Australian Government
Department of Health
Therapeutic Goods Administration

Illegal Products – what can be done?

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TGA Health Safety Regulation

Outline

Part 1: Illegal products

- Collaboration with other agencies to prevent/capture illegal products
- Collaboration with agencies on the diversion of illicit drug manufacture
- TGA international approach to therapeutic product vigilance; monitoring overseas trends and experiences

Part 2: Quality considerations

- Defining Quality
- Measuring Quality
- Ensuring Quality
- Unacceptable Quality
- TGA's quality monitoring programs

Part 1: Illegal products

- Includes goods that are imported, manufactured, supplied or exported and NOT INCLUDED IN THE ARTG, or exempted from being in the ARTG
  - Counterfeit goods can include unapproved manufacturer/manufacturing site, falsified documentation, unapproved product
  - The TG Act contains many offence provisions

Illegal manufacture - in progress

The manufacture of a range of vitamin and mineral tablets, all of which were found to contain no active ingredients at all - only colours, flavours, fillers & binders

Manufacturing offences

Making capsules inside a house

Manufacturing offences

- Clandestine laboratories
- Producing illicit therapeutic goods
- Public health risk due to conditions of manufacture

Counterfeit - bulk substitution of unapproved product

Capsules manufactured in unapproved factory in Thailand, substituted for capsules manufactured in approved factory in Canada.

Counterfeiting - in progress

Imported sea container of machinery, ingredients, packaging, etc. delivered to counterfeiter and used to manufacture a counterfeit herbal

Collaboration with other agencies to prevent/capture illegal products

- TGA works closely with Customs to prevent import of illegal products, including 'herbal dietary supplements' adulterated with prescription medicines.
- Customs maintains a list of prohibited products/substances which will be turned back at the border. New products suspected of adulteration will be referred to the TGA for investigation.
- TGA collaborates with State and Territory police forces and Health departments to prevent and recall the sale of unsafe, illegal and unregistered medicines within Australia.
- TGA puts out safety alerts on illegal and unsafe products on the TGA website (http://www.tga.gov.au/current-year-alerts)

TGA international approach to therapeutic product vigilance; monitoring overseas trends and experiences

- Policy level – SSFFC - **Substandard/spurious/falsely-labelled/falsified/ counterfeit medical products (http://apps.who.int/gb/ssffc/)**
- **Enforcement - PFIPC (http://www.pfipc.org/)**
- **Laboratory – International Laboratory Forum on Counterfeit Medicines**

Operation Pangea VII

International Collaboration

- Operation Pangea is a PFIPC Initiative
- Co-ordinated by Interpol
- Annual collaboration between international drug regulators, Customs and Police.
- PANGEA VII (13-10 May 2014),
- 113 Participating Countries
- 198 Participating Agencies

Pangea VII Results (2014)

- 9.6 million fake and illicit medicines seized, including slimming pills, cancer medication, erectile dysfunction pills, cough and cold medication, anti-malarial, cholesterol medication and nutritional products;
- Seizures worth more than USD 32 million;
- 434 arrests;
- 1,249 investigations launched;
- 22,800 adverts for illicit pharmaceuticals removed from social media platforms;
- More than 11,800 websites shut down

Part 2: Quality considerations

- Objects of the TG Act
  - Provide for the establishment and maintenance of a national system of controls relating to the QUALITY, SAFETY, EFFICACY and TIMELY AVAILABILITY of therapeutic goods that are:
    - Used in Australia, whether produced in Australia or elsewhere; or
    - Exported from Australia

Defining Quality (1)

- ARTG entry defines the product
- Listed Goods are SEPARATE AND DISTINCT if:
  - Different active ingredients
  - Different quantities of active ingredients, or
  - A different dosage form
  - Or different characteristics as prescribed in regulations (name, indications, excipients etc)

Defining Quality (2)

- 'Official' Standards
  - Therapeutic Goods Orders
  - Pharmacopoeias (BP, EP, USP-NF)

- Conditions of inclusion may specify quality requirements
- All batches must comply with official standards, unless an exemption is granted

Defining Quality (3)

- Quality must be built in to a product
- Monographs apply to ingredients and finished products
- Monographs are limited to what is known about an ingredient or finished product or what can reasonably be expected to be known
- Monographs support other regulatory controls such as compliance with manufacturing requirements

Measuring Quality

- Methods and limits in Official Standards are definitive
- Alternative methods may be used if they are equivalent or superior
- GMP allows for reduced testing based on justifications
- GMP allows for vendor qualification rather than full testing on receipt

Ensuring Quality

- Finished product – GMP (licence, certification or clearance)
- API – supplier verification, API acceptance testing
- MANUFACTURER'S RESPONSIBILITY

Unacceptable Quality - Consequences

- Possible impact on safety and/or efficacy
- Possible impact on consumer confidence and company reputation
- Possible regulatory actions include:
  - Batch recall, product de-listing, conditions on supply (eg folic acid dissolution, *Ginkgo biloba* ID test), conditions on manufacturing licence, use of civil/criminal penalties

TGA's Quality monitoring work

- GMP
- Listing verifications
- Laboratory programs
- Complaints

TGA's Quality monitoring work – Laboratory programs (1 - programs)

- Response to safety issues, complaints, GMP findings
  - Prioritised according to risk
- Monitoring programs
  - Developed in conjunction with other areas of TGA

TGA's Quality monitoring work – Laboratory programs (2 - methods)

- Full range of compendial testing, including micro, as required
- Screening for undeclared substances using LC-MS or GC-MS
  - LC- PDA spectrophotometers, various mass spectrometry techniques including Ion Trap, Triple Quadrupole, Time of Flight, and Orbitrap. Provide capability for tandem MS (i.e. multi-fragmentation steps) and/or high resolution mass analysis (allows identification via molecular formula determination).
  - Screen for pharmaceutical adulterants using an in-house library of reference standards (> 500 pharmaceutical compounds). Confirmatory testing is often conducted by LCMS.

TGA's Quality monitoring work – Laboratory programs (3 – some recent examples)

- Heavy metals - Recent survey of 33 products to check heavy metal content (As, Hg, Cd, Pb)
  - 2 products were found to have unacceptable levels of Arsenic (SUSMP limit is 1 ppm):
  - One sample contained 2.2 ppm of arsenic.
  - One sample contained 1,180 ppm - consumer level recall instituted on 14/05/2015.
- Toxic components:
  - aristolochic acid (condition of listing that evidence for each batch of potentially contaminated product must be provided to TGA to demonstrate absence of AA),
  - aconitine,
  - ephedra
- Current survey of listed medicines claiming indications for weight loss or libido enhancement screened for pharmaceutical adulterants

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