ASMI Complaints Panel Determination

Meeting held on August 10, 2010

GlaxoSmithKline Consumer Healthcare v. Reckitt Benckiser Australia Pty Limited – Nurofen for Children.

1. GSK complains that advertisements by RB in May and June 2010 promoting Nurofen for Children and directed to doctors, pharmacists and pharmacy assistants breached the ASMI Code of Practice 2009.

   "The NEW range of Nurofen for Children"

2. GSK says this breaches Code 5.1.3 because there is no new range of Nurofen for Children products. The only new product is the concentrated strength formulation for children aged 5-12 years. The formulations of the other products in the range are not new, the only change being a revision of packaging.

3. RB says the word NEW is accurate and is warranted by:

   (a) new posology for every product in range, standardised to 10 mg/kg. This was 5-10 mg/kg. It would be irresponsible not to draw attention to this;
   (b) the maximum dose was 3-4 times per day and is now 3 times per day;
   (c) the new formula for ages 5-12;
   (d) new age breaks; and
   (e) new packaging and promotional material.

   Panel consideration

4. The Panel finds that use of the words *"The NEW range of Nurofen for Children"*, by way of introduction to the changes, to be justified and accurate. The Panel agrees that it would be irresponsible to change the dosage without announcement. This aspect of the complaint is dismissed.

   "Nurofen for Children provides babies from 3 months old effective temporary relief from teething pain, which may interfere with a good night's sleep."

5. GSK says that, in breach of Code 5.1.4, RB has declined GSK's request to provide literature to support the claim that teething pain may interfere with a good night's sleep. Citing *Wake M, Hesketh K. Lucas J. Teething and tooth eruption in infants: a cohort study. Pediatrics 2000; 106(6):1374-1379* and *Macknin ML, Piedmonte M, Jacobs J, Skibinski C. Symptoms associated with infant teething: a prospective study. Pediatrics 2000 April. 105(4Pt 1): 747 -752,* GSK says there is

no cause-and-effect relationship between teething and disturbed sleep and that RB's claim is not supported, in breach of Code 5.1.3.

6. RB says no claim is made for relief from pain and sleep disturbance, only *temporary* relief for pain, which *may* interfere with sleep. It is common knowledge that pain may interfere with a good night's sleep so there is no need to supply evidence. The mean age of children in *Wake et al* was 14.4 months so *Wake* may have missed most first tooth episodes. See *Tighe M, Roe MF. Does a teething child need serious illness excluding? Arch Dis Child 2007 March;92(3):266-268. Macknin et al* found wakefulness to have some association with teething.

Panel consideration

7. The Panel finds that the claim "*effective relief from teething pain, which may interfere with a good night's sleep"* is not a claim for relief from sleep disturbance. Accordingly there is no need to supply evidence that Nurofen for Children provides relief from sleep disturbance. The Panel agrees that it is common knowledge that pain may interfere with a good night's sleep. There is no breach of Code 5.1.3 or 5.1.4. This aspect of the complaint is dismissed.

"*It also relieves fever for up to 8 hours"*

8. GSK says this claim, in the advertisements directed to teething, has serious safety implications. The last sentence of the advertisement states that all of the product benefits cited in the advertisements are "*good reasons to recommend Nurofen for Children*". The literature is very clear that disturbed sleep and the presence fever are NOT good reasons for giving a medication to a teething child. High temperature should not be attributed to teething and should be investigated: *Owais AI, Zawaideh F, Bataineh O. Challenging parents' myths regarding their children's teething. Int J Dent Hyg 2010 February;8(1):28-34.* This is underlined by data showing that 96% of children presenting to a hospital with 'teething' had other more serious medical conditions and one had bacterial meningitis: *Swann IL. Teething complications, a persisting misconception. Postgrad Med J 1979; 55:24-5,* cited in *Owais 2010* and *Tighe 2007.* By implying that pain and fever relief are *good reasons to recommend* Nurofen for Children to a teething infant, RB is in breach of Clause 5.1.3 of the ASMI Code because the literature does not support this contention and of Clause 3.2.4 of the ASMI Code because recommending a product when there is no basis to do so or when the child should better be evaluated by a medical practitioner, is not responsible. This is a severe breach - it has safety implications because it actively encourages Pharmacists and Pharmacy Assistants to recommend Nurofen for Children for a teething infant without due consideration that the symptoms being displayed might be caused by something else.

9. RB says the claim of relief from fever for 8 hours is substantiated by *Autret-Leca E, Gibb IA, Goulder MA. Ibuprofen versus paracetamol in pediatric fever: objective and subjective findings from a randomized, blinded study. Curr Med Res Opin 2007; 25(9): 2207 – 2211.* The existence of another study (*Swann 1979)* concerning children who presented with teething complaints and largely required hospitalisation for medical conditions does not undermine or render unjustified the claim of relief from fever for 8 hours. Whether or not fever present in a teething child requires investigation is a matter for the child's parents and healthcare professionals, depending on the extent and severity of symptoms.

Panel consideration

10. The headline of these advertisements reads: "*GETTING 8 HOURS SLEEP WITH TEETHING PAIN. YOU'RE DREAMING!* The copy reads:

> *"Nurofen for Children provides babies from 3 months old effective temporary relief from teething pain, which may interfere with a good night's sleep. It also relieves fever for up to 8 hours, with a tolerability equal to paracetamol. The pleasant tasting range is available for kids from 3 months to 12 years. All good reasons to recommend Nurofen for children."*

11. GSK does not dispute the claim to temporary teething pain relief. The Panel considers the claim for relief from fever for 8 hours in children aged 3 months to 12 years to be substantiated by *Autret-Leca 2007*. The advertisement encourages pharmacists and pharmacy assistants to recommend Nurofen for Children for teething pain and for fever, which may or may not be associated with teething. Nurofen for Children has been shown to be effective for the relief of both and it is therefore legitimate to claim that these are good reasons to recommend the product. The advertisements do nothing to discourage due consideration as to whether the symptoms being displayed might be caused by something else. There is no breach of Code 5.1.3. Code 3.2.4 is not an operative provision capable of breach. This aspect of the complaint is dismissed.

"*It also starts to relieve fever from 15 minutes onwards* [referenced to *Pelen 1998*], *giving more play time and less pain time*" (emphasis added)

12. GSK says the emphasised words are not referenced. The *Pelen 1988* study provides no data on analgesia. There is a direct link between the two statements - they appear in the same sentence separated only by a comma. Therefore, the advertisements imply a direct link between fast onset of fever relief (from 15 minutes) and pain relief. In effect, the advertisements are saying that because Nurofen for Children starts to relieve fever from 15 minutes onwards, then pain will also be relieved. RB has declined GSK's request to provide data to support the claim, in breach of Code 5.1.4. The claim is unsubstantiated, confusing and misleading, in breach of Code 5.1.3.

13. RB says the first two sentences of the relevant advertisements, excluding the titles, read as follows:

> *Nurofen for Children provides effective temporary relief from pain associated with earache. It also starts to relieve a fever from 15 minutes onwards*, giving more play time and less pain time.*
>
> *Nurofen for Children provides effective temporary relief from a headache. It also starts to relieve a fever from 15 minutes onwards*, giving more play time and less pain time.*

14. RB says that in each case, the first two sentences must be read together rather than in isolation. The opening sentences refer to temporary relief from pain for a child, from which it logically follows that there is less pain time and more time for children's normal activities, such as play. The words "*more play time and less pain time*" refer back to the opening sentence, not to the substantiated claim relating to fever relief.

Panel consideration

15. The Panel accepts that the two sentences should be read together. The word "*also"* makes this clear. In that context the advertisements do not imply a direct link between fast onset of fever relief (from 15 minutes) and pain relief. There is no breach of Code 5.1.3 nor of 5.1.4. This aspect of the complaint is dismissed.

"*Nurofen for Children offers more time without fever in the first four hours than paracetamol"*

16. GSK says this claim, which is referenced to *Hay AD, Costelloe C, Redmond NM, Montgomery AA, Fletcher M, Hollinghurst S, Peters TJ. Paracetamol plus ibuprofen for the treatment of fever in children (PITCH): randomised controlled trial. BMJ 2008;337 a1302,* is not supported by that study and is in breach of Code 5.1.3.

17. GSK says the *Hay 2008* study did not specifically assess the antipyretic efficacy of Nurofen for Children since the active drugs used in the study were Calpol/Calprofen purchased from Pfizer. Importantly the results of the *Autret-Leca 2007* study, which was conducted by RB and which did use Nurofen for Children, do not support the claim being made.

18. GSK says the claim is made in advertisements promoting the entire range of Nurofen for Children yet the *Hay 2008* study evaluated only children aged 6 months to 6 years (not 3 months to 12 years). RB has provided no evidence to show that ibuprofen would provide a similar antipyretic effect in children in the older age group. *Kauffman RE, Nelson MV. Effect of age on ibuprofen pharmacokinetics and antipyretic response. J Pediatr 1992 December; 121(6):969-973* has shown that when ibuprofen is given to older children (6 years

or more) it takes longer for fever relief to start (109 minutes versus 69 minutes, p=0.03) and their temperature is not reduced as much (mean maximum change in temperature 1.8°C vs 2.8°C, p=0.002) compared to in younger children. It is not valid to imply that the *Hay 2008* data is relevant to older children.

19. RB says the *Hay 2008* study was conducted in respect of the analgesic ibuprofen of which the Nurofen for Children products consist and therefore it is entirely appropriate for the finding of the study to be relied upon in respect of those products.

20. RB concedes that *Hay 2008* did not cover the age groups 3-6 months and 6-12 years but says: "However, there is no documented evidence to show that ibuprofen would not provide similar antipyretic effects in these age groups". RB also seeks to rely on other studies combined with *Hay 2008* to substantiate the claim across the entire 3 months-12 years age range.

Panel consideration

21. The Panel finds that since the *Hay 2008* study was conducted with ibuprofen suspension, it is appropriate to make claims in relation to Nurofen for Children products in reliance on it.

22. The advertised claim represents that it is wholly substantiated across the 3 months-12 years age range by *Hay 2008*. RB admits that this is not so. The absence of "documented evidence to show that ibuprofen would not provide similar antipyretic effects in the 3-6 months and 6-12 age groups" does not establish that ibuprofen would provide similar antipyretic effects in those age groups. Accordingly the Panel finds the claim based solely on *Hay 2008* to be in breach of Code 5.1.3. This is a Moderate Breach since it will impact on the perceptions of consumers (pharmacy assistants) and healthcare professionals regarding the product. The Panel makes no finding as to whether or not other studies in combination with *Hay 2008* substantiate the claim across the entire 3 months-12 years age range.

23. GSK also says the *Hay 2008* data are not consistent with the body of clinical evidence. There are only three papers that compare the antipyretic efficacy of paracetamol and ibuprofen at Australian recommended doses. The *Hay 2008* study is the only one that supports the claim being made. The other two studies, *Autret-Leca 2007* and *Walson PD, Galleta G, Chomilo F, Braden NJ, Sawyr LA, Scheinbaum ML. Comparison of multidose ibuprofen and acetaminophen therapy in febrile children. Am.J.Chin Med. 146[5], 626-632, 1992*, show no difference between the two products and do not support the claim being made. GSK says RB has deliberately chosen to pick one study from that literature in order to make a claim that is more favourable than has been demonstrated by the body of clinical experience.

24. RB says *Hay 2008* is more robust than the studies on which GSK relies. Although *Autret-Leca* showed no statistically significant difference in antipyretic efficacy between paracetamol and ibuprofen, there were "*definite trends*" in favour of ibuprofen. *Walson* only involved 61 children evaluable for efficacy v. *Hay* (156) and *Autret-Leca* (304).

Panel consideration

25. The Panel finds the *Hay 2008* data used are not inconsistent with the body of clinical evidence on which GSK relies and declines to find breach of Code 5.1.3 on this ground. This aspect of the complaint is dismissed

"…with a safety and tolerability equal to paracetamol (example),

26. GSK says this unqualified comparative claim is referenced to *Southey ER, Soares-Weiser K, Kleijnen J. Systematic review and meta-analysis of the clinical safety and tolerability of ibuprofen compared with paracetamol in paediatric pain and fever. Curr Med Res Opin 2009 September;25(9):2207-2222,* a comprehensive systematic review of the literature. Each of the three authors received funding from RB for the preparation of this article, which concludes that the safety and tolerability profile of ibuprofen in paediatric use is similar to that of paracetamol. However, the results are based on the findings of randomised controlled trials, which are subject to specific exclusion criteria. There is no discussion in the paper as to the impact of the exclusion criteria employed in each of these studies on the results. A more recent review (*Pierce CA, Voss B. Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review. Ann Pharmacother 2010 March;44(3):489-506,)* produced an odds ratio which favours paracetamol, although this was not statistically significant. In contrast to the RB sponsored study, this independent study did discuss the impact of exclusion criteria on their findings.

27. GSK says clinical trial exclusion criteria are such that any participant with a warning, precaution or contraindication to the study medication would automatically be excluded from the trial. It follows that the conclusion that ibuprofen has equal or similar safety and tolerability to paracetamol is true only in those subjects who have strictly adhered to the warnings, precautions or contraindications of each study medication. In prior advertising campaigns to healthcare professionals discussing the comparable safety and tolerability of adult ibuprofen and paracetamol formulations, RB has always used a qualifying statement to reflect the above-mentioned limitations of the data. No such qualifying statement has been included in the current advertising. The advertisements could lead pharmacy assistants to overlook pack warnings.

28. RB agrees that the odds ratio which favours paracetamol in *Pierce 2010* was not statistically significant. The same study concluded:

> *"This analytical review demonstrates that ibuprofen is as or more efficacious than acetaminophen for the treatment of pain and fever in both children and adults and that the 2 drugs are equally safe."*

29. *Southey 2009* concludes:

> *"We investigated the tolerability and safety profile of ibuprofen and paracetamol when used as antipyretic/analgesic agents in children up to 18 years. Overall the results from this systematic review demonstrate that ibuprofen, paracetamol and placebo appear to have a similar tolerability and safety profile (in terms of GI symptoms, asthma and renal adverse effects), with serious Aes being rare occurrences."*

30. RB says that although the authors received funding from RB for the preparation of the article, they stated that they had "*no role in creating, writing or reviewing this article"* and that they took "*full responsibility for the contents and views expressed in the article, and have had full editorial control whilst preparing the article*". The article was reviewed by the editorial board of the well regarded journal "Current Medical Research and Opinion" and published in that journal.

31. RB says the product packaging is prominently endorsed to refer to contraindications relevant to the products. No qualification in the advertising is required. The suggestion that the advertisements could lead pharmacy assistants to overlook pack warnings is unwarranted and mischievous.

Panel consideration

32. The Panel sees no reason to reject the conclusions of the Southey study, which supports the claim. It agrees that it is not necessary to include contraindications and warnings in the advertisements and, given the well-known contraindications for ibuprofen, it does not accept that, in the absence of such warnings in the advertising, pharmacy assistants would be likely to overlook the pack warnings. Accordingly the Panel finds no breach of the Code. This aspect of the complaint is dismissed.

Sanctions

33. With respect to the Moderate breach found by the Panel in paragraph 22, the Panel has considered the factors set out in the Code, clause 9.1.3. On the material before the Panel:

- the Panel does not know whether publication has ceased;

- the Panel does not know whether steps have been taken to withdraw the material published;
- the Panel does not know whether corrective statements have been made;
- the Panel is prepared accept that the breach was inadvertent;
- RB has breached the Code before in comparing duration of fever relief in Nurofen for Children and paracetamol: Complaint 04/08; and
- there are no safety implications but the perceptions of health care professionals and consumers (pharmacy assistants) will have been affected.

34. Accordingly, the Panel requires RB to give an undertaking in writing to the Executive Director of ASMI to cease forthwith the publication in any media, including on any website, in relation to children aged from 3 months to 12 years, of the claim "*Nurofen for Children offers more time without fever in the first four hours than paracetamol"* and any claim to like effect, where the sole reference on which reliance is placed to support the claim is *Hay AD, Costelloe C, Redmond NM, Montgomery AA, Fletcher M, Hollinghurst S, Peters TJ. Paracetamol plus ibuprofen for the treatment of fever in children (PITCH): randomised controlled trial. BMJ 2008;337 a1302.*

35. Attention is drawn to section 10.1 of the Code.

Apportionment of costs

36. Having regard to the number of aspects of this complaint which the Panel has dismissed, which occupied considerable time, the single breach found by the Panel, which was far less time-consuming, justifies an apportionment of costs in this case. Accordingly pursuant to Code 8.4.2.2, the Panel determines that GSK should contribute 90% and RB 10% of ASMI's out-of-pocket expenses associated with the determination of this complaint.

Dated 26 August, 2010.
For the ASMI Complaints Panel

Alan L. Limbury

Chairman