TGA Complementary Medicines Reforms

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Disclosure of interests

• Member:
  – Expert group that formulated the 1988 WHO Ethical Criteria for medicinal drug promotion.
  – Therapeutic Guidelines Limited.
  – PHARM Committee that devised the Quality Use of Medicines plank of Australian Medicines Policy.

• Consumer representative (Choice):
  – Government Working Group on Promotion of Therapeutic Products.
  – TGA Transparency Review Panel.
Talk outline

• Why did I get interested in CM?
• What provoked the TGA reforms?
• What’s proposed?
• Are they relevant to Naturopaths?
• What’s evidence?
• Conclusions.

Why did I get interested in CM?

Re: Spatone
Posted: 02/02/2006
This is an obscene product that I have been asked for and seen advertised & sold by pharmacies. It’s being promoted as an iron supplement for women. What is it? MINERAL WATER. PAH!
While the TGA is doing their headless chook routine making sure everything is dotted & crossed, this sort of crap is available for sale.
What we need is an AusPharmList Quack Buster section where pharmacists can put this crap up as it appears and easily reference its validity & authenticity.

**Moderator's note: what do others think? **

Re: Spatone
Posted: 09/02/2006
Great idea - there are good candidates in virtually every section of retail pharmacy.
• The working group was primarily made up of pharmacists with an interest in AusPharm Consumer Health Watch aims.
• They aimed to critically evaluate claims made by non-prescription products in the pharmacy marketplace in order to help consumers make informed choices.
• Methodology:
  – Review the literature;
  – Produce a draft report;
  – Send the report to the product sponsor for comment;
  – Disseminate a final report via their web site.

Why Tebonin®?

TEBONIN PRODUCT LAUNCH OVER TWO HUGE MONTHS. MAJOR ADVERTISING INCLUDES:

- Half page article in The Australian Journal of Complementary Medicine
- Half page article in all major remunerated issues of NAPRA
- 1 full page advertisement in the Journal of Complementary Medicine
- 4 full pages in a major consumer magazine (June)
- 4 full pages in Australian Nursing
- 4 full pages in Heron's Digest

LIMITED STOCK - ORDER YOUR 4 PACK DIVIDED UNIT BEFORE THE 31ST APRIL 2006 AND SAVE 18.5% DISCOUNT!

BULLETIN

The companies behind the marketing and distribution of Remifemin and 30 Plus are jointly launching a new product - Tebonin (Egb 761) for relief of Tinnitus and Vertigo.
Why Tebonin®?

Summary of claims made

- “Tebonin® … has shown through clinical research to be an effective treatment for a range of conditions relating to microcirculation including Tinnitus, Vertigo, …”
- “EGb761® has been clinically proven in over 60 human studies published in international medical journals”.
- “Not only are there many trials showing the effectiveness of EGb761® extract in relieving the symptoms of tinnitus, it is also used to relieve …”
Smith, Zheng & Darlington 2005

- Department of Pharmacology and Toxicology, School of Medical Sciences, University of Otago, Dunedin, New Zealand.
  - Performed a comprehensive literature review.
  - Concluded that some clinical trials have yielded positive results, however, these studies are few and have been limited either by design flaws, the small size of the significant effects, or else the results have not been published in peer-reviewed journals and therefore the quality of the research is not assured.
  - By contrast, the two most systematic clinical trials, both double-blind and placebo controlled, and published in respected peer-reviewed journals, have yielded negative results and suggest that Ginkgo biloba extracts are of little more use in the treatment of tinnitus than a placebo.
  - Treatments for tinnitus that do not have therapeutic efficacy not only waste money but can potentially prevent patients from seeking therapy that is efficacious.
  - Furthermore, the unsupervised use of Ginkgo biloba extracts with other medications could lead to adverse side effects which are unnecessary and not justified in terms of therapeutic benefit.

Subsequent events

- Dowden JS. Injunction impedes independent information. Aust Prescr 2006; 29: 120 (October).
- Burton B. Regulator finds advertising of complementary product "misleading". BMJ 2006; 333: 1141 (2 December).
Our team compared the regulation of listed complementary medicines with registered drugs, using weight-loss products as an example.

We found over 1000 listed weight-loss products of dubious efficacy on the Australian market.

Their numbers (and complaints about their promotion) were increasing yearly at a much greater rate than registered products.

This appeared to be the consequence of not evaluating listed products for efficacy and also the substantially lower fees for listing compared to registration.
Therapeutic goods regulation

- In Australia, the Therapeutic Goods Administration (TGA) is responsible for regulating therapeutic goods including medicines (prescription, OTC and complementary), medical devices, blood and blood products.
  - “Complementary medicines” (CMs) contain herbs, vitamins, minerals, nutritional supplements and traditional medicines such as homoeopathic products.
- Unless specifically exempt or excluded, all therapeutic goods must be registered, listed or included on the Australian Register of Therapeutic Goods (ARTG) prior to their supply.
- The TGA does not regulate healthcare practitioners.

Therapeutic goods regulation

- The TGA uses a risk-based pre-market assessment of therapeutic goods.
- Registered medicines (labelled AUST R) are thoroughly evaluated for quality, safety and efficacy prior to market release (with the exception of some “grandfathered” products)
- All prescription medicines are AUST R.
- Listed medicines (labelled AUST L) are regarded as lower risk self-medication products. They are required to meet quality and safety standards but are not accessed for efficacy.
- Most CMs are listed (AUST L) on the ARTG
The TGA’s electronic listing facility (ELF) allows listed medicines rapid and low cost entry onto the ARTG.

Sponsors self-certify via ELF that:
- Their product is manufactured according to GMP standards;
- The ingredients are picked from a consolidated list that the TGA regards as relatively low risk;
- Their products only carry indications and claims for the symptomatic relief of conditions (but not for proscribed serious disease, disorders, or conditions), health maintenance, health enhancement and risk reduction;
- They hold evidence sufficient to substantiate that the indications and claims are true, valid and not misleading.

Limited random and targeted post-marketing surveillance is performed.

Medical devices are regulated by the TGA using a risk classification system:
- Class I (low-risk),
- Class IIa (low-medium risk),
- Class IIb (medium-high-risk),
- Class III (high-risk),
- AIMD (Active implantable medical device).

Certification (evaluation) by the TGA or an overseas notified body is required for higher risk devices.
- EU rules for licensing medical devices (70 private agencies) are “fragmented, privatised, and largely opaque; safety is dealt with in an unsatisfactory way and efficacy not at all”.

As with Listed medicines, sponsors of lower-risk devices self-certify they are “fit for purpose”.
Shonky devices included on the ARTG

- Ear candles
- Magnets
- Electro-dermal devices
- Bio-feedback / energy devices
- Electro-acupuncture
- Frequency micro-current devices
- Haemaview diagnostic devices
- Metal on metal hip implants, etc.

QXCI (Quantum Xeroid Conscious Interface)

- The QXCI / SCIO is a safe, powerful and effective software controlled, TGA registered biofeedback device designed for natural healing.
- It works wholistically and naturopathically to stimulate and harness the self healing capacity of the human system.
- The QXCI works based on the cybernetic BIOFEEDBACK PRINCIPLE but with added computer software and biofrequencies of thousands of homoeopathic, herbal formulas and flower essences to add into the biofeedback, this allows for much greater rebalancing of the flow of the whole person to truly vibrant health.

QXCI (Quantum Xeroid Conscious Interface)

- When analysing the person's energy, it functions similar to those of a virus scan on a computer. They detect weaknesses such as viruses, nutritional deficiencies and allergies by calculating the biological reactivity and resonance in your body.
- After measuring the body's frequencies it feeds back its own frequencies to neutralise destructive wave patterns. Healing takes place through energetic intervention, giving the body the true healthy energy patterns which enhance wellness, facilitate recovery and tune up your inner healing intelligence's ability to manifest fully.


QXCI (Quantum Xeroid Conscious Interface)

- In the late 1980s, an out-of-work math instructor in Colorado built an electronic device he claimed could diagnose and destroy disease.
- The U.S. FDA, which regulates medical devices, ordered Nelson to quit selling his machine and making false claims.
- Nelson refused, was indicted on felony fraud charges. He fled the country, never to return.
- His latest machine “INDIGO” has now replacing QXCI/SCIO (Quantum Health) and is promoted and used by the Cellagenics (and other) Naturopathic practices.

http://seattletimes.nwsource.com/html/localnews/2004020058_miracle18m2.html
Live blood analysis

“Another gimmick to sell you something”
Stephen Barrett, M.D.

Shonky medicines listed on the ARTG
Shonky medicines listed on the ARTG

Xantrax, Fatblaster, Fatblaster Max, Fat Magnet, HungerBuster, SlimRight Detox n Burn, Undoit...

Problems with the TGA

- The TGA’s “risk-based assessment” is judged solely on the likelihood of the therapeutic good to produce physical adverse effects.
- Other “risks” are not taken into account:
  - Providing an imprimatur for shonky products, “approved by the TGA”;
  - Consumers forgoing evidence-based treatment to the detriment of their health (and sometimes life) while pursuing quackery;
  - Wasting consumers money.
Problems with the TGA

- Self-certification by the sponsor of so-called “low-risk” therapeutic goods depends on trust.
- The TGA only performs limited post-marketing reviews of self-certified products. Until recently these results have been regarded as “commercial-in-confidence”.
- A 2009-10 review (of 31 randomly selected complementary medicines) has now been made public by the ANAO. It found:
  - 20 (65%) had labelling issues such as non-compliance with labelling requirements and/or breaches which may mislead consumers.
  - 22 (71%) were found to have manufacturing and/or quality issues.
  - 14 (45%) did not have adequate evidence to substantiate claims made.
- There is no data available on TGA post-marketing reviews of “low-risk” devices.
- Numerous upheld complaints reiterate evidential deficiencies.

In short, a system based on trust has been shown to fail.
- Removal of products from the ARTG by the TGA for regulatory non-compliance (after protracted due process) does not necessarily stop continued promotion and use.
- In addition, sponsors can readily relist identical products or those with minor changes.
- Unscrupulous sponsors know that the TGA is a paper tiger and the current system can be gamed to their commercial advantage.
Cancelling a product from the ARTG

- Does not impact on promotion from overseas and does not necessarily mean that users stop using and promoting the good; the TGA has no control over health practitioners.

Regulation of promotion

- Therapeutic Goods Advertising Code
  - Aim: the marketing and advertising of therapeutic goods to consumers should promote rational use, be socially responsible and not mislead or deceive the consumer.
  - Underpinned by legislation
    - Therapeutic Goods Act 1989 (TGA) and the Competition and Consumer Act 2010 (ACCC).
  - Limited pre-clearance by industry associations of advertisements for medicines (but not devices) in some media such as print and TV (but not the Internet).
Problems with promotion

- The CRP is under-resourced, overloaded and lacks power to enforce sanctions.
- It currently takes 5-8 months for complaints to be heard and the determination made public.
- Non-compliance with CRP “requests” is common; these are passed to the final regulator, the TGA.
- Due to the low financial penalties currently available in the Act it is not cost-effective for the TGA to initiate legal action against advertising breaches; no prosecution has ever been attempted.

Homeopathy websites ignore retraction orders

Australian Broadcasting Corporation
Reported: 08/04/2010
Speaker: Stevon Cannane

The Therapeutic Goods Administration is being criticized after revelations that last year a third of the companies found to have breached advertising rules failed to publish retractions and withdraw misleading information.

Transcript

TONY JONES, PRESENTER: The panel that handles complaints against misleading advertisements for medical products and services is being criticized tonight for failing consumers.

Letafine can reveal that last year a third of the companies were found to have breached the Therapeutic Goods Administration’s rules on advertising and they failed to publish retractions and withdraw misleading information.

FRAN SHEFFIELD: Well, obviously I’m disagreeing with them, and that’s why the retraction hasn’t gone up. http://www.abc.net.au/lateline/content/2010/s2867990.htm
Cat Media Pty Ltd (Pharmacare laboratories) have commenced proceedings in the Federal Court to have the TGA cancellation of FatBlaster Reducta overturned. Oct 25, 2012

Problems

- Last year the TGA agreed to publish the outcome of certain investigations into complaints about therapeutic goods advertising directed to consumers which have been referred to the TGA by the CRP for follow-up action.
- Since then there have been at least 20 such referrals to the TGA. To-date, only eight outcomes have been reported; some have taken 12 months or more and are still under dispute.
- The TGA may write “Reregulation 9” letters “ordering” compliance but, due to the low financial penalties available, the TGA has NEVER prepared a brief of evidence for consideration of prosecution (ANAO report).
- In short, the current TGA “Regulation 9” processes are appallingly slow, inefficient and appear loaded in favour of the sponsors.

Problems

- The current “light-touch” regulation of CMs, especially the lack of timely and significant penalties for breaches of the Therapeutic Goods Advertising Code and the Therapeutic Goods Act, encourages unscrupulous sponsors to flood the market with shonky products and unethical claims.
- The TGA (and industry) has failed to educate consumers and health professionals that CMs (especially herbals) are usually complex products and the concept of therapeutic equivalence of generic ingredients that is applicable to PBS products does not apply to CMs.
- Just as all red wine is not Grange Hermitage neither are all preparations of St John’s Wort, or glucosamine for example, therapeutically equivalent. Clinical trial results only apply to the specific, well characterised product that was tested, they CANNOT be extrapolated to other products containing the same generic ingredient.

Case study

Of the 328 formulations of glucosamine on the ARTG; what should I choose and/or recommend?

Problems

- AUST R labelling for CMs is flawed by grandfathering unevaluated products and failure to update old assessments in light of new knowledge.
- Research has shown that the public does not understand the difference between AUST R and AUST L labelled products.
- Thus, there is currently little incentive for sponsors to undertake expensive research, compile an extensive dossier and pay the higher fees required for TGA registration.
- A better return on investment comes from spending the money on marketing.

Flordis Iberogast registration dossier

- 14,200 pages Clinical data
- 7000 pages Toxicological data
- 5,600 pages Quality data
- 105 pages Local data

Total: 27,455 pages
$150,000 submission cost
Problems

- TGA consultations on regulatory reform have been opposed by industry and never brought to a conclusion. For example:
  - Regulation of homoeopathic and anthroposophic medicines in Australia (2008)
  - Guidelines for Levels and Kinds of Evidence for Listed Medicines with Indications for Weight Loss (2009)
  - Advertising consultation (2010).

Harm caused by the present system

- **Direct harm**, resulting in adverse patient outcomes, e.g. when a complementary medicine interacts adversely with a prescription medicine.
- **Indirect harm**, resulting from a delay of appropriate treatment or from unreasonable expectations that discourage patients and their families from accepting and dealing more effectively with their medical condition and lack of incentives to research and develop evidence-based products.
- **Economic harm**, as a result of expenditure on harmless but inefficacious treatment or products, important because many patients already forgo necessary PBS medicines because of the cost of co-payments.
What was the result?


What did we want?

- A regulatory system with teeth!
- Mandatory labelling, “This product has NOT been evaluated by Australian Health Authorities to see if it works”.
- Distinguish the few properly evaluated Registered complementary medicines from the many that were “grandfathered” into the ARTG.
What did we want?

• Increased and better targeted post-marketing surveillance and transparent reporting of problems and cancellations.
• Legislation for timely and meaningful sanctions for advertising violations (civil penalties, enforceable undertakings).
• Sponsor’s “evidence” on the ARTG web site for evaluation.

What did we get?

Over 4 years the TGA will:

• Update and include in the regulations the TGA document, *Guidelines for the levels and kinds of evidence to support indications and claims* (two drafts have already been produced);
• Amend the Electronic Listing Facility (ELF) to provide increased guidance to sponsors and risk profile information to the TGA (to assist targeted reviews);
• Increase the number of coded indication in ELF to eliminate “creative” use of free text;
• Broaden pre-clearance requirements to include medical devices and advertisements on pay TV (but not the Internet);

What did we get?

Over 4 years the TGA will:

- Provide more detailed and targeted post-marketing monitoring and reporting by the TGA;
- Create a central point at the TGA for all complaints about advertising, with the TGA to deal with those regarding efficacy or the intended purpose, not the Complaint Resolution Panel;
- Explore enhanced sanctions and penalties for regulatory violations including advertising breaches;
- Improve labelling to assist consumers make informed choices;
- Harmonise industry self-regulatory codes of conduct to support consistent ethical standards across the therapeutic goods industry.

Relevance to Naturopaths?

TGA reforms: A blueprint for TGA’s future
December 2011
Relevance to Naturopaths?

- Promotion of therapeutic goods (medicines, devices) to the general public by health professionals (including naturopaths) must comply with the Therapeutic Goods Advertising Code 2007.
- Irrespective of the target audience, therapeutic goods may only be advertised with claims which are consistent with their indications or intended purpose, as entered in ARTG.
- However, these requirements do not apply to advice or information given directly to a patient by a healthcare professional, in the course of treatment of that patient.
- Therapeutic goods which are labelled for 'practitioner dispensing only' are not required to state what the product is indicated for. Such goods should only be supplied to an individual after consultation with a healthcare professional.


Relevance to Naturopaths?

s.12(3) A health practitioner must not make claims, either directly or in advertising or promotional material, about the efficacy of treatment or services provided if those claims cannot be substantiated.
What's evidence?

- Patients, colleagues, social media (and testimonials) might say, “It worked for me”.
- But the plural of anecdote is not evidence.
- There are a number of reasons why consumers (and practitioners) convince themselves that a treatment is effective when it is not. These include:
  - The natural history of disease,
  - The placebo effect (expectation of benefit),
  - Confirmation bias (seeing what you expect to see) and
  - Cognitive dissonance (ignoring results not in accord with expectations).
  - Endorsement by “celebrities” who receive multi-million payments (be especially suspicious).
- In short, personal evaluation is quick, convincing and often wrong, while double-blind, placebo-controlled clinical trials are slow, complex, and costly.
- However, the latter are important as they often show that initially promising results are not replicated by larger and better conducted studies.

What's evidence?

- Systematic Reviews
- Randomized Controlled Trials
- Cohort Studies
- Case-Control Studies
- Case Series, Case Reports
- Editorials, Expert Opinion

THE COCHRANE COLLABORATION

PubMed
What’s evidence?

- Many media stories about new medicines
  - Overstate benefits
  - Understate risks
  - Understate costs
  - Fail to disclose relevant financial ties.
- 207 stories from 1994 to 1998
  - 40% did not report benefits quantitatively
    - Of those that did, 83% reported only relative benefits
  - 53% did not mention potential harm
  - 70% did not mention cost of therapy
  - 39% disclosed ties where it was relevant.

Moynihan R et al. NEJM 2000;342:1645–50
Relative and absolute benefits / risks

- There was a statistically significant 8% reduction in total cancer incidence with multi-vitamin use (Centrum Silver provided by Pfizer) compared to placebo.
- In fact, there were 17.0 and 18.3 cancer event per 1000 person years in the multi-vitamin and placebo groups respectively.
- $1.3 \times 100 / 17 = 7.64\%$; $P=0.04$, a 1 in 25 chance this result could have arisen by chance.
- Always ask for the absolute numbers involved, not just the percentage risk or benefit and assess the likelihood the result could have arisen by chance ($P=?$).

Finally questions to ask

- How strong is the evidence to support the claims being made about the diagnostic device &/or therapy:
  - levels of evidence (anecdotes, tradition, trials)?
  - trials registered?
  - results published?
  - accurately reported?
  - replicated by others?
- Could the therapeutic goods be shonky:
  - glowing testimonials but no trial results?
  - do those promoting it profit from it?
  - listed in Quackwatch?
  - complaints upheld by the CRP?
  - product removed from the ARTG by the TGA?
Finally

questions to ask

• What’s the size of the potential benefit and risk offered by the therapeutic good, and for what types of patients:
  – statistically significant?
  – clinically significant?
  – absolute benefits and risks (not relative)?
  – Numbers needed to treat?
  – Numbers needed to harm?
• What are the costs of the therapeutic good and are the potential risks and benefits worth the cost?

In conclusion

• To give good advice about CMs:
  – ALWAYS ask patients about ALL the medicines they take including CMs.
  – Subscribe to an NPS recommended CM resource regarding ingredients / indications / interactions.
  – Ask the sponsor for all published clinical trials performed on their specific product.
  – Use Medline, Cochrane and other resources to see what else has been published.
  – Check the CRP complaint register to see if complaints about a product’s claims have been upheld.
  – Keep up-to-date with the literature as clinical trials are ongoing.
  – Polish your critical appraisal skills (try putting in complaints).
Finally

http://www.nps.org.au/health_professionals/prescribing_competencies_framework

Resources

- Harvey K. Regulation of Complementary Medicines, in Perspectives on complementary and alternative medicines, Edited by Prof Ian Oliver & Monica Robotin, Imperial College Press, Oct 2011