

Active Pharmaceutical Ingredients (API's) in Australia One Manufacturer's View

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APIMAA

Active Pharmaceutical Ingredient Manufacturers' Association of Australia

Acknowledgement

This presentation was initially developed by Tim Bowser, Operations Manager, Glaxo SmithKline for the Active Pharmaceutical Ingredient Manufacturers Association of Australia
APIMAA

Overview

- Introduction to the API Manufacturers Industry Representative Body-APIMAA
- APIMAA background & objectives
- Our TGA experience
- API manufacture in Australia
- API manufacture in Australia - Special Challenges
- API manufacture – GMP in the 21st Century
- Future Activities
- A View of one Manufacturer

APIMAA

- Peak industry body representing Active Pharmaceutical Ingredient manufacturers in Australia
- APIMAA membership represent >80% of API value manufactured in Australia
- Employ over 400 staff, exports total in excess of A\$250m, dominant world players in Natural Product Extraction & Alkaloid API production

APIMAA

- APIMAA was formed when the main API manufacturers joined forces in 1997 in response to TGA introducing the API code of GMP (1996-2001, ICH Q7A)
- APIMAA was invited by TGA to be involved in the policy development, and played a key role in the review of ICH Q7A.

APIMAA Objectives

- Represent the interests of API manufacturers in Australia
- Regular communication with the TGA
- Raise the profile of the Australian API industry
- Technical skills support network for members

Our TGA Experience

- Consultation
 - Our own code of Good Manufacturing Practice (cGMP) – Q7A
 - Regularly meet with TGA executive
 - APIMAA provides open forum for common concerns of members
 - Advice obtained on specialist issues
 - Association provides point of contact for consultation on regulatory policy change

Our TGA Experience

- Audits

- All members audited in past 2 - 4 years
- Observed increase in Audit consistency
- Man-hours per audit quadrupled
- Main observations – environmental control, validation and risk management



API Manufacture in Australia

- Definition of an API according to the cGMP
- API Manufacture presents unique GMP challenges

API Manufacture in Australia

- A limited number of manufacturers operate in Australia:-
- Alkaloids of Australia
 - Hyoscine (Scopolamine) derivatives
- Glaxo SmithKline
 - Codeine and Morphine
- Phytex Australia
 - Hyoscine and Castanospermine derivatives
- Tasmanian Alkaloids
 - Morphine, Thebaine

API Manufacture in Australia



API Manufacture in Australia



API Manufacture in Australia

- API's manufactured:
alkaloids, flavenoids, extraction of bioactives, biopharmaceuticals, etc
- API's are used for finished product manufacture, drug development and clinical trials
- Significant R&D product development programs for new API's

API Manufacture in Australia



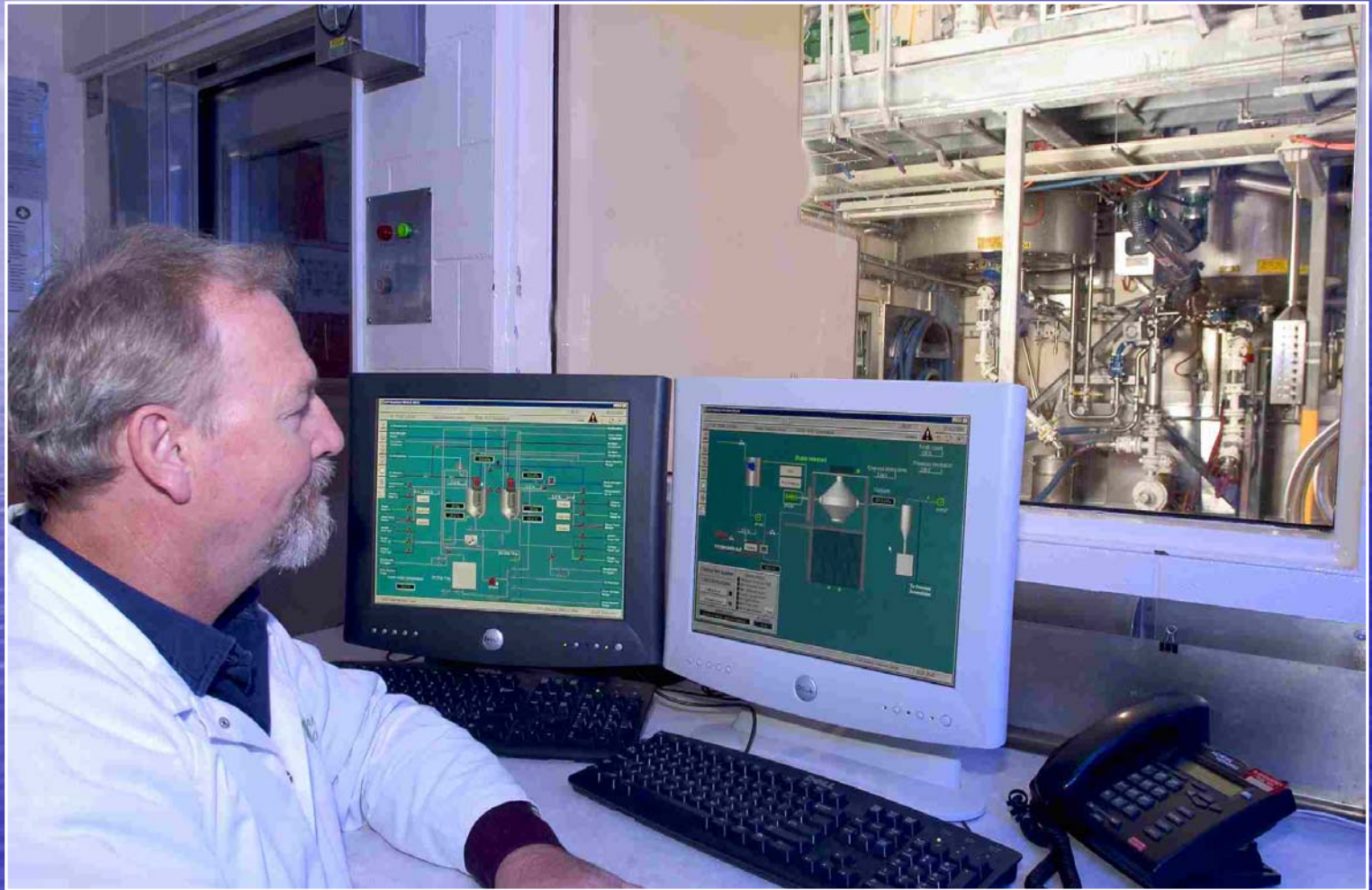
API Manufacture in Australia



API Manufacture in Australia



API Manufacture in Australia



API Manufacture in Australia

Special Challenges

- The (not) Level Playing Field
 - Formulators importing from non-regulated API suppliers
 - High level of productivity required to compete internationally
 - TGA GMP expectations - “highly regulated environment”
- The offshore competition’s size and globalisation

API Manufacture in Australia

Special Challenges

- Limited support network for Technical skills
 - Small number of API manufacturers
 - Facilities often located in regional areas
 - Limited pool of technical staff that understand API manufacture and have GMP experience
 - No equivalent Fine Chemicals Industry

API Manufacture in Australia

Special Challenges

- Hazardous Chemicals
 - Natural Product Extraction & API manufacture
 - Hazardous area regulations
 - Safe manufacture requires specialist technical skills
 - GMP requirements – residual solvents

API Manufacture in Australia

Special Challenges

- Natural Product Complexities
 - Natural Products variable by their nature
 - Special requirements
 - eg. pesticides, herbicides for plant materials
 - Process understanding requires advanced chemistry & engineering know-how
 - Robust manufacturing processes required to produce consistent quality
 - Contamination control / sterility for tissue derived materials

API Manufacture in Australia

Special Challenges

- Biotechnology Product Complexities
 - Closed system, “sterile” manufacturing process
 - Some process equipment can not be sterilised, requires sanitisation
 - Inherent API heterogeneity & highly complex analytical methods
 - Manufacturing process is integral part of product quality definition

API Manufacture

Dealing with GMP in the 21st Century

- Increased Scientific Understanding
 - Greater understanding of Quality Critical Parameters
 - Emphasis on Processes Understood, Capable & Controlled
 - Increased use of Statistical methodology
- Validation
 - proof of process control capability

API Manufacture

Dealing with GMP in the 21st Century

- Particulate Contamination
 - Environmental Control of Product Isolation
- Systematic approach to Risk Management
 - ICH Q9 - Risk in small enterprises
- Quality Management Systems
 - ICH Q10 and ISO 13485
 - why is ISO 9000 not enough for regulators!

Future Activities

- Qualified Person
 - Industry input into developing a certification model for the 'Qualified Person' welcomed
 - Should enhance International image of Australian API manufacturers
- Level Playing Field
 - Tighter GMP control of API importers welcomed

- A VIEW OF ONE
API MANUFACTURER

Alkaloids of Australia

- Operations are based on synthesis of Scopolamine (Hyoscine) derivatives from extracts of the Duboisia plant
- A locally owned, the sole Australian Hyoscine API manufacturer located in Kingaroy
- Vertically integrated company selling commodity API's almost entirely to export
- A small but significant and competitive part of the world market

Alkaloids of Australia

- Scopolamines are tropane alkaloids, a quaternary ammonium compound the common forms of which are the butyl and hydro bromides.
- They are muscarinic antagonists (CNS interferers)
- Used in
 - Travel sickness tablets
 - Pre and post operative injectables
 - General analgesics – particularly overseas
 - Ophthalmic solutions (pupil dilation)

Alkaloids of Australia

- Commercial Duboisia plants are hybrids of a cross developed in the late 60's from 2 Australian natives
- Almost all the world's commercial scopolamine is grown around Kingaroy



Alkaloids of Australia

- Leaf contains from 1 – 3% scopolamine along with other related compounds
- Harvested, stripped and dried October to May and stored for processing



Alkaloids of Australia

- Unique extraction process yields the scopolamine base



Alkaloids of Australia

Synthesis and purification of the hydro and butyl bromides follows



Alkaloids of Australia

- Preparation of the dried product for packaging to 1 kg containers



Alkaloids of Australia

- Dispatch to order in quantities of 1 – 1000 kg



Thank you for this opportunity to share our
view of the smallest part of Australia's
pharmaceutical industry