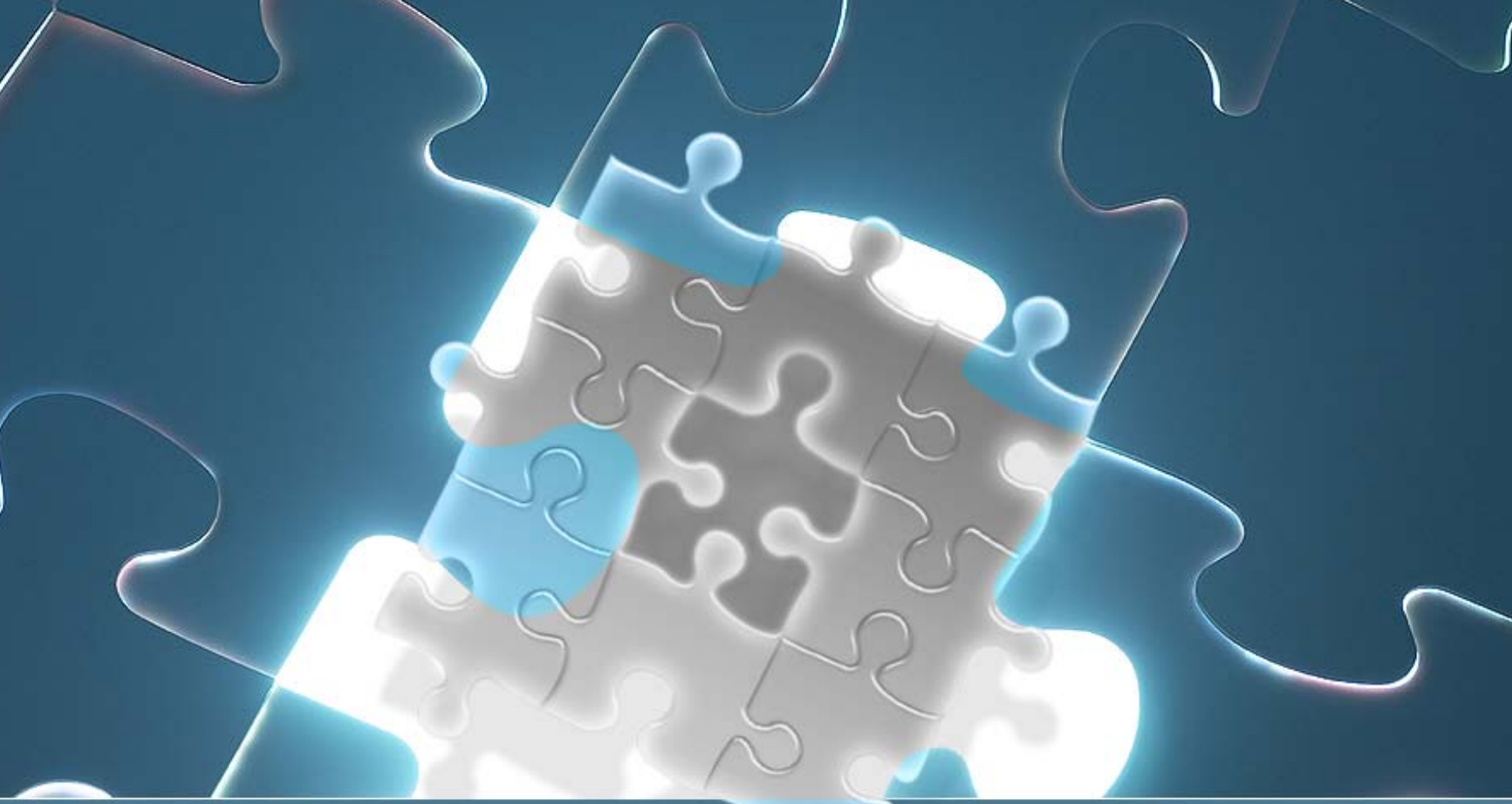


GMP in Complimentary Manufacturing

GMP ?

Good

Manufacturing

Practice

GMP ?

Great

Mounds

Paper

GMP ?

Best Practice

Efficient & Effective way of accomplishing a task based on repeatable proven procedures

COMPLEMENTARY MEDICINES

Traditional or alternative medicines

Examples include vitamins, minerals, nutritional supplements and herbal, aromatherapy and homoeopathic products.

GMP HISTORY

- First Australian Code of GMP 1991
- PICs adopted (in part) in 2002
- Guide to interpretation of the Code of GMP applicable to Complementary Medicine Manufacture 2003
- Australian Regulatory Guidelines for Complementary Medicines 2005
- Starting materials & Finished Product Analytical Procedure Validation for Complimentary Medicines 2006

Requirements for Complimentary Medicines

Are they different from Pharmaceuticals?

Requirements for Complimentary Medicines

1. Quality Management
2. Personnel
3. Premises & Equipment
4. Documentation
5. Production
6. Quality Control
7. Contract Manufacture & Analysis
8. Complaints & Recall
9. Self Inspection

Requirements for Complimentary Medicines

- Annex 7 – Manufacture of herbal medicinal products
- Annex 8 – Sampling of Starting & Packaging Materials
- Annex 9 – Manufacture of Liquids, Creams & Ointments
- Annex 11 – Computerised Systems
- Annex 15 – Qualification & Validation

GMP

Good **M**anufacturing **P**ractice

- Code of GMP gives us the **"WHAT"**
- We need to find out the **"HOW"**

GMP the "HOW"

Premises –

CONTROLLED ENVIRONMENT

Influenced By –

- Temperature
- Humidity
- Air Movement
- Microbial & Physical Contamination

GMP the "HOW"

Premises –

CONTROLLED ENVIRONMENT

- Air Filters in Manufacturing areas should be at least EU7 grade or equivalent
- Monitoring of HVAC use Grade D from the Annex 1 for Sterile Medicinal Products
- Pressure differentials and air flows must be appropriate.

GMP the "HOW"

Premises –

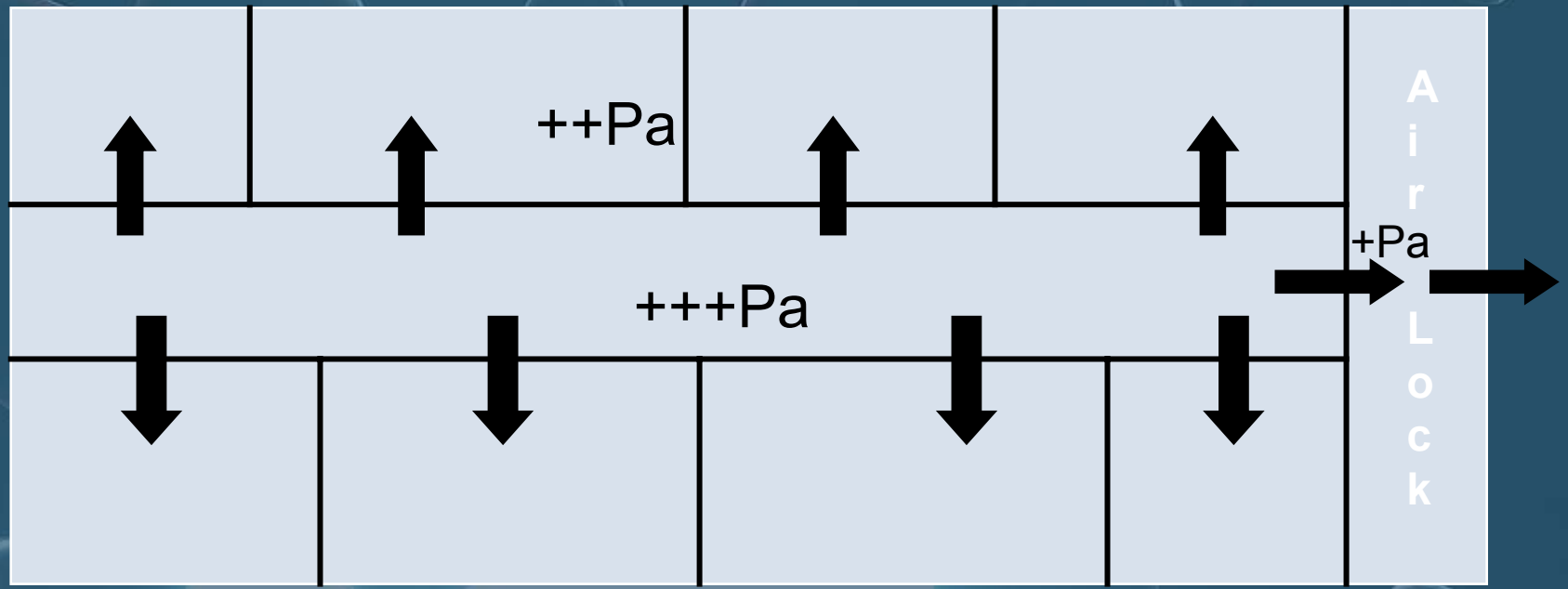
CONTROLLED ENVIRONMENT

- Differential pressures are used to control cross contamination
- Contain activities in each room
- Corridors at Health World have the highest pressure

GMP the "HOW"

Premises –

CONTROLLED ENVIRONMENT



GMP the "HOW"

Processes –

PROCESSES MUST BE UNDER CONTROL

GMP the "HOW"

UNCONTROLLED PROCESSES

- Degradation of Product
  Stability and shelf life problems
- Contamination of Product
  Threat to consumer
- Reworks
  Lost time
- Loss of batch
  Loss of profits

GMP the "HOW"

Standardise Processes

Eliminate Variation

Variation = Waste

GMP the "HOW"

Standardise Processes

Elimination of Waste –

- **Time**
- **Reworks**
- **Failed Batches**

GMP the "HOW"

Processes – **Standardise - Warehouse**

- Set all in order
- Instil Discipline

GMP the "**HOW**"

Processes –

Standardise - Production

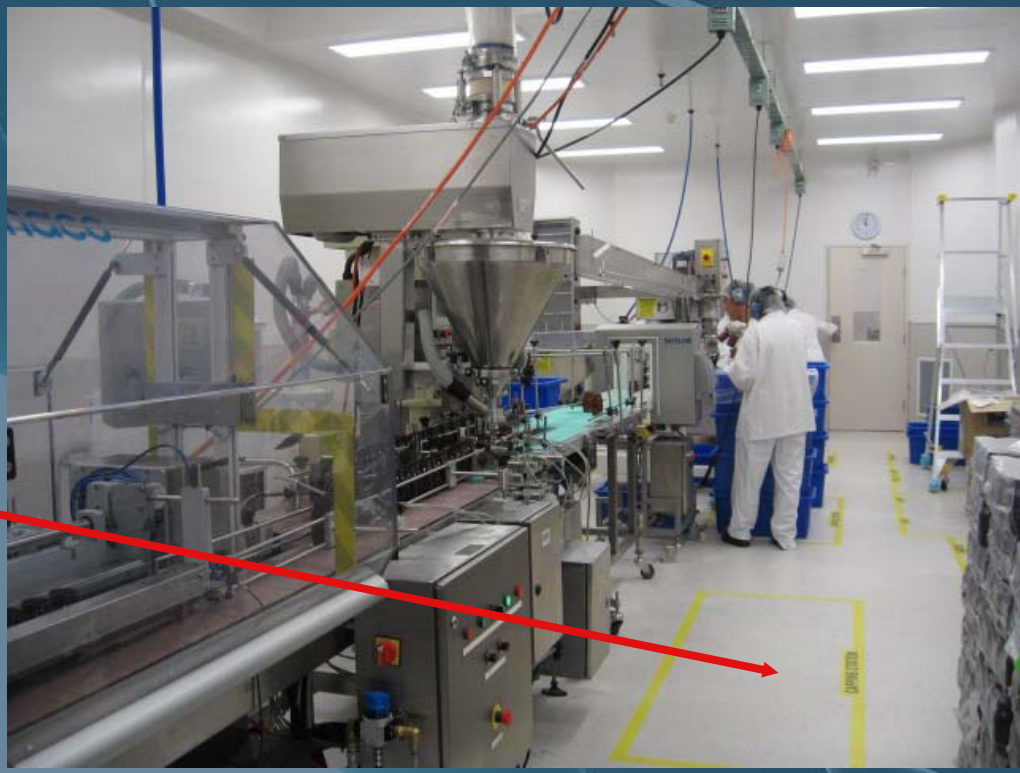
- Set all in order
- Instil Discipline

GMP the "**HOW**"

Processes – **Standardise - Production**

A place for everything

Visual labels



GMP the "**HOW**"

- Processes – **Standardise - Laboratories**
  - Set All in Order
  - Instil Discipline

GMP the "HOW"

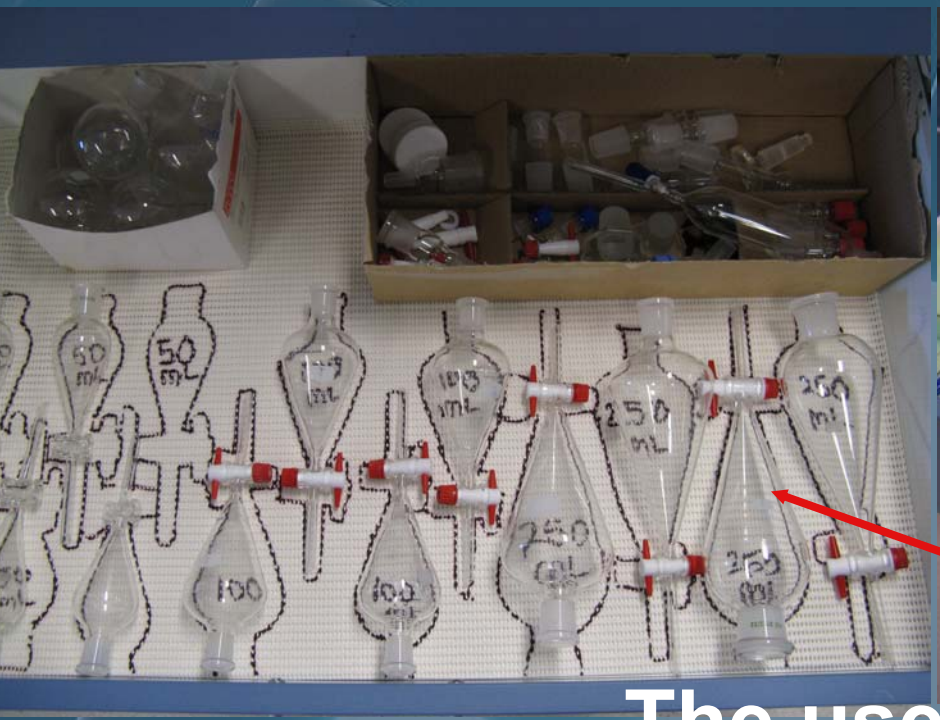
- Processes – **Standardise - Laboratories**

A place for everything

Visual labels

GMP the "HOW"

- Processes – **Standardise - Laboratories**



The use of shadow cut outs

GMP the "HOW"

- Processes – **Standardise - Offices**
  - Set All in Order
  - Instil Discipline

GMP the "HOW"

- Processes – **Standardise - Offices**
  - Set All in Order
  - Instil Discipline

GMP the "HOW"

Processes – **Standardise**

Simplify Documentation –

- **Standardise formats**
- **Document content should shadow the process flow**
- **More diagrams – less words**

GMP the "HOW"

Processes – **Standardise**

Simplify Documentation –

Procedures

Use of pictures – less words

GMP the "HOW"

Processes – **Standardise**

Simplify Documentation –
Batch Records

Format clearly and logically

Follow the process flow

GMP the "HOW"

Validation –
Process Validation

Consideration of Critical Points

Can be Grouped for similar products/ formulations

Use of Worst Case Situations – equipment train used

GMP the "HOW"

Validation –
Cleaning Validation

Can be Grouped

Use of Worst Case Situations

GMP the "HOW"

Validation –
Cleaning Validation

"Visibly Clean"

What does this mean?

How do we assess "Visibly" ?

GMP the "HOW"

"Visibly Clean"

Is there a standard way to assess this?

GMP the "HOW"

"Visibly Clean"

What did we do!

GMP the "HOW"

Separate Equipment Trains

Worst Case Groups –

- **Highly coloured**
- **Fish Oil Products**
- **High Maltodextrin Content**

Visibly Clean

We used **Black** & **White** swatches of material moistened with purified water to wipe surfaces

- **Inspected the residues on the swatches**
- **Inspected the appearance of the equipment**

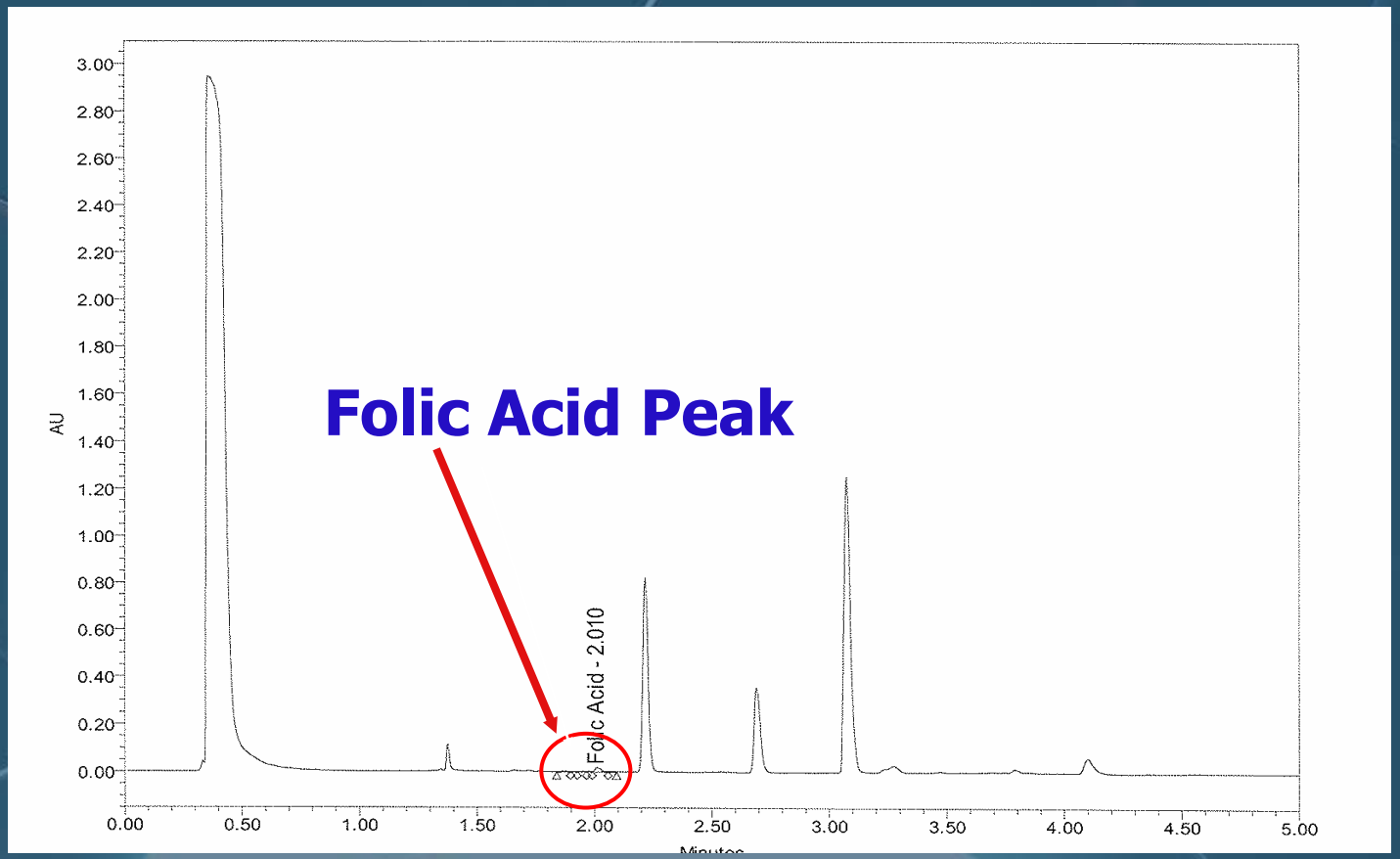
Development of Analytical Methods

Complexity of Matrix

- Some products can have over 60 ingredients!
- Interference of herbal components
- Specificity
- Extraction of active
- Appropriate detection methods

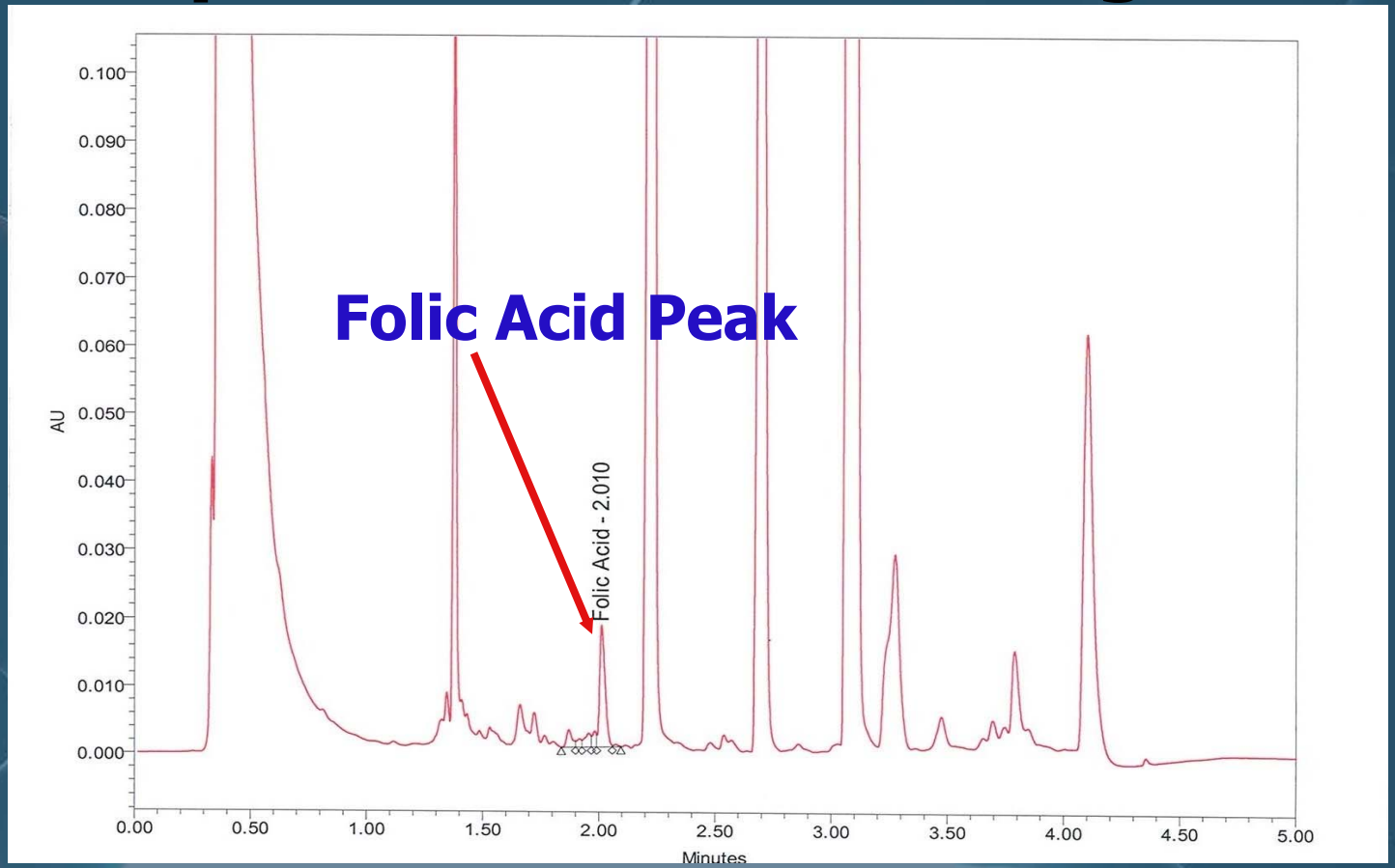
Development of Analytical Methods

Example of HPLC Chromatogram



Development of Analytical Methods

Example of HPLC Chromatogram



Product Specifications

Using "Quantified by Input"

- Herbal Extracts
- Component below quantitation
- Component cannot be assayed

Schedule 1 in TGO56

- Extended input range for multivitamins
- **Herbal Materials must be authenticated against a botanically authenticated reference**

TRAINING

Well TRAINED operators perform to expectations and reduce errors

- Knowledge of GMP & Code of GMP
- Hygiene
- Housekeeping
- Cross contamination
- Handling Deviations
- Quality Systems
- Documentation Practices

VENDOR ASSSURANCE

Sampling of EACH container

- Permissible to take a proportion of the batch if there is a validated procedure to ensure identity of each container.
- Excipients may be reduced sampled

VENDOR ASSSURANCE

To validate the procedure – Need to Know

- **The nature & status of the manufacturer**
- **Do they have a quality assurance system & use it**
- **Manufacturing conditions**
- **The products the material will be used in**

GMP the "HOW"

Good Manufacturing Practice in Complimentary Manufacturing

- Standardise work practices
- Simplify documentation
- Understand the complexities of your products
- Train operators well

GMP

Why just "Good"
Why not "GREAT"

Great

Manufacturing

Practice