ASMI Complaints Panel Final Determination

Meeting held on July 14, 2015

AFT Pharmaceuticals Pty Limited ("AFT")
v.
Reckitt Benckiser (Australia) Pty Limited ("RB")

Nuromol advertising

Jurisdictional issue

1. This complaint raised for the first time the question whether the Complaints Panel has jurisdiction to determine industry-generated complaints brought against Members of ASMI by non-members who do not agree to be bound by all of the provisions of the ASMI Code of Practice ("the Code").

2. After some informal correspondence between the parties, this complaint was initiated by AFT by formal complaint dated May 4, 2015, which AFT lodged with ASMI on May 23, 2015. That day AFT agreed:

> "to be bound by section 9.4.2.2 [of the Code] to reimburse ASMI its out-of-pocket expenses in the event that the complaint is unsuccessful".

3. On May 26, 2015, no formal response having been provided by RB, AFT submitted to ASMI that RB should not be granted an extension of time to respond.

4. On May 28, 2015, RB submitted that it should be allowed to provide a formal response, contending *inter alia* that the Industry-Generated Complaints Procedure under section 9.4 of the Code cannot apply to this complaint because it applies solely to complaints between Members (defined, according to RB, to include "non-member companies agreeing to be bound by the Code") and that AFT is not a Member because it had refused to be bound by the Code other than in relation to costs. RB provided its formal response that same day.

5. On June 3, 2015 the Panel Chair decided under section 9.4.2.8 of the Code that RB's formal response should be received by the Panel, saying *inter alia*:

> "There is no dispute that AFT carries on business within the "industry", as that term is defined in section 1 of the ASMI Code of Practice.
>
> By letter dated May 4, 2015, AFT sent to RB a formal complaint in conformity with section 9.4.2.4 of the Code. At that time AFT was not a Member of ASMI. "Member" is defined in section 1 of the Code to include non-member companies which agree to be bound by "all or part of the provisions of the Code". AFT became a Member on May 23, 2015, when it agreed to be bound by the provisions of section 9.4.2.2 of the Code and hence agreed to reimburse ASMI its out-of-pocket expenses should its complaint be

unsuccessful. Does this mean that the complaint should be rejected as invalid when sent to RB on May 4th?

Section 9.4 is headed “Industry-Generated Complaints”, an expression wide enough to encompass complaints by non-Members against Members. Although section 9.4.1 refers to Members, that reference should not be interpreted, in my opinion, as operating to confine the entire section 9.4 process to complaints brought by Members against Members.

There is nothing in the Code to require non-member companies to agree to be bound by all or part of the provisions [of] the Code in order to be entitled to submit an industry-generated complaint. It may be argued that by invoking the formal ASMI complaints resolution procedure under section 9.4.2.6, a non-member company becomes bound by section 9.4.2.2 of the Code. Securing an express undertaking to that effect, as ASMI did in this case, is a prudent course for ASMI to adopt. However, in my opinion such an undertaking, whenever given, is not a pre-requisite to the invocation of that process by a non-member industry participant.

Accordingly, I do not accept RB’s contention that the Industry-Generated Complaint process applies solely to complaints between Members. I consider that the formal complaint, when sent by AFT to RB on May 4th, was a valid Industry-Generated Complaint to which section 9.4 applies and that the Panel has jurisdiction to determine the complaint.

This is the first occasion on which the jurisdictional issue has been raised. It was not clear until now whether RB was obliged to respond before AFT undertook to be bound by the Code or part thereof or at all.

On May 7th RB asked AFT to submit to the jurisdiction of ASMI by May 13th. AFT did not do so until May 23rd. RB’s failure to provide a formal response in the meantime is understandable, given the doubt cast over the validity of the complaint by the unresolved jurisdictional issue.

The Panel is likely to be in a better position to determine the complaint on its merits if the response is before it.”

6. Accordingly the Panel has considered both AFT’s formal complaint and RB’s formal response.

The advertisements

7. AFT complains that advertisements for Nuromol breach sections 3.2.3, 3.2.4, 4.2 and 5.1.3 of the Code. The advertising comprises an advertorial in The Australian Journal of Pharmacy (“AJP”) Vol. 96 March 2015; Blooms The Chemist Weekly Dose; a Nuromol Detailer, RECB8889; and an email from RB Health Hub.

The AJP advertorial

8. AFT says it has two concerns regarding "the advertisement placed by RB in AJP March issue". First, AFT says the following statement is unsubstantiated:

> "*The result of the simultaneous and rapid dissolution of ibuprofen and paracetamol in Nuromol with Synchro-Tech is faster absorption of these active ingredients into the blood stream, than had it been taken alone. Faster absorption has been shown to lead to faster onset of pain relief lasting up to 8 hours."*

9. AFT cites *Tanner, Aspley, Munn & Thomas, (2010) The pharmacokinetic profile of a novel fixed-dose combination tablet of ibuprofen and paracetamol:*

> "For ibuprofen, the median rate of absorption was unchanged (1.25 hr, n.s difference) when administered as monotherapy or in Nuromol. However, the median difference and 95% CI suggests that absorption of ibuprofen takes slightly longer (median difference 7.5 minutes) in the combination".

10. AFT says that, contrary to the claim made, this shows that the rate of absorption of ibuprofen is in fact subject to a marginal *decrease* following concomitant administration with paracetamol and with Synchro-Tech and that the statement "*faster absorption of these active ingredients into the blood stream"* is not accurate.

11. Second, AFT says the advertisement makes unsubstantiated claims referring to Reference 8, which is not listed in the references:

> *"Nuromol might also improve tolerability compared with single agents alone because it limits the daily dose of active ingredients. 8"*

12. In response, RB says the AJP advertisement including its wording was not "placed by RB", nor was it authored or authorised by RB. On that basis, the allegations are denied. Further, as to AFT's second point, in any event the claim made is that improved tolerability *might* occur, a non-absolute and self-evident statement.

13. Prior to the Panel meeting, the ASMI Regulatory and Scientific Director passed on to RB some questions from the Panel Chair. These are set out below, together with RB's answers:

> 1. Do you know how the advertisement came to be published?
>
> RB purchased advertising space within the March edition of AJP which included a number of advertising pages and an advertorial. The advertorial was to be written by the Editor of AJP, [name] as part of the overall media buy. As such, RB took no part in the writing, construction or design of the advertorial in question as it was being written by the editor and was not an RB piece. RB understood at the time, that this was AJP's normal policy.

RB first received a PDF of the article on the 10th February, which was within a day or so of the publication going to print for the March issue. RB understood the provision of the PDF by AJP to RB, was as a matter of courtesy, RB did not at that time, provide a 'sign off' and was not provided an opportunity to review the advertorial before the publication went to print.

2. Did RB provide any materials from which the article could have been developed?

[Name], as part of their role as RB's health PR agency, manages any journalist enquiries and facilitates the distribution of media materials and supporting documents directly with the publications in relation to RB's health products. As part of the Nuromol product launch, the journalists received the Product Information, the media backgrounder and media release. In addition, journalists can ask for additional supporting materials such as clinical papers and face to face interviews through [name of agent]. These materials would have been made available to [name of Editor].

3. If materials were provided to AJP could you provide copies of those materials?

Please see attached. However, please note that these supporting materials are to the best of RB's knowledge and records as documents which are likely to have been provided to AJP through [name of agent]. However, as set out above, RB did not manage journalist enquiries directly.

14. The attachments initially provided by RB comprised copies of the Nuromol Product Information and 6 published articles. Following a further request from the Panel Chair, RB provided the media backgrounder mentioned in RB's answer to question 2 and two media releases.

Panel consideration

15. The Panel notes that RB purchased advertising space in the March 2015 AJP, including an advertorial (an advertisement that is written and presented in the style of an editorial or journalistic report).

16. All the information and much of the wording in the statement of which AFT complains (set out in paragraph 8 above) is contained in the backgrounder. Under these circumstances, even if RB was not given sufficient time to provide sign-off prior to the advertorial going to print, RB cannot escape responsibility for the publication by claiming the AJP advertorial, including its wording, was not placed by RB and was not authored or authorised by RB. The Panel finds that, through its authorised agent, RB provided to AJP the information contained in the statement of which AFT complains and thereby authorised its publication.

17. The substance of the statement is the claim that, when combined in Nuromol with Synchro-Tech, ibuprofen and paracetamol are absorbed faster into the blood stream than when taken alone. The *Tanner et al 2010* article was not provided to the Panel by AFT but RB has not sought to dispute the passages on which AFT relies to show that ibuprofen is not absorbed faster in Nuromol with Synchro-Tech than when taken alone.

18. *Tanner et al 2010* compared the rate of absorption of ibuprofen 400mg and paracetamol 1000mg when taken alone versus when taken in the Nuromol with Synchro-Tech combination. The Panel understands 400mg to be the standard adult dose of ibuprofen when taken alone, as either two 200mg tablets or a single 400mg capsule. Tanner et al 2010 found that the Nuromol Synchro-Tech combination resulted in an increased rate of paracetamol absorption, however the rate of absorption of ibuprofen was unchanged.

19. Since the approved Australian dose of Nuromol with Synchro-Tech is ibuprofen 200mg with paracetamol 500mg, the question arises whether the rate of absorption of ibuprofen 200mg when taken alone versus when taken with paracetamol 500mg in the Australian approved dose of Nuromol with Synchro-Tech is different from rate of absorption as found by *Tanner et al 2010* in relation to ibuprofen 400mg.

20. In the absence of any evidence or argument by RB to the contrary, the Panel proceeds on the basis that there is no difference. It follows that the statement: "*The result of the simultaneous and rapid dissolution of ibuprofen and paracetamol in Nuromol with Synchro-Tech is faster absorption of these active ingredients into the blood stream, than had it been taken alone"* is incorrect and misleading, in breach of section 5.1.3 of the Code.

21. As to AFT's complaint that the claim: *"Nuromol might also improve tolerability compared with single agents alone because it limits the daily dose of active ingredients.8"* is unsubstantiated, the Panel notes that *Mehlisch DR et al 2010*[1] supports the claim (at p.1047): "*Using a combination of ibuprofen and paracetamol that is more effective than either agent alone may improve tolerability by limiting the daily dose of individual components, in particular paracetamol".*

22. As to Reference 8 not being listed in the references, the Panel notes that the backgrounder contained a reference 8. Its description, although incomplete, was sufficient to identify *Mehlisch DR et al 2010* which, as mentioned, supports the claim. Under these circumstances the Panel does not find the absence of any reference 8 from the advertorial to be misleading. There is no breach of the Code.

[1] Mehlisch DR et al, *A Single-Tablet Fixed-Dose Combination of Racemic Ibuprofen/Paracetamol in the Management of Moderate to Severe Postoperative Dental Pain in Adult and Adolescent Patients: A Multicenter, Two-Stage, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Factorial Study,* Clinical Therapeutics Vol. 32, No. 6, June 2010, pp.1033-1049.

Blooms The Chemist Weekly Dose

23. AFT says Blooms confirmed that the advertising copy for this publication was provided by RB. AFT says the advertisement claims that Nuromol has greater efficacy versus full dose of the single ingredients, whereas Maxigesic does not, and infers that Nuromol is more effective than single agents, which is not substantiated in the literature. The claims are inaccurate and misleading. The only Nuromol dose superior to full OTC ibuprofen dosing is the Nuromol two tablet dose, which in Australia is an unapproved dose. Reference is made to literature data which includes the two tablet dose. Either the claim is incorrect or is only supported for the two tablet dose which is not approved in Australia.

24. AFT also refers to a study[2] which shows that Maxigesic at the Australian approved daily dose (2 tablets 4 times a day) results in 35% lower pain scores than ibuprofen 1200mg/day, statistically significant results: [p <0.01]

25. In response, RB says the Blooms material does not claim nor infer that Maxigesic does not have greater efficacy versus single actives in a dose. It is claimed that both Nuromol and Maxigesic are greater than single actives in a dose. This is substantiated for Nuromol by *Mehlisch DR et al, 2010*:

> "*In terms of efficacy over the 8 hour study duration, SPRID8 scores for one tablet of Nuromol were significantly better vs paracetamol 500mg (p<0.001), and ibuprofen 200mg (p<0.001)."*

26. RB denies that it has sought to rely on or "promote" the unapproved two tablet dose of Nuromol as support for its claim, saying the two tablet dose data was included for data completeness only, which is proper and ethical in the circumstances. There is a disclaimer that makes clear that the two tablet dose is not approved. It is entirely proper that data should be presented without being edited or redacted. Finally, this material was sent only to [the Category Manager] at Blooms and RB has no further plans to publish or disseminate the material.

Panel consideration

27. Since Nuromol is an S3 product, the Panel understands the Blooms material to have been addressed to healthcare professionals, namely Blooms pharmacists.

28. The material compared Nuromol (with Synchro-Tech) at the dosing strength of ibuprofen 200mg/paracetamol 500mg with Maxigesic at the dosing strength of ibuprofen 150mg/paracetamol 500mg. Three claims were made in relation to efficacy, of which two are relevant here:

    (i) "greater than single actives in a dose", with "Yes" for each product;
    (ii) "greater than double dose of single actives", with "Yes" for Nuromol and "No published data" for Maxigesic.

[2] Merry AF et al 2010, *combined acetaminophen and ibuprofen for pain relief after oral surgery in adults: a randomized controlled trial.* British Journal of Anaesthesia 104, 80-88.

29. As to (i), the Panel considers that despite possible ambiguity, the words "greater than single actives in a dose" would be understood by Blooms pharmacists as representing that both Nuromol and Maxigesic, in the respective dosing strengths just mentioned, have greater efficacy than ibuprofen and paracetamol taken alone in their single tablet strengths, namely ibuprofen 200mg and paracetamol 500mg for Nuromol and ibuprofen 150mg and paracetamol 500mg for Maxigesic. The study by *Mehlisch DR et al, 2010* substantiates this claim in relation to Nuromol. The claim does not breach the Code.

30. As to (ii), the Panel considers that the words "greater than double dose of single actives", with "Yes" for Nuromol and "No published data" for Maxigesic would be understood by Blooms pharmacists as representing that Nuromol with Synchro-Tech at the dosing strength of ibuprofen 200mg/paracetamol 500mg specified in the advertisement has greater efficacy than paracetamol 1000mg and ibuprofen 400mg taken alone, i.e. double their single tablet strengths, and that there is no published data as to whether Maxigesic at the Australian approved dosing strength of ibuprofen 150mg/paracetamol 500mg has greater efficacy than ibuprofen 300mg and paracetamol 1000mg taken alone. The findings of *Mehlisch DR et al, 2010* at p.1040 show this representation to be incorrect and misleading in relation to Nuromol versus ibuprofen:

> *"…although FDC ibuprofen 200mg/paracetamol 500mg was significantly more effective over 8 hours than was paracetamol 1000mg (P <0.001), it was not significantly different from ibuprofen 400mg."*

31. Accordingly the Panel finds the claim "greater than double dose of single actives", with "Yes" for Nuromol to be in breach of section 5.1.3 of the Code.

32. AFT did not provide to the Panel a copy of the *Merry et al* article as required by clause 9.4.2.4 of the Code. The extracts AFT did provide do not reveal whether that study compared the efficacy of Maxigesic ibuprofen150mg/paracetamol 500mg versus ibuprofen 300mg and paracetamol 1000mg taken alone. Accordingly the claim "No published data" for Maxigesic has not been shown to be incorrect or misleading.

33. In the (single page) Blooms material provided to the Panel by AFT there is no reference to a double dose of Nuromol nor to any literature which might contain any such reference. The Panel finds that the Blooms material does not promote use of an unapproved dose of Nuromol.

The Detailer

34. AFT says this claims that Nuromol is proven versus "single-agent analgesics", which infers that it is proven to be more effective than either paracetamol or ibuprofen alone, whereas this is true only for an unapproved double dose of Nuromol.

35. RB says the inference for which AFT contends does not arise. The ordinary sensible construction of the word "proven" is that "proven" means to prove the genuineness of something, that is, by way of clinical testing. Nuromol *is*

"clinically tested" versus single agent analgesics: *Mehlisch DR et al, 2010*. Even if that construction be not accepted, data does exist to support an inference that Nuromol is more effective than a [sic] single agent analgesics, citing the passage from *Mehlisch DR et al, 2010* set out in paragraph 25 above.

Panel consideration

36. The Panel accepts AFT's contention that the claim that Nuromol is proven versus "single-agent analgesics" represents to pharmacists, to whom the detailer is addressed, that the Australian approved dose of Nuromol is proven to be more effective than the standard adult dose of paracetamol (i.e. 1000mg) and ibuprofen (i.e. 400mg) taken alone. Because this is not correct in relation to the standard adult dose of ibuprofen, namely 2 x 200mg, the Panel finds this to be incorrect and misleading, in breach of clause 5.1.3 of the Code.

The email from RB Health Hub

37. AFT says this includes the claim: *"One Nuromol with Synchro-Tech is the only paracetamol/ibuprofen analgesic to provide more powerful pain relief than two tablets of a paracetamol/codeine combination".* This is inaccurate and misleading because it infers that Maxigesic would not have more powerful pain relief than paracetamol/codeine and that there is no data to support this claim.

38. RB says no comparison is made between Maxigesic and Nuromol and in fact Maxigesic is not mentioned at all. So far as RB is aware, Maxigesic has not been tested against 2 tablets of a paracetamol/codeine combination. *Daniels 2011*[3] supports the claim that Nuromol provides more powerful pain relief than a paracetamol/codeine combination:

> "*For the pain measure SPRID 0-12h, one tablet of Nuromol was statistically superior to two tablets of a paracetamol/codeine combination (p=0.0001)."*

39. RB interprets the complaint as asserting that the claim in the email of which AFT complains can be valid only when applied to the unapproved double dose of Nurofen. RB says this is not correct and in any event it does not make that claim.

Panel consideration

40. Pharmacists, to whom the Panel considers the email was directed, would be well aware that, prior to the recent launch of Nuromol, Maxigesic was the only combined paracetamol/ibuprofen analgesic available in Australia. Accordingly they would understand the claim to mean that while Nuromol provides more powerful pain relief than two tablets of a paracetamol/codeine combination, Maxigesic does not. Since, so far as RB is aware, Maxigesic has not been tested against two tablets of a paracetamol/codeine combination, RB has failed to substantiate its representation that Maxigesic does not provide more powerful

[3] Daniels SE et al, *A randomised, five-parallel-group, placebo-controlled trial comparing the efficacy and tolerability of analgesic combinations including a novel single-tablet combination of ibuprofen/paracetamol for postoperative dental pain,* PAIN® 152(2011) 632-642.

pain relief than two tablets of a paracetamol/codeine combination. This constitutes a breach of the Code, clause 5.1.3.

41. The Panel does not interpret AFT's complaint as raising the unapproved double dose issue in relation to this email. Rather it appears to be a general comment about RB's advertising.

Classification of breaches

42. The Panel considers each of the breaches found in paragraphs 20, 31, 36 and 40 above to be a Moderate Breach of the Code, having no safety implications but which will impact on the perceptions of healthcare professionals regarding the product and competitor product.

Section 10.1.3 factors

43. On the material before the Panel, the Panel has considered these factors as follows:

- *Whether publication has ceased*
  It appears the Blooms and AJP publications have ceased. The Panel does not know whether publication of the email or the detailer has ceased.

- *Whether steps have been taken to withdraw the material published.*
  There is nothing before the Panel to indicate that any such steps have been taken.

- *Whether corrective statements have been made.*
  No corrective statements appear to have been made.

- *Whether the breach was deliberate or inadvertent.*
  Although the material presented in the advertorial and the other advertisements was deliberately provided by RB itself or through its agent, there is no evidence that the breaches were deliberate.

- *Whether the Member that is the subject of the complaint has previously breached the Code.*

  In determinations dated July 17, 2008, August 3, 2009, August 26, 2010, May 27, 2012 and August 28, 2013, RB was found by this Panel to have breached the Code. None of those determinations related to Nuromol.

- *Whether there were or are safety implications.*
  There are no safety implications.

- *Whether the perceptions of healthcare professionals or consumers have been or will be affected.*
  The perceptions of healthcare professionals are likely to have been affected.

Sanctions

44. The Panel requires RB:

(a) to give an undertaking in writing to the Executive Director of ASMI to cease publication forthwith in any media of any of the following representations, express or implied, until the representation can be supported by clinical evidence:

(i) that ibuprofen in Nuromol with Synchro-Tech is absorbed faster into the blood stream than if taken alone*;*

(ii) that Nuromol with Synchro-Tech at the Australian approved dose of ibuprofen 200mg/paracetamol 500mg has greater efficacy than ibuprofen 400mg taken alone;

(iii) that Maxigesic does not provide more powerful pain relief than two tablets of a paracetamol/codeine combination.

(b) to request the Category Manager at Blooms to circulate to all Blooms pharmacies the statement annexed hereto, with similar prominence to the original publication and with no other material referring to Nuromol on the same page, and to send copies of the request and of the statement when published by Blooms to the Executive Director of ASMI;

(c) to cease distribution and to destroy all existing stocks of the Detailer and to notify the Executive Director of ASMI that this has been done; and

(d) to pay a fine of $20,000, being $5,000 for each of the Moderate Breaches found by the Panel.

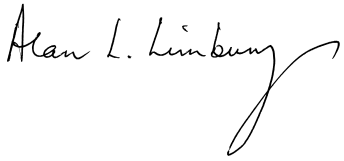
45. Since the Code breach in the AJP advertorial related to absorption, not efficacy, the Panel does not consider it appropriate to require RB to publish a correction in AJP.

46. The Panel recommends to RB that, in any future advertising of Nuromol, it be made clear what dosage is being referred to and with what dosage any comparison is made.

47. The Panel makes no determination to alter the usual operation of section 9.4.2.2 of the Code.

48. Attention is drawn to sections 10.2.6 and 11.1 of the Code.

Dated: August 11, 2015.
For the ASMI Complaints Panel



Alan L. Limbury
Chairman

Note: although this is called a Final Determination, each party has a right of appeal to the Arbiter. If no appeal is lodged this determination will be published on the ASMI website once the time for lodging an appeal has expired. If there is an appeal, the Arbiter's determination will be published on the ASMI website together with this determination. Until publication on the website, parties and their representatives should maintain the privacy of these proceedings.

Annexure

Correction: incorrect and misleading information about Nuromol

In March this year Blooms Weekly Dose published material provided by Reckitt Benckiser (Australia) Pty Limited comparing Nuromol® with Maxigesic®.

The comparison represented that Nuromol with Synchro-Tech at the Australian approved dosing strength of ibuprofen 200mg/paracetamol 500mg has greater efficacy than paracetamol 1000mg and ibuprofen 400mg taken alone

That representation has been found by the ASMI Complaints Panel to be incorrect and misleading in relation to ibuprofen:

> *"…although FDC ibuprofen 200mg/paracetamol 500mg was significantly more effective over 8 hours than was paracetamol 1000mg (P <0.001), it was not significantly different from ibuprofen 400mg."*[1]

The ASMI Complaints Panel has required Reckitt Benckiser to ask Blooms to circulate this correction.

1. Mehlisch DR et al, *A Single-Tablet Fixed-Dose Combination of Racemic Ibuprofen/Paracetamol in the Management of Moderate to Severe Postoperative Dental Pain in Adult and Adolescent Patients: A Multicenter, Two-Stage, Randomized, Double-Blind, Parallel-Group, Placebo-Controlled, Factorial Study,* Clinical Therapeutics Vol. 32, No. 6, June 2010, pp.1033-1049 at 1040.