



# An Industry Perspective on Herbal Medicinal Products Past, Present and Future

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# Key issues to cover

1. Introduction
2. The past
3. The present
4. The future
5. Threats & opportunities
6. Conclusion



# Introduction

## An aspiration

Herbal medicines, whether sold through retail channels , or prescribed and dispensed by qualified medical herbalists, should form part of an integrated approach to healthcare and well-being in the 21<sup>st</sup> century.

Such treatment should be both safe and appropriate, with as wide an access as possible for the patient to both OTC herbal medicines and herbal medicines prescribed by qualified medical herbalists.



# The Past – year 2000

Unlicensed herbal medicines becoming more popular

- Growing evidence base for St John's Wort
- High quality German herbal (unlicensed) medicines marketed in the UK eg.
  - Black Cohosh
  - Echinacea
  - Milk Thistle
  - Ginkgo biloba
  - Kava kava
  - Devil's Claw



# The Past – year 2000

## St John's Wort drug interaction risk

- Effect of St. John's wort (*Hypericum perforatum* L.) on cytochrome P-450 2D6 and 3A4 activity in healthy volunteers.
- Markowitz JS, DeVane CL, Boulton DW, Carson SW, Nahas Z, Risch SC  
Life Sciences, January 2000, vol./is. 66/9(PL133-9), 0024-3205.
- The growing knowledge of St. John's wort (*Hypericum perforatum* L.) drug interactions and their clinical significance
- Biffignandi P.M., Bilia A.R.  
Current Therapeutic Research - Clinical and Experimental, 2000, vol./is. 61/7(389-394).
- Inhibition of human cytochrome P450 enzymes by constituents of St. John's Wort, an herbal preparation used in the treatment of depression
- Obach R.S.  
Journal of Pharmacology and Experimental Therapeutics, July 2000, vol./is. 294/1(88-95).

# The Past – year 2002

## Kava kava and hepatotoxicity risk

- Kava kava: investigations into liver injury.

- WHO Drug Information, 01 January 2002, vol./is. 16/1(24-25).

- Herbal kava: reports of liver toxicity

- Wooltorton E.

- Canadian Medical Association Journal, 19 March 2002, vol./is.

- 166/6(777-777).

- Hepatic failure in female adolescent taking kava.

- Author(s): Perel J.M.

- Brown University Child & Adolescent Psychopharmacology Update, 01

- June 2002, vol./is. 4/6(8-8).

# The Past – year 2002/2003

## Black Cohosh and hepatotoxicity risk

Black cohosh and other herbal remedies associated with acute hepatitis  
Whiting P.W., Clouston A., Kerlin P.  
Medical Journal of Australia, October 2002, vol./is. 177/8(440-443).

Acute liver failure associated with the use of herbal preparations  
containing black cohosh

Lontos S., Jones R.M., Angus P.W., Gow P.J.  
Medical Journal of Australia, October 2003, vol./is. 179/7(390-391).

Does *Cimicifuga racemosa* cause hepatotoxicity? A comment on the  
Australian case reports [German] Hepatotoxizität durch Cimicifuga  
racemosa?

Thomsen M., Schmidt M.

Citation: Zeitschrift für Phytotherapie, 2003, vol./is. 24/1(11-14).

## Key safety risk questions:

- How many products are on the UK market
- What is the active herbal ingredient
- What is the quality of the products
- How many patients are using them
- How long are they using them for
- How many annual Defined Daily Doses have been consumed



**ETC**

**We don't know!**



## Well – documented quality & safety issues of unlicensed herbal products:

- ✘ Wrong herb used!
- ✘ Wrong dose or strength
- ✘ Heavy metal contamination – lead, mercury, cadmium
- ✘ Microbial contamination – Salmonella, coliforms
- ✘ Pesticides – dioxins, DDT
- ✘ Residual solvent contamination



## Unlicensed Herbal Medicines

### No independent MHRA approval

- ✘ No independent approval process
- ✘ Variable product quality
- ✘ No independent safety assessment
- ✘ No indication allowed
- ✘ No appropriate consumer information



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- ✘ No GMP requirements
  - ✘ Variable distribution standards
  - ✘ No safety monitoring (PhV) required
  - ✘ No advertising allowed



# Herbal Food Supplements (Botanicals)



- No approval by the MHRA
  - Quality
  - Safety
  - Efficacy } variable
- No Good manufacturing practice
- No Good distribution practice
- No Pharmacovigilance
- No approved Patient information



**No Consumer & Professional Confidence**

# European Traditional Herbal Medicines Directive (THMPD)

- ✓ Independent approval by the MHRA
  - ✓ Quality & manufacturing standards
  - ✓ Safety & risk/benefit assessment
  - ✓ 30 years traditional use
  - ✓ Patient information (+ SPCs)
  - ✓ All other medicine requirements





## **New Regulations**

### **Benefits for consumer safety**

1. Availability of safe herbal medicines
2. Availability of high quality herbal medicines
3. Reliable patient information

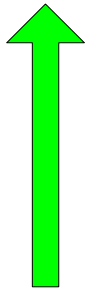
### **Benefits to Healthcare Professionals**

1. Trust in the quality & safety of THR herbal products
2. Availability of reliable medical information (SPCs)
3. Confidence when dealing with patients

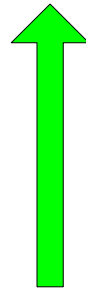
# THMPD – Timelines - UK



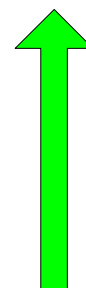
2004												2005												2006												2011											
J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D



Enactment  
Date "A"



Registration  
applications  
begin  
Date "B"



First  
registration  
approval



Transitional  
protection  
ends  
Date "C"



# The Present



## Up-to-date THR registration statistics

228 x THR applications received

115 x THR granted (includes 13 Transfer from PL)

39 x Companies applied for THR

28 x Companies have at least one THR

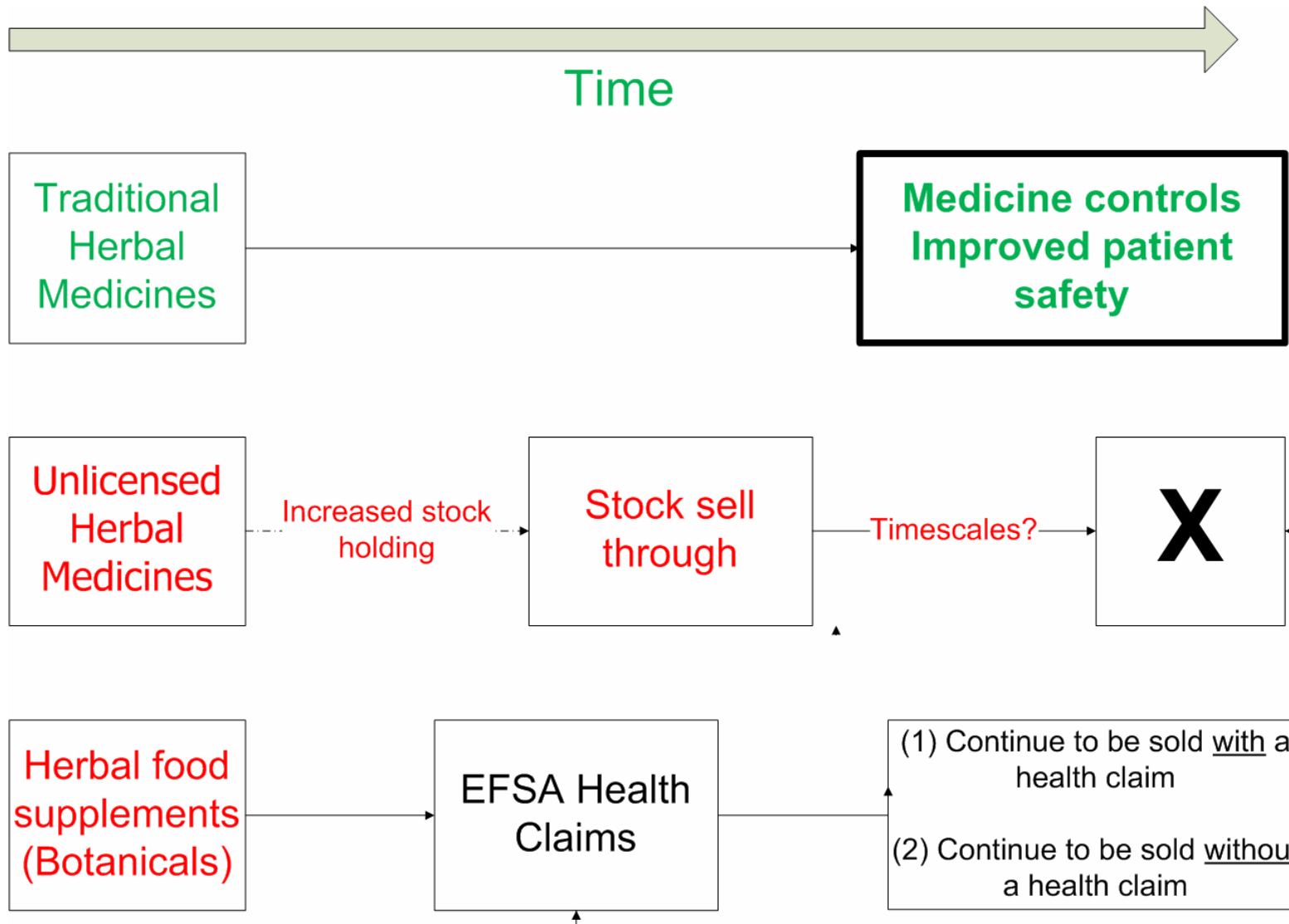
79 x Herbs in all THR applications

38 x Herbs in granted THR

34 x Combination applications received; 17 granted

MHRA – 28.06.2011

# The Present



# Regulatory differences



## Milk Thistle

### THR Medicine

### Unlicensed Herbal Medicine/ Food supplement

Quality controlled through GMP  
Patient information controlled  
MHRA Inspection driven  
Pharmacovigilance controlled  
Distribution controlled  
Indication controlled

**Improved patient safety**

**Expensive cost of goods**

Quality NOT controlled  
No patient information  
No medicine control  
No pharmacovigilance requirements  
No distribution control  
No indication/health claim

**Poor patient safety**

**Very cheap cost of goods**



# Consumer Feedback

## THR versus unlicensed products

“Will be looking else where as price increase too much. This product was very good and value for money but no more.”

“Was astounded to see the massive price increase for Milk Thistle and would like to know the reason for this. Have purchased this product for years from \_ \_ \_ \_ \_ but sadly will now have to look elsewhere. ”

“I cannot believe the increase in price and the decrease in quantity of this product. I will certainly have to consider buying this product from an alternative source”

“great product but why has it gone from £5.95 for 120 tablets to £12.95 for 30 tablets ? this increase cannot be justified in my mind - sorry will be looking some where else . ”

# Unlicensed Companies - strategy



*“New legislation coming into effect at the end of April 2011 means that 70% of the range we sell will have to be licensed. As the MHRA is run by pharmacists, they have required a lot of laboratory testing and made the licenses prohibitively expensive, favouring larger companies. We can only afford a few licences but we are doing what we can to stay in business. We will be able to sell existing stocks through over the next year or two while we get as many licenses as we can, however, this crazy policy from the MHRA threatens the future of organic herbal medicine.”*

**Anonymised Website 1<sup>st</sup> July 2011**

# The future - threats



## Threats to THRs in the immediate future

- Continuing widespread availability of cheap unlicensed herbal medicines and dual regulated herbs eg Saw palmetto
- High cost of THR GMP manufactured herbal medicines compared to unlicensed herbal medicines and herbal food supplements (three fold difference in price)
- Precautionary warnings & indications on THRs alongside unlicensed/herbal food supplement competitors with no such requirements



# The future

## - opportunities

- Attractive to Healthcare Professionals – high quality & reliable patient information
- Non-herbal users will find THR herbal medicines less confusing than unlicensed herbal medicines and may gain the confidence to purchase and use them
- THR Indications are for minor, self-limiting conditions. Government and health initiatives in self-care could increase consumer demand for these products in the wider population



# The UK future for THRs – success or failure?

This will depend on whether short-term commercial threats lead to a reversal back to unlicensed (botanical) status for dual regulated herbs

AND

How quickly the MHRA is willing and/or able to ensure compliance with the THR regulations and thereby create a commercially equitable and safe marketplace



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