CASE AUTH/1946/1/07

PFIZER CONSUMER HEALTHCARE v Reckitt Benckiser Healthcare

'Quick Guide' on childhood fever

Pfizer Consumer Healthcare complained about a two page 'Quick Guide' article, 'Supported with an unrestricted educational grant from Reckitt Benckiser Healthcare', which appeared as a bound in insert in The Practitioner in November. The 'Quick Guide' was entitled 'Best practice in childhood fever – the comfort cycle' and referred to Nurofen for children (ibuprofen suspension) which was marketed by Reckitt Benckiser Healthcare.

Pfizer Consumer Healthcare's two key issues were the misleading and selective interpretation of the supporting data used and, more broadly speaking, the fact that this article was a promotional item as defined by the Code. The item was promotional because it incorporated a stylised image of the Nurofen for Children logo and the brand name appeared throughout the text. Furthermore Reckitt Benckiser Healthcare had effectively selected the subject matter by supplying specific data (including data on file) to the journal editors and had reviewed the copy prior to publication. Reckitt Benckiser Healthcare was thus able to influence the article in such a way as to favour its own interests. This article should thus be considered as an 'advertorial', covered by the Code, rather than an independently written best practice guide as implied by the statement 'supported with an unrestricted educational grant'. Overall, this article clearly appeared to have been written by or under the editorial control of Reckitt Benckiser Healthcare. Pfizer Consumer Healthcare alleged that the insert was misleading and constituted disguised promotion in breach of the Code.

The overall message, reinforced by the title, 'Best practice in childhood fever – the comfort cycle', was that Nurofen for Children represented best practice in treating childhood pain and fever. Several references to Nurofen for Children being 'treatment of choice' further strengthened this message. This was misleading and implied that the article was based on sound, accepted principles, preferably peer reviewed and supported by strong independently, published data. However two of the cited references were unpublished data on file and the third discussed anxiety in adolescents with chronic pain (Eccleston *et al* 2004). No link had been demonstrated between fever and anxiety in children or parents. Neither Nurofen for Children, nor indeed ibuprofen, was established as best practice in treating children's pain and/or fever. In fact a UK paediatric formulary recommended paracetamol as first line in fever. In conclusion both the title and contents misleadingly implied that they discussed genuine scientific opinion in breach of the Code.

The Dover study was one of the principal data on file references cited and was available on the Nurofen website. Pfizer Consumer Healthcare noted that this company sponsored randomised study compared the single dose efficacy and multiple dose tolerability of paracetamol with ibuprofen in paediatric fever. The single dose part of the trial was blinded while the second and subsequent doses were open-label. The primary endpoint of the study was the reduction of temperature from baseline at 6 hours following single dose administration of either paracetamol or ibuprofen. Secondary endpoints included subjective assessment of parent treatment preference.

Data from this study had been cherry picked to suit the 'Nurofen for Children Comfort Cycle' story that had been created in the article. The Dover study did not show a statistically significant difference between paracetamol and ibuprofen in reducing temperature (the primary endpoint). The article completely disregarded this less favourable primary endpoint and focussed instead on the more positive secondary endpoint of parent preference. Data extracted from this open-label element of the study was little more than market research. However it was presented in the article as fact and described as best practice in order to underpin and encourage confidence in the comfort cycle argument. There was no mention that this was a secondary endpoint or that it was open-label.

The open-label element of this study also meant that parents knew which medicine their child was to receive in subsequent dosing. This introduced significant bias into the study as parents were likely to be familiar with both medicines; it was likely that previous experience with taste, colour, brand recognition and dosing would influence their choice. This issue was discussed very briefly in the study but ignored in the article which unequivocally favoured Nurofen for Children over paracetamol. Despite this obvious source of bias the article recommended Nurofen for Children as the treatment of choice with parents *'which cannot be explained by product bias'*.

The comfort cycle was referenced specifically to the Dover study and implied that reducing parental anxiety reduced anxiety in children which in turn tackled fever. It did not appear that the study even assessed anxiety and, in fact, the study report described this speculative link as a 'working hypothesis'. This misinterpretation of the data breached the Code.

Eccleston *et al* was another study cited in support of the comfort cycle story but as it investigated a very

different patient group than that discussed in the article it could not be used as supporting evidence. Eccleston *et al* measured distress associated with *chronic pain* in *adolescents* and how they coped while the article at issue discussed anxiety associated with acute pain in children. Nurofen for Children was licensed to treat mild to moderate pain and fever in children up to the age of 12 years; it was not intended for long term use. Eccleston *et al* investigated adolescents (mean age 14.45 years). Pfizer Consumer Healthcare accepted that the lower end of this age range was 11 years and so within the Nurofen for Children's licence. However the article at issue did not refer to adolescents and implied that the published evidence used for their anxiety-pain hypothesis applied to a much younger age group.

Eccleston *et al* investigated anxiety relating to *chronic* pain and did not investigate a relationship between anxiety and acute pain. The article did not state that the supporting data referred specifically to chronic pain in adolescents. The article, without the benefit of further clinical evidence, then went on to extend on this anxiety/pain association by stating that it followed that anxiety must also result from fever as well, thus completing the comfort cycle. Though not specifically referenced beyond the initial anxiety-pain statement the citation of Eccleston *et al* added a degree of apparent credibility to the article. It was clear that this data had been misrepresented so that it fitted in with the comfort cycle story. Pfizer Consumer Healthcare alleged that it was inappropriate to cite this reference in an article that specifically discussed the use of a medicine for the treatment of acute pain in children.

In summary the concept of the comfort cycle formed the basis for the whole piece and had been presented as fact in order to influence prescribing decisions in childhood fever. However this was conjecture and based on a working hypothesis as discussed in the Dover study. Little or no factual data had been presented in support of the comfort cycle model.

Pfizer Consumer Healthcare noted that a bar chart at the top of the first page clearly implied that, at the end of the Dover study, more than twice as many parents would use Nurofen for Children again compared with paracetamol. In reality this difference was about 9%. This use of suppressed zeros was grossly misleading and was clearly and specifically prohibited in the Code.

The article described Nurofen for Children as '… achieving excellent analgesia (at least as good as paracetamol) …' which clearly implied superiority of Nurofen for Children over paracetamol. If the intention was to communicate parity then a statement to the effect of 'as good as paracetamol' would have been sufficient. As pain was not measured in any of the studies cited in the article at issue this statement was not substantiated, either in terms of being 'excellent' or in its comparison with paracetamol. The reference cited related to fever and not analgesia. Pfizer Consumer Healthcare alleged this unsubstantiated claim together with a misleading reference to an irrelevant study constituted a breach of the Code.

Pfizer Consumer Healthcare alleged further breaches of the Code in that the non-proprietary name was not adjacent to the most prominent display of the brand name, there was no statement on the first page of the advertorial as to where the prescribing information might be found, and nor was there information describing the adverse event reporting mechanism.

In summary the article was misleading in its overall message, presentation and interpretation of the data. It was branded and promotional but presented as an independently written 'best practice' article. The information had been presented as established scientific opinion, rather than a working hypothesis requiring further investigation, in such a way as to influence prescribing decisions in childhood fever.

The Panel had first to consider whether the 'Quick Guide' article was covered by the Code. Nurofen for Children was a product which, for childhood fever, the subject of the article in question, could be bought over-the-counter (OTC) or prescribed; sales data showed that most packs of Nurofen for Children were purchased OTC. The supplementary information stated that the Code did not apply to the promotion of OTC medicines to members of the health professions when the object of that promotion was to encourage their purchase by the public. Where an advertisement was designed to encourage doctors to prescribe the medicine, then it came within the scope of the Code. An item that promoted for both prescribing and recommending purchase would need to comply with both the ABPI Code and the PAGB Professional Code.

The 'Quick Guide' article referred to the comfort cycle and how important a parent's perception of therapy was in the management of a child's pain. The article stated that 'Prescribing or recommending a treatment of choice will ultimately benefit both [parent] and child'. The Panel acknowledged that although very few packs of Nurofen for Children were prescribed this was not a relevant factor in deciding whether the ABPI Code applied or not. The article referred to prescribing and thus would encourage some doctors to prescribe Nurofen for Children. The Panel considered that the 'Quick Guide' article fell within the scope of the Code.

It was acceptable for companies to sponsor material. It had previously been decided, in relation to material aimed at health professionals, that the content would be subject to the Code if it was promotional in nature or if the company had used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its contents, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the

material for promotional purposes.

The article at issue was developed after Reckitt Benckiser Healthcare had contacted the publishers with a view to introducing GPs to, *inter alia*, the concept of the comfort cycle. Reckitt Benckiser Healthcare provided relevant information and was able to comment on the final article and had paid for it to be included in the journal; the production of the article had thus not been a strictly arm's length arrangement. The article featured, as part of the heading to both pages, a logo which incorporated the red/orange/yellow 'target' associated with the Nurofen brand. The Panel considered that this, together with the company's involvement in the development of the article, meant that Reckitt Benckiser Healthcare was responsible for its content under the Code.

At first glance the article appeared to be an educational discussion about how best to manage childhood fever; an impression strengthened by the statement that the insert had been 'Supported with an unrestricted educational grant from Reckitt Benckiser Healthcare'. The 'Quick Guide' had been provided as an insert in The Practitioner and was intended to be kept for future reference. The only treatments discussed in the article, however, were paracetamol and Nurofen for Children. The Panel noted the way in which the material had been developed; Reckitt Benckiser Healthcare was inextricably linked to the production of the insert. Given the company's involvement the Panel considered that the article was disguised promotional material for Nurofen for Children; the declaration of sponsorship implied that it was an independently written educational piece which was not so. A breach of the Code was ruled.

The Panel noted Pfizer Consumer Healthcare's submission that a UK paediatric formulary recommended paracetamol as first line in fever. The title of the article was 'Best practice in childhood fever – the comfort cycle' but the only treatments referred to were Nurofen for Children and paracetamol. It was stated that Nurofen for Children had emerged as a treatment of choice with parents. A diagram of 'The comfort cycle' featured 'Nurofen for Children' in the middle of a cycle of arrows; one arrow was labelled 'Becomes parent's treatment of choice'. The Panel considered that the diagram implied that Nurofen for Children became the treatment of choice for parents. The Panel further considered that as the article was principally about Nurofen for Children, the title 'Best practice in childhood fever – the comfort cycle' implied that Nurofen for Children had been clinically shown to represent best practice which was not so. The Panel considered that the overall message of the article was misleading as alleged. A breach of the Code was ruled.

Reckitt Benckiser Healthcare had not provided any information about the Dover Study other than that mentioned in its response. The diagram depicting 'The comfort cycle' was referenced to the Dover study and depicted a four stage cycle of 'Reduces anxiety in children', 'Tackles fever', 'Becomes parent's treatment of choice' and 'Reduces anxiety in parent' around 'Nurofen for Children' in the centre. The Panel considered that the diagram implied that because it tackled fever, Nurofen for Children became the parent's choice. A description of the study in the text stated that when compared with paracetamol suspension, parents rated Nurofen for Children as more efficacious. According to Pfizer Consumer Healthcare there was, however, no difference between the two medicines with regard to the primary clinical outcome of reduction in temperature/fever. The Panel also noted that the concept of the comfort cycle was a 'working hypothesis'. The Dover study had not measured anxiety in either the parents or the children. The Panel thus considered the article was misleading as it was not a fair reflection of the results of the Dover study. A breach of the Code was ruled.

Eccleston *et al*, cited in support of the statement 'Anxiety is a measure of pain…', reported on adolescent chronic pain, not childhood fever, the subject of the insert in question. The patients in Eccleston *et al* ranged from 11 to 17 years (mean 14.45 years) and the study examined emotional distress in adolescent chronic pain patients and their parents and the relationship between the two and adolescent coping. The Panel questioned the relevance of the study in the context of a piece about childhood fever which required only short-term treatment. There was no data to show that the relationship between anxiety and pain in adolescents with chronic pain was the same as in infants with acute pain or fever. Nurofen for Children was indicated for children from 3 months to 12 years of age. The Panel considered that citing Eccleston *et al* was misleading as alleged. A breach of the Code was ruled.

The y axis of the bar chart which depicted the percentage of parents who would use either Nurofen for Children or paracetamol again (as reported in the Dover study) started at 82%. The resultant height of the bars made it look as if twice as many parents preferred Nurofen for Children as preferred paracetamol which was not so. The Panel considered that the use of the suppressed zero was misleading in breach of the Code.

The Panel noted that on the available information the Dover Study had not measured analgesia. Reckitt Benckiser Healthcare Healthcare submitted that it was widely accepted that ibuprofen was at least as good as paracetamol and that the superiority of ibuprofen was capable of substantiation citing McGaw *et al* in this regard. The claim 'At least as good as paracetamol' was not referenced as such nor did the Code require it to be referenced. The Code did not require substantiation to be provided in the article itself but the claim must be capable of substantiation. The Panel considered that readers might assume that the Dover study measured pain/analgesia given that the article stated the data was presented at the International Symposium on Paediatric Pain.

McGaw *et al* compared ibuprofen with acetaminophen in the relief of postextraction dental pain in children aged 8 - 16 with the majority of the children in the 14 - 16 age range. The authors commented that postoperative pain associated with dental surgery was associated with pain and oedema and that ibuprofen's superior analgesic efficacy might be due in part to its anti-inflammatory properties which were not shared by acetaminophen. The Panel considered that in the circumstances the reference to 'excellent analgesia (at least as good as paracetamol)' was misleading and a breach of the Code was ruled.

The Panel considered that the most prominent display of the brand name was not accompanied by the non-proprietary name. A breach of the Code was ruled.

The 'Quick Guide' was provided as a bound-in insert in The Practitioner' it was thus a two page advertisement where the prescribing information appeared overleaf. There was, however, no statement as to where the prescribing information could be found. A breach of the Code was ruled.

The Code required that all promotional material, other than promotional aids, must include prominent information about adverse event reporting mechanisms. No such information was given in the 'Quick Guide' at issue. A breach of the Code was ruled.

Pfizer Consumer Healthcare complained about a 'Quick Guide' article, 'Supported with an unrestricted educational grant from Reckitt Benckiser Healthcare', which appeared as an insert in The Practitioner in November 2006. The subject of the 'Quick Guide' was 'Best practice in childhood fever – the comfort cycle'.

COMPLAINT

Pfizer Consumer Healthcare stated that its two key issues, from which further more specific concerns arose, were the misleading and selective interpretation of the supporting data used and, more broadly speaking, the fact that this article was a promotional item and fulfilled the Code's definition of such an item. Pfizer Consumer Healthcare believed the item was promotional because:

- it was clearly branded in the top right corner with a stylised image of the Nurofen for Children logo;
- the brand name Nurofen for Children (ibuprofen suspension) appeared throughout the text;
- Reckitt Benckiser Healthcare (UK) Limited had effectively selected the subject matter by supplying specific data (including data on file) to the journal editors – some of this subject matter such as the graph showing patient preference had been used in the article unaltered;
- Reckitt Benckiser Healthcare had reviewed the copy prior to publication.

It was clear that Reckitt Benckiser Healthcare was able to influence the article in such a way as to favour its own interests. This article should thus be considered as promotional and covered by the Code, rather than an independently written best practice guide as implied.

Disguised promotion

The Code stated that 'when a company pays for, or otherwise secures or arranges the publication of promotional material in journals, such material must not resemble independent editorial matter'.

The statement that Reckitt Benckiser Healthcare had provided an unrestricted educational grant to support the article, clearly implied that the item was independently produced. On closer inspection it was plain that there was significant company involvement. The article was heavily branded with numerous inclusions of the brand name, Nurofen for Children, as well as the prominent inclusion of a stylised version of the Nurofen 'target' logo at the top of the piece. This impression was reinforced by the fact that two out of the three supporting references were unpublished data on file and therefore not available without company permission.

With the inclusion of branding, prescribing information and the adherence to the two-page limit for journal advertisements, Pfizer Consumer Healthcare suggested that this article constituted an 'advertorial' rather than an independently produced editorial as the title and general style suggested.

Overall, this article clearly appeared to have been written by or under the editorial control of Reckitt Benckiser Healthcare. Pfizer Consumer Healthcare alleged that the insert was misleading and constituted disguised promotion in breach of Clause 10.1 of the Code.

Pfizer Consumer Healthcare queried who had authored this piece and in particular if any public relations or advertising agencies were involved.

The overall theme of the article

The overall message, reinforced by the title, 'Best practice in childhood fever – the comfort cycle', was that Nurofen for Children represented best practice in treating childhood pain and fever. In addition there were several references to Nurofen for Children being 'treatment of choice' which further strengthened this message.

This was misleading and implied that the article was based on sound, accepted principles, preferably peer reviewed and supported by strong independently, published data. However two of the cited references were unpublished data on file and the third discussed anxiety in *adolescents* with *chronic pain* (Eccleston *et al* 2004). Pfizer Consumer Healthcare also noted that no link had been demonstrated between fever and anxiety in children or parents. Neither Nurofen for Children, nor indeed ibuprofen, was established as best practice in treating children's pain and/or fever. In fact

'Medicines for Children' which was jointly published by the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists' Group recommended paracetamol as first line in fever.

In conclusion both the title and contents misleadingly implied that they discussed genuine scientific opinion in breach of Clause 7.2.

The 'comfort cycle'

The Dover study was one of the principal data on file references cited. Its methodology and results were available on the Nurofen website. Pfizer Consumer Healthcare noted that the objective of this company sponsored randomised study was to compare the single dose efficacy and multiple dose tolerability of paracetamol with ibuprofen in paediatric fever. The single dose part of the trial was blinded while the second and subsequent doses were open-label.

The primary endpoint of the Dover study was the reduction of temperature from baseline at 6 hours following single dose administration of either paracetamol or ibuprofen. Secondary endpoints included a number of measures including subjective assessment of parent treatment preference.

Data from this study had been cherry picked to suit the 'Nurofen for Children Comfort Cycle' story that had been created in the article. The Dover study did not demonstrate a statistically significant difference between paracetamol and ibuprofen in reducing temperature (the primary endpoint). The article completely disregarded this less favourable primary endpoint and focussed instead on the more positive secondary endpoint of parent preference. It was clear from this open-label element of the study that the data extracted was little more than market research. However it was presented in the article as fact and described as best practice in order to underpin and encourage confidence in the comfort cycle argument. There was no mention that this was only a secondary endpoint or that it was open-label.

The open-label element of this study also meant that parents were aware of which medicines their child was to receive in subsequent dosing. This introduced significant bias into the study as parents were likely to be familiar with both medicines; it was likely that previous experience with taste, colour, brand recognition and dosing would influence their choice. This issue was discussed very briefly in the study but ignored in the article which unequivocally favoured Nurofen for Children over paracetamol. Despite this obvious source of bias the article still recommended Nurofen for Children as the treatment of choice with parents *'which cannot be explained by product bias'*.

The comfort cycle was referenced specifically to the Dover study and implied that reducing parental anxiety reduced anxiety in children which in turn tackled fever. It did not appear that the study even assessed anxiety and, in fact, the study report described this speculative link as a 'working hypothesis'. Pfizer Consumer Healthcare alleged that this misinterpretation of the data was a breach of Clause 7.2.

Eccleston *et al* was another key study used to build up credibility and support for the comfort cycle story. However that paper investigated a very different patient group than that discussed anywhere in the article and so could not be used as supporting evidence. Eccleston *et al* measured the extent of distress associated with *chronic pain* in *adolescents* and how they coped while the article at issue discussed anxiety associated with acute pain in children.

Nurofen for Children was only licensed for children up to the age of 12 years. Eccleston *et al* investigated adolescents (mean age 14.45 years). Pfizer Consumer Healthcare accepted that the lower end of this age range was 11 years and so within the Nurofen for Children's licence. However the article at issue did not refer to adolescents and implied that the published evidence used for their anxiety-pain hypothesis applied to a much younger age group.

Nurofen for Children was an over-the-counter (OTC) medicine licensed to treat mild to moderate pain and fever; it was not intended for long term use. Eccleston *et al* investigated anxiety relating to *chronic* pain and did not investigate a relationship between anxiety and acute pain. The article did not state that the supporting data referred specifically to chronic pain in adolescents.

The article, without the benefit of further clinical evidence, then went on to extend on this anxiety/pain association by stating that it followed that anxiety must also result from fever as well, thus completing the comfort cycle.

Though not specifically referenced beyond the initial anxiety-pain statement the citation of Eccleston *et al* added a degree of apparent credibility to the article. It was clear that this data had been misrepresented so that it fitted in with the comfort cycle story. Pfizer Consumer Healthcare alleged that it was inappropriate to cite this reference in an article that specifically discussed the use of an OTC medicine for the treatment of acute pain in children, in breach of Clause 7.2.

In summary the concept of the comfort cycle formed the basis for the whole piece and had been presented as fact in order to influence prescribing decisions in childhood fever. However this was pure conjecture and based on a working hypothesis as discussed in the Dover study. Little or no factual data had been presented in support of the comfort cycle model.

Misrepresentation of data

Pfizer Consumer Healthcare noted that by the use of suppressed zero, a bar chart at the top of the first page clearly implied that, at the end of the Dover study, more than twice as many parents would use Nurofen for Children again compared with paracetamol. In reality this difference was about 9%. The use of a suppressed zero was misleading and clearly in breach of Clause 7.8.

Implied superiority without substantiation

The article described Nurofen for Children as '… achieving excellent analgesia (at least as good as paracetamol) …'. This clearly implied superiority of Nurofen for Children over paracetamol. If the intention was to communicate parity then a statement to the effect of 'as good as paracetamol' would have been sufficient. As pain was not measured in any of the studies cited in the article at issue this statement was not substantiated, either in terms of being 'excellent' or in its comparison with paracetamol. The reference cited related to fever and not analgesia. Pfizer Consumer Healthcare alleged this unsubstantiated comparative claim together with a misleading reference to an irrelevant study constituted a breach of Clause 7.2.

Clause 4 breaches

Pfizer Consumer Healthcare alleged that the following had been omitted.

- the non-proprietary name which must appear adjacent to the most prominent display of the brand name (breach Clause 4.6);
- a statement on the first page of the advertorial describing where the prescribing information might be found (breach Clause 4.7);
- a prominent display of information describing the adverse event reporting mechanism (breach Clause 4.10).

Summary

In summary the article was grossly misleading in its overall message, presentation and interpretation of the data. It was branded and promotional but presented as an independently written 'best practice' article. The information had been presented as established scientific opinion, rather than a working hypothesis requiring further investigation, in such a way as to influence prescribing decisions in childhood fever.

RESPONSE

Reckitt Benckiser Healthcare did not consider that this complaint was appropriate for consideration by the Authority because it related to an educational article concerning an OTC product; this particular piece was outside of the scope of the ABPI Code.

Clause 1.1 of the Code stated that the Code did not apply to the promotion of OTC medicines to members of the health professions when the object of that promotion was to encourage their purchase by members of the public. As indicated below, Reckitt Benckiser Healthcare did not consider that this publication was promotional, but even if it was, it was exempted by the final paragraph of Clause 1.1.

The 'Quick Guide' insert was published in The Practitioner, a journal targeted at, and circulated solely to UK GPs. However, if the article was considered to be promotional, Reckitt Benckiser Healthcare considered that it would encourage GPs to recommend Nurofen for Children to parents, for their later purchase, rather than prescription. A small number of GPs did prescribe Nurofen for Children, though it was principally an OTC product; the ratio of OTC sales to prescription sales was tiny, approximately 28:1. The design of the packaging was also clearly aimed at consumer sales, rather than prescription, and was noticeably different from the majority of prescription medicines currently available, ie predominantly plain white packs. In other words, prescription accounted for a mere 3.5% of total UK sales of Nurofen for Children.

The last paragraph of column 2 of the article in question stated that 'Prescribing or recommending a treatment of choice will ultimately benefit both [parent] and child'. The word 'parent' was consistent with the theme of the article on the comfort cycle and allaying parental anxiety. The use of the word 'recommending' was also consistent with Reckitt Benckiser Healthcare's view of the intention of the article, and a single use of the word 'prescribing' was not of itself significant in the circumstances.

Reckitt Benckiser Healthcare explained that it had contacted the publishers of The Practitioner with a view to introducing GPs to the concepts of the comfort cycle and a bound-in insert in The Practitioner was agreed upon. Reckitt Benckiser Healthcare made an educational grant to assist in the cost of circulation. No agency was involved in the production of this item. The publishers generated the initial concept insert; Reckitt Benckiser Healthcare provided data and information on ibuprofen and the comfort cycle to assist in the writing of the article. Whilst Reckitt Benckiser Healthcare was able to comment on the finished manuscript, the editors of The Practitioner had final editorial control.

Reckitt Benckiser Healthcare provided the publishers with the essential information [prescribing information], as was required under the Proprietary Association of Great Britain (PAGB) Professional Code of Practice, as appeared in the final version of the insert. This was in the belief that this item was targeted at GPs and to be kept by the intended audience for their future reference and recommendation to parents for purchase.

As stated above, a single paragraph in the insert included the word 'prescribing'. This was the author's choice and Reckitt Benckiser Healthcare did not have editorial control over the article.

Alleged disguised promotion

Reckitt Benckiser Healthcare noted that Clause 10.1 of the Code stated that promotional material and activities must not be disguised.

As stated prominently on the item, Reckitt Benckiser Healthcare had provided an unrestricted educational grant in order to make the publication and circulation of this important information possible. Thus the requirements of Clause 10.1 and, indeed, Clause 9.10,

of the Code had been met.

Notwithstanding this, Reckitt Benckiser Healthcare strongly believed that it would be wrong to suggest that the article constituted disguised promotion. Firstly, the article was not designed to be promotional in nature; it discussed the comfort cycle and communicated the results of the Dover study presented at the recent international symposium on paediatric pain (which utilised Nurofen for Children as a treatment arm).

Secondly, Reckitt Benckiser Healthcare's involvement was not disguised; there was a prominent statement at the top of the article, that the company had provided the educational grant to allow its circulation to GPs. If a company wished to disguise a piece of promotional material it would not have declared its financial interest to the readers so openly. Reckitt Benckiser Healthcare had made this declaration very clear to the reader, to allow them to make an informed judgment.

The brand name Nurofen for Children was used in the article as it was the product used as an active treatment arm in the Dover study.

The inclusion of the Nurofen logo, use of the brand name Nurofen for Children and the fact that Reckitt Benckiser Healthcare provided information for the insert and was able to comment on it prior to its publication, was immaterial, as these elements did not in themselves make the item promotional, whether disguised or not.

The use of data on file as supporting data was accepted practice in the pharmaceutical industry. Use of such data meant that Reckitt Benckiser Healthcare was required to provide it on request to health professionals or appropriate administrative staff. In contrast to Pfizer Consumer Healthcare's allegation, this did not mean that it was not available without Reckitt Benckiser Healthcare's permission.

Reckitt Benckiser Healthcare therefore contested the allegation that the article was in breach of Clause 10.1; it did not consider it to be promotional in nature, disguised or otherwise.

Overall theme of the article

Reckitt Benckiser Healthcare noted that Pfizer Consumer Healthcare took issue with the overall theme of the insert. In particular, Pfizer Consumer Healthcare appeared to believe that the insert represented the use of ibuprofen as best practice in treating childhood pain and fever, and that Nurofen for Children was emerging as a treatment of choice with parents. This was wrong; the best practice referred to, even within the title, was to the comfort cycle and not ibuprofen suspension.

With regard to a treatment of choice the authors had carefully chosen the indefinite article 'a' rather than the definite article 'the' when referring to 'treatment of choice'. The insert did not claim Nurofen for Children to be 'the' treatment of choice with parents, but merely 'a' treatment of choice with parents. This careful selection of wording presumably resulted from a thorough reading and understanding of the Dover study. Reckitt Benckiser Healthcare noted that the complaint studiously avoided the use of any definite article when referring to treatment of choice.

Reckitt Benckiser Healthcare also noted that, within the text of the insert, this parental preference was repeatedly referred to as a treatment of choice with parents, rather than for parents or, for that matter, physicians.

Whilst some professional health organisations might have recommended paracetamol as the first line treatment in fever, the Dover study had shown in its secondary endpoint that Nurofen for Children could be 'a' treatment of choice for parents, in that 96.7% of parents had stated that they would use Nurofen for Children again, compared with 87.9% who would use paracetamol again ($p < 0.01$).

Recommendation of a treatment that, in addition to treating the child was also the preferred choice of the parent, was likely to allay parental anxiety, and was thus a clear link to the comfort cycle. Moreover, the reason that Nurofen for Children was specifically referred to in the insert was because it was used in the Dover study. Reckitt Benckiser Healthcare considered that this parental preference was accurately and fairly represented as 'a' treatment of choice, and that the Dover study, being a very recent piece of work, represented an up-to-date evaluation.

Reckitt Benckiser Healthcare noted that Pfizer Consumer Healthcare had objected to the fact that parts, and not all, of the Dover study end points and results were presented. Reckitt Benckiser Healthcare submitted that it was standard practice by clinical investigators to publish findings of a large study in separate sections, in different journals, at different times. The Dover study was a large study with many findings. The results of the primary efficacy and safety end points had been submitted to a reputable journal and the manuscript was currently undergoing peer-review. The results of comparative efficacy between ibuprofen and paracetamol were also the subject of current peer-review. For reasons of confidentiality as well as observing the Code with regard to peer-review, Reckitt Benckiser Healthcare could not currently discuss the details of the primary end points. Added to this was the fact that word-count limitations were often set by journals, so it was not always possible to include discussion of all findings in the primary manuscript when submitted for publication. However, sufficient details of the study had been made publicly available on Reckitt Benckiser Healthcare's website which Pfizer Consumer Healthcare had downloaded and included in its complaint. This demonstrated the open approach taken by Reckitt Benckiser Healthcare in communicating these study results.

In view of these various facets, secondary end points were often discussed in a journal different to the one in which the primary manuscript was published. Selecting the particular secondary end point of parental preference was most appropriate here, given that the

insert was intended to give that much more focus to this very issue, and to a tightly targeted audience.

Reckitt Benckiser Healthcare submitted that selecting secondary end points in such a publication was an accepted practice; as there was no bias in the presentation of this secondary end point, there was no breach of any specific clause of the Code, or its spirit.

With regard to concerns raised by Pfizer Consumer Healthcare over the phrase 'which cannot be explained by product bias', Reckitt Benckiser Healthcare believed that this was a fair, balanced, undistorted portrayal of the interpretation made by the authors of the trial report.

Although the parents' perception of efficacy was a subjective criterion, the randomised, double blind, double dummy nature of the study meant that parental preference would be equally split between the two groups, and that the significant difference between treatment groups was most probably as a result of better resolution of all associated symptoms, rather than bias as suggested by Pfizer Consumer Healthcare.

Parental preference was already evident at the end of the randomised, double blind, double dummy element of the study, and continued into the second, open element. In contrast, had this been a fully open-label study, Pfizer Consumer Healthcare's criticism might have been valid.

It was acknowledged that the second part of this study was conducted as an open study: parents knew whether their child was taking paracetamol or Nurofen for Children. This 'product bias' was hence known to all parents involved. Yet the level of preference expressed at the end of the study when compared to that expressed after the first phase did not differ to any great degree. After initial dose (the randomised, double blind phase of the study), 96.5% (138/143) of parents said they would use ibuprofen again, compared to 88.8% (127/143) of the paracetamol group ($p < 0.05$). At end of treatment (at the end of open phase of the study), 96.7% (145/150) of parents said they would use ibuprofen again, compared to 87.9% (131/149) in the paracetamol group ($p < 0.01$). After initial dose, 59.2% (87/147) of parents graded ibuprofen as very efficacious, compared to 37.2% (55/148) of the paracetamol group ($p < 0.001$). At end of treatment, 59.6% (90/151) of parents graded ibuprofen as very efficacious, compared to 43.3% (65/150) in the paracetamol group ($p < 0.01$).

The fact that parents whose children were taking Nurofen for Children preferred it to a greater extent than the preference expressed for paracetamol by parents whose children were taking that product, indisputably showed that 'product bias' was not the only factor affecting parental choice.

Hence the conclusion 'which cannot be explained by product bias' was indeed accurate. All data on parental preference were accurately reflected in the text, and described correctly so as not to mislead the reader. If Pfizer Consumer Healthcare wished to contest the interpretation of the data, it should write to the investigators of the Dover study. Interpretation of the study findings was independent from Reckitt Benckiser Healthcare; it was important for all parties to respect this independence. Additionally, the accusation that this was little more than market research data was unacceptable and constituted denigration of the academic work by the investigators of the Dover study.

With regard to alleged inappropriate referencing, Reckitt Benckiser Healthcare noted that Eccleston *et al* was not cited in support of a promotional claim, but merely to explain that anxiety was a measure of pain. This was a well-conducted study using a large number of sophisticated psychological instruments to measure the emotional status of young patients and their parents. Study of anxiety with acute pain was difficult, given the short-term and relatively transient nature of acute pain; hence this study had taken chronic pain as a study model. It included children aged 11 to 17, and provided a reasonable surrogate for children younger than 12 (the upper age limit for which Nurofen for Children was licensed), who could have practical difficulties in participating in anxiety assessment. Reckitt Benckiser Healthcare believed that it provided a sound scientific basis for the discussion on the complex area of anxiety and pain, and was both objective and fair.

When considering all of the above, Reckitt Benckiser Healthcare believed that it had demonstrated that the article in question did not mislead and did not distort or exaggerate. The company thus denied a breach of Clause 7.2.

Alleged misrepresentation of data

Reckitt Benckiser Healthcare acknowledged that the bar chart had a suppressed zero on the y-axis, but reiterated that the article was written by the editor of The Practitioner, primarily as an educational piece, and did not fall within the scope of the Code. There was thus no breach of Clause 7.8.

Where Reckitt Benckiser Healthcare did have editorial control, it would of course take the use of suppressed zeros into account and ensure that information was clearly represented in educational and scientific material produced by it.

Alleged implied superiority without substantiation

It was widely accepted clinically that ibuprofen was at least as good as paracetamol. As no claim of superiority was made in this piece, the authors undoubtedly considered that it was thus unnecessary to elaborate further on this point. This was despite the fact that superiority of ibuprofen was capable of substantiation (McGaw *et al*, 1987).

Clauses 7.4 and 7.5 stated that information, claims or comparisons must be capable of substantiation and that such substantiation must be provided in no more than ten days, on request. The Code did not stipulate that substantiation must be within the text of the article. Clause 7.2 required such information, claims or

comparisons to be accurate, balanced, fair, objective and unambiguous. This was indeed the case in this particular instance. Reckitt Benckiser Healthcare therefore considered that there were no breaches of these clauses to answer with regard to this matter.

Alleged breaches of Clause 4

As discussed above, this was not an advertisement. This was an educational article written by the editors of The Practitioner, and so was not required to carry the non-proprietary name adjacent to the most prominent display of the brand name. In fact, as this was not an advertisement, there was no prominent branding used in the article. There was therefore no breach of Clause 4.6 and Reckitt Benckiser Healthcare reiterated that it did not have final editorial control of the article in its final print format.

Reckitt Benckiser Healthcare submitted that if, when it had provided information to the writers and editors of The Practitioner, it had considered this to be a promotional item, it would have considered the PAGB Professional Code rather than the ABPI Code. The PAGB Professional Code required the inclusion of essential information [prescribing information] but had no requirement for a statement as to where this could be found (Clause 4.6.13 of the PAGB Professional Code referred).

Reckitt Benckiser Healthcare also understood that Clause 4.7 of the Code referred to large journal advertisements where the prescribing information often ran overleaf. The article here was not such an advertisement, but an educational discussion of the comfort cycle and the paediatric asthma algorithm. Reckitt Benckiser Healthcare therefore failed to see how Clause 4.7 applied.

Notwithstanding the above, where there were minor technical differences between the PAGB and ABPI Codes, Reckitt Benckiser Healthcare urged the Authority to exercise restraint in its interpretation of the ABPI Code and subsequent rulings. Ruling a breach of one Code when the same practice was permitted under another could raise complexity and difficulties in administration of the self-regulatory framework of both the ABPI and PAGB, and cause confusion throughout the pharmaceutical industry.

Reckitt Benckiser Healthcare submitted that as this was an educational piece rather than promotional material, the requirement for inclusion of information on adverse event reporting mechanisms did not apply. The argument above also applied: the PAGB Professional Code did not require inclusion of adverse event reporting mechanisms, and Reckitt Benckiser Healthcare would thus not necessarily have communicated this point to the journal editors had they considered the article to be promotional. Where such differences existed between the PAGB Professional Code and the ABPI Code, Reckitt Benckiser Healthcare did not believe that the Authority should rule a breach of Clause 4.10 in the circumstances of this case.

Conclusion

Reckitt Benckiser Healthcare contested that this article was within the scope of the ABPI Code. If the article was considered to be promotional (which Reckitt Benckiser Healthcare disputed), it would encourage GPs to recommend Nurofen for Children to parents, for their later purchase, rather than prescription. This would exempt the article from the ABPI Code and would bring it under the auspices of the PAGB Professional Code. Even if the article fell under the ABPI Code it was educational and not promotional.

If the Authority considered that this educational article came within the scope of the ABPI Code, Reckitt Benckiser Healthcare contested the allegation that it was in breach of Clause 7.2 and Clause 10.1.

Reckitt Benckiser Healthcare noted the technical differences between the PAGB Professional Code and the ABPI Code. Had it considered the article to be promotional, Reckitt Benckiser Healthcare would have borne in mind the PAGB Professional Code and not the ABPI Code when communicating with the editors of The Practitioner, as Nurofen for Children was primarily an OTC product. Reckitt Benckiser Healthcare thus contested the alleged technical breaches of Clause 4.

PANEL RULING

The Panel had first to consider whether the 'Quick Guide' article was covered by the Code. Nurofen for Children was a product which, for childhood fever, the subject of the article in question, could be bought OTC or prescribed; sales data showed that most packs of Nurofen for Children were purchased OTC. The supplementary information to Clause 1.1 of the Code stated that the Code did not apply to the promotion of OTC medicines to members of the health professions when the object of that promotion was to encourage their purchase by the public. Where an advertisement was designed to encourage doctors to prescribe the medicine, then it came within the scope of the Code. An item that promoted for both prescribing and recommending purchase would need to comply with both the ABPI Code and the PAGB Professional Code.

The Panel noted that the 'Quick Guide' article referred to the comfort cycle and how important a parent's perception of therapy was in the management of a child's pain. The article stated that 'Prescribing or recommending a treatment of choice will ultimately benefit both [parent] and child'. The Panel acknowledged that although very few packs of Nurofen for Children were prescribed this was not a relevant factor in deciding whether the ABPI Code applied or not. The article referred to prescribing and thus would encourage some doctors to prescribe Nurofen for Children. The Panel considered that the 'Quick Guide' article fell within the scope of the Code.

The Panel noted that it was acceptable for companies to sponsor material. It had previously been decided, in relation to material aimed at health professionals, that

the content would be subject to the Code if it was promotional in nature or if the company had used the material for a promotional purpose. Even if neither of these applied, the company would be liable if it had been able to influence the content of the material in a manner favourable to its own interests. It was possible for a company to sponsor material which mentioned its own products and not be liable under the Code for its contents, but only if it had been a strictly arm's length arrangement with no input by the company and no use by the company of the material for promotional purposes.

The Panel noted that the article at issue was developed after Reckitt Benckiser Healthcare had contacted the publishers with a view to introducing GPs to the concepts of the comfort cycle and the paediatric asthma algorithm. Reckitt Benckiser Healthcare provided relevant information and was able to comment on the final article. Reckitt Benckiser Healthcare paid for the article to be included in the journal. The Panel thus considered that the production of the article had not been a strictly arm's length arrangement. The Panel further noted that the article featured, as part of the heading to both pages, a logo which incorporated the red/orange/yellow 'target' associated with the Nurofen brand. In this regard, the Panel considered that the article was promotional in nature. The Panel thus considered that the company's involvement in the development of the article, together with the use of brand logos, meant that Reckitt Benckiser Healthcare was responsible for its content under the Code.

The Panel considered that at first glance the article appeared to be an educational discussion about how best to manage childhood fever. This impression was strengthened by the statement that the insert had been 'Supported with an unrestricted educational grant from Reckitt Benckiser'. The 'Quick Guide' had been provided as an insert in The Practitioner and was intended to be kept for future reference. The only treatments discussed in the article, however, were paracetamol and Nurofen for Children. The Panel noted the way in which the material had been developed; Reckitt Benckiser Healthcare was inextricably linked to the production of the insert. Given the company's involvement the Panel considered that the article was in effect promotional material for Nurofen for Children. The Panel considered that it was disguised promotion; the declaration of sponsorship implied that it was an independently written educational piece which was not so. A breach of Clause 10.1 was ruled.

The Panel noted Pfizer Consumer Healthcare's submission that 'Medicines for Children' jointly published by the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists' Group recommended paracetamol as first line in fever. The title of the article was 'Best practice in childhood fever – the comfort cycle' but the only treatments referred to were Nurofen for Children and paracetamol. It was stated that Nurofen for Children had emerged as a treatment of choice with parents. A diagram of 'The comfort cycle' featured 'Nurofen for Children' in the middle of a cycle of arrows; one arrow was labelled 'Becomes parent's treatment of choice'. The Panel considered that the diagram implied that Nurofen for Children became the treatment of choice for parents. The Panel further considered that as the article was principally about Nurofen for Children, the title 'Best practice in childhood fever – the comfort cycle' implied that Nurofen for Children had been clinically shown to represent best practice which was not so. The Panel considered that the overall message of the article was misleading as alleged. A breach of Clause 7.2 was ruled.

Reckitt Benckiser Healthcare had not provided any information about the Dover Study other than that mentioned in its response. The Panel noted that the diagram depicting 'The comfort cycle' was referenced to the Dover study which compared the single dose efficacy and multiple dose tolerability of paracetamol 15mg/kg and Nurofen for Children 10mg/kg in paediatric fever. According to Pfizer Consumer Healthcare there was no difference in terms of efficacy between the two medicines as measured by reduction in temperature. However the diagram depicted a four stage cycle of 'Reduces anxiety in children', 'Tackles fever', 'Becomes parent's treatment of choice' and 'Reduces anxiety in parent' and so on. 'Nurofen for Children' appeared in the centre of the cycle. The Panel considered that the diagram implied that because it tackled fever, Nurofen for Children became the parent's choice. A description of the study in the text stated that when compared with paracetamol suspension, parents rated Nurofen for Children as more efficacious. According to Pfizer Consumer Healthcare there was, however, no difference between the two medicines with regard to the primary clinical outcome of reduction in temperature/fever. The Panel also noted that the concept of the comfort cycle was a 'working hypothesis'. The Dover study had not measured anxiety in either the parents or the children. The Panel thus considered the article was not a fair reflection of the results of the Dover study and was thus misleading. A breach of Clause 7.2 was ruled.

Eccleston *et al* was cited in support of the statement 'Anxiety is a measure of pain…'. Eccleston *et al* reported on adolescent chronic pain, not childhood fever, the subject of the insert in question. The patients in Eccleston *et al* ranged from 11 to 17 years (mean 14.45 years) and the study examined emotional distress in adolescent chronic pain patients and their parents and the relationship between the two and adolescent coping. The Panel questioned the relevance of the study in the context of a piece about childhood fever which required only short-term treatment. There was no data to show that the relationship between anxiety and pain in adolescents with chronic pain was the same as in infants with acute pain or fever. Nurofen for Children was indicated for children from 3 months to 12 years of age. The Panel considered that citing Eccleston *et al* was misleading as alleged. A breach of Clause 7.2 was ruled.

The Panel noted that the y axis of the bar chart which depicted the percentage of parents who would use either Nurofen for Children or paracetamol again (as

reported in the Dover study) started at 82%. The resultant height of the bars had the effect of making it look as if twice as many parents preferred Nurofen for Children as preferred paracetamol which was not so. The Panel considered that the use of the suppressed zero was misleading. A breach of Clause 7.8 was ruled.

The Panel noted that on the available information the Dover Study had not measured analgesia. Reckitt Benckiser Healthcare submitted that it was widely accepted that ibuprofen was at least as good as paracetamol and that the superiority of ibuprofen was capable of substantiation citing McGaw *et al* in this regard. The Panel noted that the claim 'At least as good as paracetamol' was not referenced as such nor did the Code require it to be referenced. The Code did not require substantiation to be provided in the article itself but the claim must be capable of substantiation. The Panel considered that readers might assume that the Dover study measured pain/analgesia given that the article stated the data was presented at the International Symposium on Paediatric Pain.

McGaw *et al* compared ibuprofen with acetaminophen in the relief of postextraction dental pain in children aged 8 - 16 with the majority of the children in the 14 - 16 age range. The authors commented that postoperative pain associated with dental surgery was associated with pain and oedema and that ibuprofen's superior analgesic efficacy might be due in part to its anti-inflammatory properties which were not shared by acetaminophen. The Panel considered that in the circumstances the reference to 'excellent analgesia (at least as good as paracetamol)' was misleading and a breach of Clause 7.2 was ruled.

The Panel considered that the most prominent display of the brand name was in the highlighted box labelled 'The comfort cycle' in the bottom left hand corner of the front page of the article. The brand name was not accompanied by the non-proprietary name. A breach of Clause 4.6 was ruled.

The Panel noted that the 'Quick Guide' was provided as a bound-in insert in The Practitioner' it was thus a two page advertisement where the prescribing information appeared overleaf. There was, however, no statement as to where the prescribing information could be found. A breach of Clause 4.7 was ruled.

The Panel noted that Clause 4.10 required that all promotional material, other than promotional aids, must include prominent information about adverse event reporting mechanisms. No such information was given in the 'Quick Guide' at issue. A breach of Clause 4.10 was ruled.

Complaint received 19 January 2007

Case Completed 4 April 2007