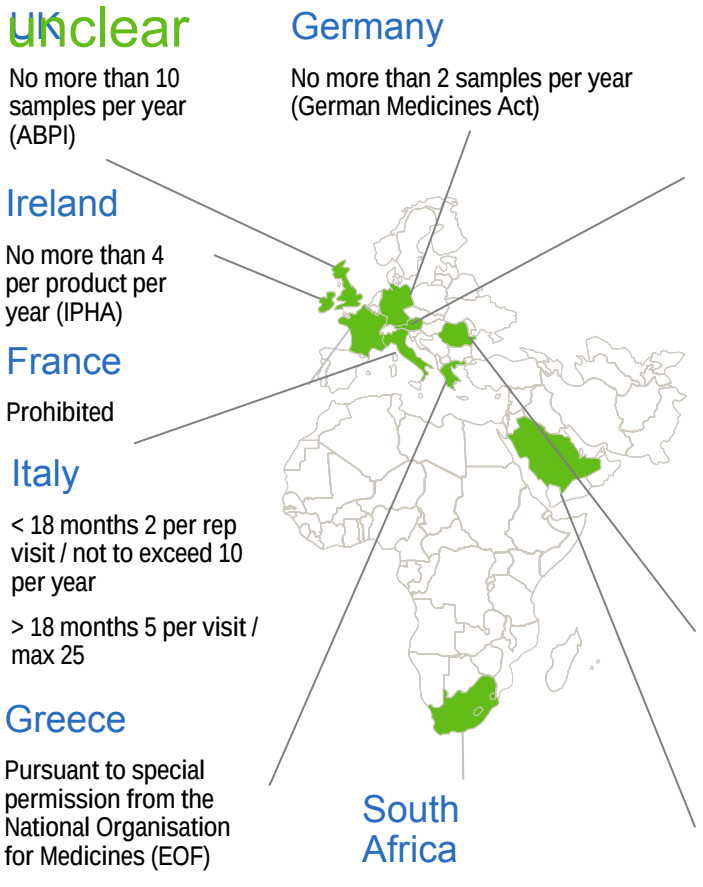
Taking Control of Product Sampling Programs

As promotional practices come under scrutiny, could product sampling programs be on the radar?

- Significant variation in sample limits imposed by codes-of-conduct
  - Increased complexity in managing compliance across the NEMIA region
- Interpretation of the rules is challenging
  - Imposed limits are often unclear e.g. Saudi Code of Good Pharmaceutical Marketing Practices limits the amount of samples to "modest quantities"
- Scale of sampling programs coupled with increased diversion and counterfeiting activity puts focus on sample accountability
  - Raises importance of ability to track product samples across the region

Significant code variation across the region and imposed limits often unclear



UK
No more than 10 samples per year (ABPI)

Germany
No more than 2 samples per year (German Medicines Act)

Austria
<1 yr
- sufficient quantity to assess therapeutic success in max 10 pts
- No more than 30 samples per recipient per product

>1 yr
- Maximum of 2 samples per request per recipient
- No more than 5 samples per year

(Pharma Industry Code of Conduct)

Ireland
No more than 4 per product per year (IPHA)

France
Prohibited

Italy
< 18 months 2 per rep visit / not to exceed 10 per year

> 18 months 5 per visit / max 25

Romania
Number to treat 10 patients / HCP / year

Greece
Pursuant to special permission from the National Organisation for Medicines (EOF)

South Africa
Prohibited

Saudi Arabia
Modest quantities

Source: Ernst & Young's 2007 Global Pharma Associations Sales and Marketing Code Matrix

Taking Control of Product Sampling Programs

The Risks

- **Breaching limits imposed by codes-of-practice**
  - Incurring associated fines and penalties and damage to reputation
- **Sample accountability requirements**
  - Incurring regulatory penalties for failing to be able to account for samples
  - Impaired product recall capability compromising patient safety due to lack of effective sample tracking systems
  - Diversion of samples / integrity against counterfeiting compromised
- **Sample pack patient information**
  - Patient safety compromised as samples supplied with inadequate patient information (e.g. Australia)
- **Fraud abuse by HCPs**
  - Prosecution for collusion in HCP reimbursement fraud (billing insurers for free-samples e.g. precedents set in the US)
- **Anticompetitive sampling practices**
  - Litigation under antitrust for using sampling programs to 'undercut' competing products

It is increasingly argued that free product samples potentially compromise HCP prescribing decisions. Calls for Sampling Programs to be banned in many parts of the world

A US study published in the Journal of Medical Ethics found that one in three doctors believes that their own decision to prescribe a drug is likely influenced by receiving samples from pharmaceutical sales representatives

Most doctors who distributed drug samples to patients said they did so because of patients' financial needs or convenience.

Less than two-thirds said they gave patients samples as the result of knowledge of the product's efficacy

"The most commonly reported problems were drug samples being supplied to patients with inadequate information regarding dosage, administration, storage and possible adverse effects,"

Report, published in the Australian Prescriber 2007

University of Michigan Health System has banned free samples and the University of Pennsylvania and Stanford University medical schools have prohibited staff members from accepting them

Ensuring Data Privacy

Privacy encompasses the rights and obligations of individuals and organizations with respect to the collection, use, disclosure, and retention of personal information about:

- Health care professionals
- Patients and trial participants
- Consumers and web site visitors
- Employees
- Other business partners

Privacy has become an increasingly critical issue as industries use personal information for a broader range of purposes:

- The lack of formalised privacy-oriented strategy has caused data to be exposed and potentially harvested
- Identity theft in the UK has increased by 500% since 1999
- Globalisation of systems, outsourcing and off-shoring of services mean that the boundaries of any given jurisdiction are unclear

Ensuring Data Privacy

The Risks

- **Brand and reputation hit**
  - Our code of conduct has it that "we never intentionally break any law"
  - Do not want to become an example of what could go wrong
- **Litigation**
  - There is increasing employee, and general public, awareness of what information is being held and their rights and responsibilities in relation to it
- **Regulatory action**
  - Increasing regulatory scrutiny
- **Direct financial loss**
  - Direct financial loss is small but cost of rectification is much higher
- **Loss of consumer and business partner confidence**
  - Third parties confidence in externalisation will require higher standards
- **Identity theft (employees, health care professionals, patients)**
  - Third parties confidence in externalisation will require higher standards
- **Loss of market value**
  - E.g. in the event that a critical database be subject to a freezing order

"In December 2005, a U.K. charity that provides aid to faith-based organizations, found its online systems breached by hackers. Besides possible stolen funds, more than 2,000 online donors' contact information was harvested in the attack. Since the incident, hackers have contacted donors directly for money."

"Eli Lilly: provided an e-mail reminder service on its Prozac.com web site that alerted customers when it was time to take their pills, get refills etc. When it cancelled the reminder service, it notified 669 subscribers with a notice that included their e-mail addresses in the cc: field. The FTC and eight states sued the company, saying it failed to protect customer information. The settlement agreements required the company to conduct an annual review of its information security program, tighten training and monitoring, and pay a $160,000 fee to be divided among the states." IT ARCHITECT, October 2005

"In West Palm Beach, Florida, a confidentiality disaster occurred in February when a HIV/AIDS statistical worker who normally gathers aggregate HIV/AIDS data for the health department inadvertently attached in an e-mail the names and addresses of 6,500 patients who tested positive for either HIV/AIDS and sent it to 800 health department employees."

Managing Risk around Risk Management Plans

EU Legislation in certain circumstances* obliges companies to submit a description of their risk-management system

- November 2005 – EMEA published guidance to the pharmaceutical industry on the establishment of EU-RMPs.
- Goal – Consistent approach for the detection, assessment, minimisation and communication of product risks in the EU
- Applicable to products in the pre-authorization and post authorization phases of either the centralised, decentralised or mutual recognition procedures

* With the application for a **new marketing authorization** for, in particular: any product containing a **new active substance**. With an application involving a **significant change in a marketing authorization**. **On request** from a Competent Authority (both in pre-and post- authorization). On the initiative of a Marketing Authorization Holders (MAA) and applicants (MAH) when they **identify a safety** concern with a medicinal product at any stage of its life cycle. Source: Article 6 of Regulation (EC) N° 726/2004 and Article 8 of Directive 2001/83/EC

Part I: Safety Plan

Safety Specification: identify any need for specific data collection to facilitate the construction of the pharmacovigilance plan

Pharmacovigilance Plan: describe routine pharmacovigilance and additional pharmacovigilance activities and action plans for each safety concern as identified

≠ with the pharmacovigilance system: product specific, not company specific

Part II: Risk

Evaluation of the need for risk minimization activities: whether there is a need for additional (i.e. non- routine) risk minimization activities

If yes, risk minimization plan: should include both routine and additional risk minimization activities and should list the safety concerns for which risk minimization activities are proposed

Managing Risk around Risk Management Plans

PART I

1. Safety specification:

- Summarize important identified risks, potential risks, and important missing information, and address populations potentially at risk and outstanding safety questions
- Help identify needs for specific data collection and facilitate construction of a pharmacovigilance plan

2. Phamacovigilance plan

- Describe pharmacovigilance activities (routine and additional) and action plans for each safety concern
- Propose actions to address identified safety concerns, complementing the procedures in place to detect safety signals

PART II

3. Evaluation of the need for risk minimization activities

- Discussing safety concerns incl. potential for Medication Errors and the need for routine or additional risk minimization strategies
- Assess for each safety concern whether risk minimization strategies are needed beyond the pharmacovigilance action plans

4. Risk minimization plan:

- List safety concerns for which risk minimization activities are proposed
- Discuss associated routine and additional risk minimization activities and the assessment of their effectiveness
- Detail risk minimization activities to reduce risks associated with an individual safety concern

Risk minimization activities may include:

– Provision of information to / training of healthcare professionals and/or patients on the specific risks of a product and the measures on how to reduce them

– Control of the conditions under which a medicine is prescribed and dispensed at pharmacy level in connection with its legal status

–"Certification" of healthcare-professionals

– Control of prescription size and validity

– Informed consent and other patient aspects

– Restricted Access Programs

– Patient Registries

(Source: Guidelines on Pharmacovigilance for Medicinal Products for Human Use)

Managing Risk around Risk Management Plans

- **43 plans submitted to the EMEA between November 2005 and September 2006**
- **EMEA examined 12 RMPs submitted as part of authorization procedures:**
- **Only 3 proved to be of acceptable quality**
- **9 considered deficient and of those 5 did not conform**
- **EMEA reinforced its communication with the industry about the spirit, rationale, and usefulness of RMPs**

Future Risks – Product Liability

Could an RMP help prove that the marketing authorization holder knew in advance the level of risk the drug posed to patients?

Could failure to carry out undertakings described in the RMP could carry risks in relation to product liability claims?

- Companies will need to pay careful attention when they draft RMPs
- Implementation and monitoring will also require a heightened level of vigilance and coordination across multiple functions

Coordinating an enterprise-wide RMP approach:

- Which functions do we need to include in the development, implementation, and monitoring RMPs? (e.g. pharmacovigilance, sales and marketing, regulatory affairs, legal, medical affairs, etc.)
- Which department will be held accountable for RMP compliance?
- Which level of the organization – for example headquarters or local subsidiaries – should draft, implement and control RMPs?
- How should we control and monitor RMP compliance when functions are outsourced to a third party?
- What is the process for updating RMPs with new controls in a coordinated manner? How can we avoid creating new control silos in the process?
- How do we determine which processes we need to create, amend, or delete to effectively implement the RMP controls?