Better Control of our Controlled Substances

A Pistoia Alliance Project

Domain Lead: Rob Lifely, GSK
Agenda

• Introduction to the Controlled Substance Compliance Services (CSCS) Project
• Benefits
• Business Challenge/Key issues
• Progress and timelines
• Summary
What are Controlled Substances?

- Compounds like marijuana, cocaine, LSD and ecstasy
- Compounds that are regulated by legislation
  - E.g., UK Misuse of Drugs Act 1971
- Such compounds must be identified, stored, handled, shipped and tracked in accordance with this regulation
Legal Highs - A Deadly Serious Problem?

- Legislation is constantly evolving and becoming more complicated as it attempts to mirror developments in substance abuse.

**Mephedrone ban comes into force in UK**

A ban on synthetic stimulant mephedrone has come into force across the UK.

The drug and its related compounds are now Class B substances after measures were rushed through Parliament.

The Advisory Council for the Misuse of Drugs (ACMD) had recommended a ban, saying the substance was "likely to be harmful" despite incomplete research.

**U.S. bans chemicals in "bath salts" street drug**

FISHERSVILLE, Va. -- A panel comprised of local law enforcement officials, substance abuse counselors and medical personnel addressed a concerned crowd of 153 people on the dangers of bath salts Tuesday night at Augusta Health.

Described as a "new designer drug," bath salts can be swallowed, snorted, injected or smoked, and some of the most common side effects include severe paranoia, delusions, suicidal thoughts and intense cravings for more consumption.
Legal Highs - A Deadly Serious Problem?

- Legislation is constantly evolving and becoming more complicated as it attempts to mirror developments in substance abuse.

The hidden dangers of legal highs

In the last five years, the market for legal highs has exploded. It's never been easier, or cheaper, to buy drugs online - but no one knows what's in them, or how dangerous they are.

The Guardian Friday 26 April 2013

U.S. bans chemicals in "bath salts" street drug

methylene dioxy pyrovalerone (MDPV)
Project History

• In 2011, AZ and GSK began exploratory talks on Compound Exchange Standards
  - Getting to know one another
  - Getting to understand what we do, how we work and what we can share
  - Getting to understand what Pistoia is and how it could benefit us
The Pistoia work-stream ‘Compound Exchange Standards’ identified the management of controlled substances as the stand-out topic under discussion to take forward to full project status.

The fundamental requirement is to answer the question “Are any of my compounds Controlled Substances?”

- Based on the legislation in all geographies
How would we use this service?

- **Internal Compound Collections**
  - Regular checks to ensure controlled substances are correctly flagged

- **Compound Shipping**
  - Ensure that controlled substances are not inadvertently shipped within or between countries

- **Compound Synthesis**
  - Ensure that controlled substances are not inadvertently synthesised

- **Compound Purchase**
  - Ensure that controlled substances are not inadvertently purchased
Controlled Substances Compliance Service

Unmet Need

- Pharmaceutical companies routinely work with controlled substances, so must have adequate controls in place.
- Legislation is increasingly complex as legislators attempt to keep up with a rapidly changing environment.
- The externalisation of pharma means compounds are produced, stored and transported across all geographies.
- No single source of global controlled substance knowledge is available; just the legislation itself or specific country / legislation-type databases/websites.
- It is imperative that pharma has a clear, detailed and accurate understanding of the regulations in all regions.

Value Proposition

- Establish a high-quality, controlled substance compliance information service that will enable pharma to maintain compliance in whatever geography they are operating.
- Each pharma company only has a small number of domain experts able to monitor and interpret the legislation. Provision of a comprehensive service will minimize the risk created by the size-limited workforce and will also eliminate the replication of effort across the pharmaceutical industry.

Business Case

- Projected Shared Project Costs - $170,000 [Project Analyst, Ethical Hack, Implementation, Project meeting]
- Estimated value for the industry of implementing this project is - $90m
  - FTE saving on employing/training domain expertise to monitor and interpret the legislation
  - FTE saving on the transformation of legislation into data that can be used to enforce control
- Risk mitigation - fines, damage to reputation, revocation of licences to operate with controlled substances

High Level Implementation Timeline

- Project Start: Q2
- Funding Agreed: Q4 - 12
- Funding Available: Q2 - 13
- Vendors build systems: Q4 - 13
- Service Available: Q4 - 13
Pistoia Alliance - Generic Project Process

1. Get Companies interested
2. Build Business Case
3. Pistoia Board Review

Phase Two
- Shared-risk funding?
- Request for Proposal
- Selection of vendors

Phase One
- Requirements
- Proof-of-concept

Obtain Funding

Production

Individual companies make their individual choice of vendor
CSCS: What is the unmet need?

- Pharmaceutical companies routinely work with controlled substances, so must have adequate controls in place.
- Legislation is increasingly complex as legislators attempt to keep up with a rapidly changing environment.
- The externalisation of pharma means compounds are produced, stored and transported across all geographies.
- No single source of global controlled substance knowledge is available; just the legislation itself or specific country / legislation-type databases/websites.
- It is imperative that pharma has a clear, detailed and accurate understanding of the regulations in all regions.
CSCS: Value Proposition

- Establish a high-quality, controlled substance information service
  - Maintain compliance in all geographies
- Each pharma company has a small number of domain experts to monitor and interpret the legislation
  - Comprehensive service to minimize risk
- Eliminate the replication of effort across the pharmaceutical industry
  - Common interpretation of legislation
CSCS: Business Case

- Projected Shared Project Costs ~$170,000 [Project Analyst / Manager, Ethical Hack, Implementation, project meetings]
- Estimated value for the industry of implementing this project is ~$90m
  - FTE saving on employing/training domain expertise to monitor and interpret the legislation
  - FTE saving on the transformation of legislation into data that can be used to enforce control
- **Risk mitigation** - fines, damage to reputation, revocation of licences to operate with controlled substances
Business Challenge

- Legislation exists at local, national and international levels to restrict the production, import/export, supply, use and possession of certain substances.

- Legislation has to be interpreted and transformed from legal wording into scientific nomenclature to be useful, e.g. words into chemical structures.
  
  ‘Acetorphine’ into

- Pharmaceutical companies must hold multiple licences to conduct research across the field of restricted substances.

- But it doesn’t stop at research...restricted substances can be found in all areas of pharmaceutical company operations, including final products.
**Business Challenge - Phenethylamines**

![Chemical Structure]

R1 = H, Me or Et

R2 = H or alkyl (saturated aliphatic, straight chain or branched)

X (illustrated in 4 position only but can be in one or all of the 2, 3, 4, 5 or 6 positions) = halo, alkyl, alkoxy or alkylenedioxy

Alkylenedioxy - most commonly methylenedioxy, resulting in a 1,3-benzodioxole, less commonly ethylenedioxy, resulting in a 2,3-dihydrobenzodioxin and so on.
Business Challenge

The global nature of externalisation - including outsourcing and collaboration - is increasingly prevalent in today’s pharmaceutical industry. Businesses need to know the international, regional and local laws wherever they operate...

The United Nations Single Convention on Narcotic Drugs 1961
- United Nations Convention against the Illicit Traffic in Narcotic Drugs and Psychotropic Substances 1988
- United Kingdom Misuse of Drugs Act 1971
- United States Controlled Substances Act 1970
- United States CHEMICAL DIVERSION AND TRAFFICKING ACT OF 1988
- Canadian Controlled Drugs and Substances Act 1996
- India - Narcotic Drugs and Psychotropic Substances Act, 1985
- Singapore – Misuse of Drugs Act
- New Zealand – Misuse of Drugs Act 1975
- Thailand - Psychotropic Substances Act
- Pakistan - Narcotic Drugs and Psychotropic Substances Act, 1985
- Australia - Standard for the Uniform Scheduling of Medicines and Poisons
- Philippines - Comprehensive Dangerous Drugs Act of 2002
- Russia - Regulations on the State Committee of Russian Federation for the control of narcotic drugs and psychotropic substances
- United Arab Emirates - UAE Federal Law 14 of 1995
- Japan - Narcotics & Psychotropics Control Law, Stimulants Control Law, Narcotics Special Law
- South Africa - Drugs and Drug Trafficking Act No. 140 of 1992
- Iceland - Regulation on habit-forming and narcotic substances and other controlled substances No. 233/2001
- Gibraltar - Drugs (Misuse) Act 1973
- Indonesia – law on narcotics (Law No. 22/1997), law on psychotropics (Law No. 5/1997)

Belgium - Royal Decree of 1930 on narcotic substances and Royal Decree of 1998 on psychotropic substances
- Czech Republic - Law no. 167/1998, On Narcotic Drugs and Psychotropic Substances
- Denmark - Executive Order 698 of 1993 on Euphoric Substances
- Germany - Narcotics Act (BTMG)
- Spain - Order of 8th July 1967 and the Royal Decree 2829/1977
- Ireland - Misuse of Drugs Regulations1988
- France – Decree Law of 22 February 1990
- Netherlands - Opium Act
- Portugal - Decree-Law 15/93
- Norway - Regulation of 1978
- Poland - 1997 Act on Counteracting Drug Addiction
- Estonia - Regulation No 39 of the Minister of Social Affairs of 4 November 1997
- Austria - ‘Narcotic Substances Act’ (Suchmittelgesetz, abbr. SMG)
- Italy - Decree 4 March 1992
- Sweden - Narcotic Drugs Punishments Act (1968:64).
- Portugal - Decree Law 15/93, of 22 January 1993
- Slovenia - Production and Trade in Illicit Drugs Act
- Slovakia - Act No. 139/1998
- Romania - Law no. 143/2000
- Malta - Medical and Kindred Professions Ordinance (Cap. 31), Dangerous Drugs Ordinance (Cap. 101)
- Bulgaria - Drugs and Precursors Control Act 1999
- Croatia - Law on Combating Narcotic Drugs Abuse 2001
- Cyprus - Narcotic Drugs and Psychotropic Substances Law 1977
- Finland - Narcotics Act (1289/1993)
- Latvia - Law on Procedures for the Legal Trade of the Narcotic and Psychotropic Substances, Law on Precursors
Business Challenge

As well as addressing controlled drugs and drug precursors the intention is to cover prohibited or regulated compounds such as those compounds covered by:

- Chemical Weapons Convention
- Ozone Depletion Legislation
- Dual Use legislation
- European REACH regulations
- UK HSE (COSHH/COMAH) and US OSHA regulations
- US Department of Homeland Security regulations

REACH – Registration, Evaluation and Authorisation of Chemicals
COSHH - Control of Substances Hazardous to Health
COMAH - Control of Major Accident Hazards
OSHA - Occupational and Safety Health Administration
## CSCS Project Team

<table>
<thead>
<tr>
<th>Company</th>
<th>Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>3E</td>
<td>Kishore Mamidi, Jeffrey Starr, Alex Ortiz</td>
</tr>
<tr>
<td>Accelrys</td>
<td>Keith Taylor, Sanjay Gupta</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>Daniel Taylor, Stuart Bowden</td>
</tr>
<tr>
<td>Binocular Vision</td>
<td>Tom Blackadar</td>
</tr>
<tr>
<td>Boehringer-Ingehelm</td>
<td>John Proudfoot</td>
</tr>
<tr>
<td>ChemAxon</td>
<td>Alex Drijver, Tim Dudgeon, Douglas Drake, Aurora Costache, Daniel Bonniot</td>
</tr>
<tr>
<td>GGA Software</td>
<td>James Martin</td>
</tr>
<tr>
<td>GSK</td>
<td>Rob Lifely (Project Lead), Derek Wilson</td>
</tr>
<tr>
<td>InfoChem</td>
<td>Josef Eiblmaier, Stephanie North, Jürgen Rochlitz</td>
</tr>
<tr>
<td>Merck</td>
<td>Jim Goggin, Michael Bernstein, Kay Nyman</td>
</tr>
<tr>
<td>LHASA</td>
<td>Chris Barber, Nicole McSweeney</td>
</tr>
<tr>
<td>Novartis</td>
<td>Marc Andreae, Greg Wendel</td>
</tr>
<tr>
<td>Robert Schwartz</td>
<td>Robert Schwartz</td>
</tr>
<tr>
<td>Roche</td>
<td>Eva-Maria Gutknecht, Reinhard Knorr</td>
</tr>
<tr>
<td>Scitegrity</td>
<td>Ian Johns, Joe Bradley, Drew Gibson</td>
</tr>
<tr>
<td>Pistoia Alliance</td>
<td>Anne Dunlop (Project Manager), John Wise</td>
</tr>
</tbody>
</table>
Core Deliverables

An Expert System to determine if a substance is controlled

• Searchable by:
  - Structures
  - Chemical / Common Names (e.g. IUPAC, INN, Trade name)
  - Common Substance Identifiers (e.g. CAS No)

• Legal Status (Global, Regional, Country, Intra-Country State/Regional legislation)

• Updated at defined intervals as agreed by the project group

• Easily accessed by each project partner

A Legislation Notification Service

• Customers notified about proposed changes to legislation

• Customers notified when new update packages are available to be downloaded

• Guidance on the impact of the legislative change

• Notification of updates to the Expert System data or code including download instructions
Core Deliverables

This dataset to be implemented in the following incremental way:

- Deliverable 1a: Controlled Drugs lists for North America/Europe
- Deliverable 1b: Controlled Drugs lists for RoW
- Deliverable 2a: Other restricted compounds lists for North America/Europe
- Deliverable 2b: Other restricted compounds lists for RoW
## Project Timelines

<table>
<thead>
<tr>
<th>ID</th>
<th>Task Name</th>
<th>Start</th>
<th>Finish</th>
<th>Duration</th>
<th>Q1 13</th>
<th>Q2 13</th>
<th>Q3 13</th>
<th>Q4 13</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Requirements Gathering</td>
<td>01/01/2013</td>
<td>23/04/2013</td>
<td>16.2w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>RFP Process (incl. Preparation)</td>
<td>25/03/2013</td>
<td>14/06/2013</td>
<td>12w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Contract(s) awarded</td>
<td>14/06/2013</td>
<td>14/06/2013</td>
<td>0w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Vendors Assign CSCS project teams</td>
<td>17/06/2013</td>
<td>28/06/2013</td>
<td>2w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Vendors build CSCS system</td>
<td>01/07/2013</td>
<td>21/11/2013</td>
<td>20.8w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Vendors compile 1st dataset</td>
<td>01/07/2013</td>
<td>19/11/2013</td>
<td>20.4w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Project Progress Review</td>
<td>25/07/2013</td>
<td>25/07/2013</td>
<td>0w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Project Progress Review</td>
<td>05/09/2013</td>
<td>05/09/2013</td>
<td>0w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Project Progress Review</td>
<td>17/10/2013</td>
<td>17/10/2013</td>
<td>0w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Write UAT test Spec</td>
<td>21/06/2013</td>
<td>12/07/2013</td>
<td>3.2w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Test Dataset Preparation</td>
<td>24/06/2013</td>
<td>17/09/2013</td>
<td>12.4w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>CSCS System ready for UAT</td>
<td>21/11/2013</td>
<td>21/11/2013</td>
<td>0w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Perform UAT</td>
<td>21/11/2013</td>
<td>05/12/2013</td>
<td>2.2w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>System security audits, incl. an ethical hack</td>
<td>05/12/2013</td>
<td>11/12/2013</td>
<td>1w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>UAT Complete</td>
<td>11/12/2013</td>
<td>11/12/2013</td>
<td>0w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>System(s) demonstrations</td>
<td>12/12/2013</td>
<td>18/12/2013</td>
<td>1w</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CSCS Project RFP process

2 vendor consortia selected
ChemAxon/Patcore and Scitegrity/Keller Heckman
Currently Monitoring Vendor Progress

- Each vendor providing regular email updates - sent to steering committee
- 6 weekly review meetings
  - Final review meeting will involve demo/testing of system prototypes
Currently Preparing for UAT

- UAT Specification - based on Requirements
- Build test dataset
CSCS Ethical Hack

- AT&T will perform the ethical hack providing objective, expert, third-party analysis
- AT&T will ethically hack the public portions of each vendor’s CSCS including the service which provides the data updates
- The bulk of the CSCS will sit behind a customer’s IT firewall and will not be hacked
- The output will be a set of recommendations for improved security which will benefit the CSCS customers and vendors
What does success look like?

- **CSCS Delivery**
  - There are no outstanding issues that would prevent the launch of the CSCS to potential subscribers.
  - All the points listed in the Scope statement have been delivered.
  - The CSCS is available for use and a number of companies have signed up to use the service.
  - **Longer Term:** Controlled Substance Compliance Services are recognized as an authoritative information source for controlled substance information by the pharma industry and regulatory authorities.
What are the Project Risks/Issues?

- Timelines are overly ambitious
- Interpretation of the legislation from the Expert System
  - Lack of confidence that CSCS data is complete and correct
- Unable to develop a business model which is equitable for the organisations funding the project and the service provider(s)
CSCS Project - Budget and Costs

- Funding from AZ, GSK, Merck, Novartis and Roche
- Projected Project costs

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Part-time Project Analyst/Manager</td>
<td>$50,000</td>
</tr>
<tr>
<td>Ethical hack</td>
<td>$20,000</td>
</tr>
<tr>
<td>Shared-risk implementation of Service</td>
<td>$80,000</td>
</tr>
<tr>
<td>G&amp;A</td>
<td>$20,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$170,000</strong></td>
</tr>
</tbody>
</table>

Note these project costs are **indicative** only
Summary

- **Pistoia Alliance motto:**
  - “If you want to go fast, go alone. If you want to go far, go together”
- **Allow time to get from first idea to project initiation**
- **CSCS project is underway with planned completion by end 2013**
  - Substantial funding has been obtained
  - Project Team (both Pharma and Vendors) and Steering Committee assembled
  - Requirements documented
  - Request for Proposal (RFP) phase complete
  - Vendors are building systems
  - Preparing for UAT and Ethical Hack
  - Project is on time and within budget
- **Main benefit is risk mitigation**
  - Avoid fines and loss of reputation