CASE AUTH/3760/4/23

COMPLAINANT v GSK

Misleading presentation of data in a Press Release

CASE SUMMARY

This case was in relation to claims about a COVID-19 vaccine made in a press release.

The outcome under the 2021 Code was:

Breach of Clause 6.1	**Making a misleading claim**

No Breach of Clause 5.1	**Requirement to maintain high standards at all times**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

A contactable member of the public complained about a press release which appeared on GSK's corporate website.

COMPLAINT

The complainant stated that they had previously complained about press releases from two different companies, which made misleading claims for the efficacy of their covid vaccines based only on the presentation of RRR [relative risk reduction] data without any mention of ARR [absolute risk reduction] data. The Panel upheld their complaints in this regard. The complainant provided links to Case AUTH/3518/5/21 and Case AUTH/3519/5/21.

The complainant stated that unfortunately, it had recently been brought to their attention that GSK issued a press release from its London HQ [headquarters] last November, announcing the approval by the EMA of its own, Covid vaccine, which made a similar misleading claim. There was once again no indication that this was RRR data only, and no discussion of ARR at all: 'The results showed a 64.7% efficacy against symptomatic SARS-CoV-2 infection in adults, regardless of their SARS-CoV-2 infection status prior to vaccination, and 75.1% efficacy in participants previously infected with SARS-CoV-2'.

The complainant provided a link to the GSK press release on GSK's corporate website.

The complainant cited Clause 1.2 of the ABPI Code of Practice which stated that:

> 'Information or promotional material about medicines which is placed on the internet outside the UK will be regarded as coming within the scope of the Code, if it was placed there by:
> • a UK company/with a UK company's authority.'

The complainant assumed as GSK was a UK company and as this press release was flagged as being issued from London, that it fell well within the scope of the UK Code.

As there had been two previous identical cases of this breach published by the PMCPA fairly recently, they were surprised that another prominent member company should be committing exactly the same breach again in such short order. It would appear that member companies either take very little interest in PMCPA decisions or had little incentive to learn from them. In the circumstances, in addition to a breach of Clause 6.1, they thought that a breach of Clause 5.1 had also taken place here.

The complainant stated that they would also like to take this opportunity to point out that this misleading information had already been posted for 6 months now and would no doubt continue to be posted and be misleading for the many months that the Panel would take to conclude its deliberations. In view of the fact that the Panel had already considered identical cases on two occasions recently and found them in breach they would also ask the Panel to consider instructing GSK to remove this press release from their website while this case was dealt with.

When writing to GSK, the Authority asked it to consider the requirements of Clauses 6.1 and 5.1 of the 2021 Code.

GSK RESPONSE

The response from GSK is reproduced below:

'Following the receipt of your letter, out of an abundance of caution and with respect to the complainant's request, we removed the material from the GSK corporate website. Following the outcome of your decision, we may reinstate the release with any necessary corrections as a matter of company record.

Background outlining Sanofi and GSK relationship and product

Sanofi and GSK together developed an adjuvanted vaccine for COVID-19, VidPrevtyn Beta, to help address the COVID 19 pandemic. VidPrevtyn Beta combines technology from both companies: S-protein COVID-19 antigen (Sanofi) and, pandemic adjuvant (GSK). Sanofi Pasteur is the EU and UK marketing authorisation holder for Vidprevtyn Beta. The European Commission (EC) granted a marketing authorisation for Vidprevtyn Beta on 10 November 2022; and it was authorised by the UK Medicines and Healthcare products Regulatory Agency (MHRA) on the 20th of December 2022.

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and it was authorised by the UK Medicines and Healthcare products Regulatory Agency (MHRA) on the 20th of December 2022.

Whilst the terms of the Sanofi-GSK agreement are confidential, GSK can confirm that, in accordance with the terms of the collaboration agreement, that joint press releases are reviewed and agreed between parties. However, press releases then undergo separate individual approvals in line with each company's own standard operating procedures prior to being issued independently by each company. It is therefore possible that the final press release issued by each company may differ. It could also be the case, that one of the parties may choose not to issue a press release. In terms of the press release which is the subject of the complaint, GSK can confirm that the procedure outlined was followed.

Background to GSK's press release – purpose and intended audience

The GSK global press release was a stock-exchange announcement to global business/financial media regarding the European Commission's approval of Vidprevtyn Beta, a significant regulatory milestone and of interest to investors and the business community. The press release had a specific purpose and was intended for a specific audience and both factors were made clear at the top of each page of the press release in large font size. The use of orange-coloured font served to further emphasize the fact this was a stock-exchange announcement:

'Stock-exchange announcement
For Media and investors only'

The press release was distributed to the intended audience using GSK's business/financial media standard distribution list. It was also published on the media section of GSK's global website, which can only be accessed through the site navigation menu under 'Media' then 'Press releases.' It was not visible on the public-facing landing page of the site, and neither was it linked to via social media.

The press release announced the approval of Vidprevtyn Beta which was made on the basis of two immunobridging studies and which was the focus of the press release. On page two of the press release information about those immunobridging studies and one efficacy study were included to provide background information so that the business analysts would be able to understand the relative efficacy compared to other Covid vaccines and what that would mean for impact on share price and the like. As discussed below, vaccine efficacy is described in this way for all routine communications across business, healthcare and the public. It is technically a relative risk reduction, but the addition of absolute risk levels is not required to ensure readers are not misled as these are results from trials of preventive vaccines, which are fundamentally different to standard efficacy trials and the way efficacy results are calculated and reported are necessarily different.

The complaint

Previous Pfizer & AstraZeneca PMCPA cases

GSK is aware of the two previous cases raised by the complainant: CASE/AUTH/3518/5/21 Member of the Public v AstraZeneca (published October 2022) and CASE/AUTH/3519/5/21 Member of the Public v Pfizer (published June 2022). The same complainant was made aware

of the GSK press release and asserts that this case is identical and therefore should be found in breach of 6.1 and also that high standards have not been maintained as GSK '*take very little interest in PMCPA decisions or have little incentive to learn from them and* so deserves an additional breach of 5.1. GSK refutes both allegations.

As the Panel are aware, each complaint is considered on a case-by-case basis determined, *inter alia,* by the materials or activities themselves, the intended audience, the arguments made and evidence presented by both the complainant and respondent. Importantly, neither Pfizer or AstraZeneca appealed the breaches of 7.2 (2019), and thus did not take full advantage of the self-regulatory process to argue their case at the Appeal Board. As such, these cases do not necessarily set a case precedent but provide scope to present different arguments for the Panel to consider.

Furthermore, whilst there are similarities between this case and the two previous cases raised by the complainant - they all relate to COVID-19 vaccine press releases and the use of Relative Risk Reduction (RRR) - there are also differences in terms of the purpose and content of the press releases and the audiences to whom they were distributed.

As seen in the AZ and Pfizer press releases and the arguments before the Panel in those cases, relative risk reduction (RRR) is the standard way for vaccine efficacy to be presented and has been for decades. GSK do not intend to repeat the epidemiological arguments put forward in those cases but hope to provide the Panel with the rationale that the presentation of RRR without absolute levels is neither misleading nor in breach of Clause 6.1 in this case.

Clause 6.1

In our response, you have asked us to consider Clause 6.1. Clause 6.1 states that "*Information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication, by distortion, exaggeration, or undue emphasis. Material must be sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine."*

It is the main clause to ensure that material does not mislead the audience and the supplementary information provides some direction for companies by listing areas where particular care should be taken to help them ensure they remain compliant with the Code. It is in this supplementary information (not the clause itself) where the reference to absolute risk and relative risk sits:

'Referring only to relative risk, especially with regard to risk reduction, can make a medicine appear more effective than it actually is. In order to assess the clinical impact of an outcome, the reader also needs to know the absolute risk involved. In that regard, relative risk should never be referred to without also referring to the absolute risk. Absolute risk can be referred to in isolation.'

The wording of the supplementary information does not state that providing relative risk without absolute risk is always contrary to the Code. The word used is 'should' not 'must' when it says '*relative risk should never be referred to without also referring to the absolute risk '*. Indeed, the Panel ruled no breach in 2936/9/17 when no absolute data were included in a claim of ''*combination NRT is 43% more effective than patch alone"* noting that there '*was no mention of*

relative risk as such' but that it was '*a comparison of the two* [treatments]'. The Odds Ratio of 1.43 was provided but does not throw any light on the absolute efficacy levels of either combination therapy or the patch alone. The claim '*43% more effective*' is exactly the same principle as the vaccine efficacy claim under consideration here - where the vaccine was *64.7% more effective* than placebo at reducing symptomatic infection, so, the vaccinated group experienced 64.7% fewer symptomatic Covid cases than they would have if they had not been vaccinated. Just like the NRT case above, the press release made no mention of relative risk as such but was a comparison of two treatment arms – placebo and vaccine. "*The results showed a 64.7% efficacy against symptomatic SARS-CoV-2 infection in adults, regardless of their SARS-CoV-2 infection status prior to vaccination, and 75.1% efficacy in participants previously infected with SARS-CoV-2.*"

Vaccine efficacy

RRR is the value most considered when discussing vaccine efficacy as it evaluates the risk of infection irrespective of the transmission setting and is the value most used when discussing vaccine efficacy. Vaccine efficacy has been reported this way for decades. It is the language used by the Joint Committee on Vaccination and Immunisation (JCVI) in their meeting minutes, and the Green Book (the Government publication on immunisation for health professionals) also refers to vaccine efficacy as an RRR without inclusion of absolute risk reduction (ARR) as it is the most meaningful way to report vaccine efficacy results and reduces the risk misunderstanding and confusion that reporting absolute rates can introduce. It is found in the eLearning materials from the Royal College of General Practitioners and it is the language used by clinicians, in routine practice and also by the financial and business analysts. It is therefore the way least likely to mislead readers which is what Clause 6.1 is designed to address.

Absolute risk reductions are simply an arithmetical deduction of event rates between two populations. In preventive vaccine trials it is very dependent on the background rate of that event, as not all patients will get infected. In contrast, when we are considering efficacy trials to show the effect of a treatment all the trial participants in both arms have the condition being treated so it makes sense to include the absolute levels to ensure that efficacy is not exaggerated by only using relative risk. Reporting vaccine efficacy in the way we do (which is technically a relative risk reduction versus placebo) allows us to compare the effects only in the proportion of the population of interest – the proportion of those who would have caught the disease/become severely ill/died if they hadn't been given the vaccine. It focuses the comparison in a way that we automatically do in treatment efficacy trials by only recruiting those with the condition, but we can't do that in trials for preventive measures of infectious diseases as we don't know who will get the infection.

Example 1: RRR can mislead without ARR in efficacy trials

If we have a product claiming a 75% RRR in mortality in patients with COPD, it is clearly important to understand what the absolute rates of mortality are as it could be that the product reduces a death rate of 20% down to 5% or a death rate of 2% down to 0.5%. Both of those event rates would enable a relative risk reduction claim of 75%, but clearly one scenario has much more clinical impact than the other, and it is for scenarios such as this that the absolute levels are a key piece of contextualising information to ensure the reader is not misled.

Example 2: RRR does not mislead without ARR in vaccine infection prevention trials

However, if we take 20,000 people in the vaccine arm of a study and 20,000 in the placebo arm and 200 people in the placebo arm got sick, and 0 in the vaccine arm we would intuitively understand that to be a vaccine efficacy of 100%. The vaccine stopped all potential infections. And this is how it is usually reported “Vaccine efficacy was 100%”.

However, if we used the same results and reported the Absolute Risk Reduction it would be 200/20,000 = 1% minus 0/20,000 = 0. Thus, the Absolute Risk Reduction would be 1 minus 0 = 1% which would to most readers make it sound not very effective at all and does not add anything of clinical relevance about vaccine efficacy to the reader.

The supplementary information to Clause 6.1 does not form part of the clause but is included as useful considerations for companies to take into account when approving materials in an effort to help them comply with the Code. In this statistical minefield, it is important to be concerned to ensure readers are not misled rather than using the supplementary information wording as if it were law. It is advisory, but even though it states that ‘*Absolute risk can be referred to in isolation,’* only providing ARR could still be misleading in the unusual scenario of preventive vaccine efficacy as evidenced by the example 2 above. Hence it is important to return to the clause itself and determine the correct course of action needed to ensure compliance for the specific material under review.

Why using RRR is the norm in communicating vaccine efficacy

If we take 20,000 patients in vaccine arm of the study and 20,000 in the placebo and 200 people in the placebo arm got sick, and 0 in the vaccine arm we would intuitively understand that to be a vaccine efficacy of 100%. The vaccine stopped all potential infections. And this is how it is usually reported “Vaccine efficacy was 100%”. However, if we used the same results and reported the Absolute Risk Reduction it would be 200/20,000 = 1% minus 0/20,000 = 0. Thus, the Absolute Risk Reduction would be 1 minus 0 = 1% which would to most readers make it sound not very effective at all and does not add anything of clinical relevance about vaccine efficacy to the reader.

Using the relative risk reduction allows us to convey that the vaccine will reduce the risk of infection by that reported percentage irrespective of the transmission setting. It is a much more relevant and meaningful statistic to both health professionals and the media and is much simpler to understand and explain than the ARR and therefore less likely to be misinterpreted. The supplementary information to clause 6.1 contains a statement that ‘*Absolute risk can be referred to in isolation’*; this example illustrates why such an approach would likely be considered misleading when discussing vaccine efficacy with an audience who are much more familiar with the use of RRR. However, the language in the SI is not definitive - it provides direction to companies about ‘*where particular care should be taken’* and that ‘*relative risk should never be referred to without also referring to absolute risk’* to ensure compliance with clause 6.1 which is definitive that materials ‘*must not mislead’*.

The pandemic introduced a level of misinformation and conspiracy theories on social media that were unparalleled and risked derailing the efforts to bring the pandemic under control. One of the main targets for this was (and remains) anti-vaccine misinformation. When a Lancet paper included ARR rates, cynics seized on them to show how companies and governments were lying about vaccine efficacy and it fuelled vaccine hesitancy as it was difficult to explain the underlying statistics quickly and simply. Thus, the addition of absolute risk does not always provide greater clarity, but can, as in this example, fuel misunderstanding.

A helpful commentary in Gut advocates and explains why relative risk should be used for preventive intervention when talking to the public.

Complying with the letter and spirit of the Code

GSK take the Code seriously and believe that this press release clearly targeted to the financial and business community did not mislead readers by not including ARR along with RRR for vaccine efficacy, but used the standard language recognised across business, government and healthcare to provide relevant information on vaccine efficacy that would be easy for the audience to understand and not mislead.

As such, GSK believes they supplied information that was accurate, balanced, fair, objective and unambiguous and based on an up-to-date evaluation of all the evidence and reflected that evidence clearly. It did not mislead either directly or by implication, by distortion, exaggeration, or undue emphasis and was sufficiently complete to enable recipients to form their own opinion of the therapeutic value of the medicine in accordance with Clause 6.1. As such GSK deny a breach of Clause 6.1

Clause 5.1

In our response you have asked us to consider Clause 5.1.

Clause 5.1 requires companies to maintain high standards at all times. GSK takes the requirements of this Clause very seriously. The complainant alleges that GSK "*either take very little interest in PMCPA decisions or have little incentive to learn from them*". GSK refute this allegation and take the opportunity to reassure the Authority that GSK continually monitors PMCPA Code cases, subscribes to publications that discuss recent cases, has regular meetings with both internal and external experts to discuss the Code, its interpretation and rulings and try to uphold the principles and practice of compliant activity.

As outlined above, GSK believe that the standard practice of using RRRs to report Vaccine Efficacy is the way least likely to mislead readers - it has been used for decades because it is the most meaningful statistic in preventive interventions such as vaccination. The fact that it is technically a relative risk reduction does not automatically mean it breaches Clause 6.1 as the Clause is about ensuring information does not mislead.

GSK has a specific framework for the review, approval and issuing of global press releases where materials are intended for global media and/or financial analysts. The Standard Operating Procedure outlines the process required to obtain approval for such materials. Adherence to the Standard Operating Procedure ensures that all global media materials comply with applicable laws and regulations and conform to the most stringent regulatory authority or Code of Practice requirements.

GSK can confirm that approval process for this press release involved senior GSK stakeholders from legal, regulatory and R&D and an ABPI Signatory.

Conclusion

GSK takes its obligations under the ABPI Code of Practice seriously and is committed to following both the letter and spirit of the Code and ask the Panel to consider this case on its own merits.'

PANEL RULING

The complaint related to a global press release issued by GSK regarding its (and Sanofi's) Covid-19 vaccine VidPrevtyn Beta.

GSK submitted the global press release at issue was a stock-exchange announcement to global business/financial media distributed using GSK's business/financial media standard distribution list and also published on the media section of GSK's global website, which could only be accessed through the site navigation menu under 'Media' then 'Press releases'; according to GSK, it was not visible on the public-facing landing page of the site, and was not linked to via social media.

The Panel noted the version provided by the complainant was a webpage copy titled 'Sanofi and GSK's next-generation COVID-19 booster vaccine VidPrevtyn Beta approved by the European Commission' beneath which was listed 'Issued: London, UK' and 'For media and investors only'.

The version provided by GSK was a standalone document which contained the same title but was headed 'Stock-exchange announcement' in orange text with 'For media and investors only' in black text immediately below. In this version both statements, appeared above the title.

The Panel noted that the supplementary information to Clause 26.2 Financial information required that business press releases should only be aimed at the intended financial and investment audience, identify the business importance of the information and were also required to be non-promotional, accurate, presented in a factual and balanced way and not misleading, taking into account the information needs of the target audience.

The complainant's allegation concerned content within the press release which was considered to be misleading. The complainant alleged 'The results showed a 64.7% efficacy against symptomatic SARS-CoV-2 infection in adults, regardless of their SARS-CoV-2 infection status prior to vaccination, and 75.1% efficacy in participants previously infected with SARS-CoV-2', was misleading as relative risk reduction data was presented without referring to absolute risk.

The Panel noted the requirements of Clause 6.1 and its supplementary information which highlighted relative risk as an area where particular care was needed.

The Panel considered the claim in the context of the press release as a whole. The press release headline announced the European Commission's approval of VidPrevtyn Beta, followed by three bullet points summarising the key messages to be conveyed, that the vaccine was a next generation adjuvanted COVID-19 booster vaccine, had shown a strong immune response against all tested variants of concern and was ready to be supplied for seasonal COVID-19 vaccination campaigns in Europe.

The indication, and brief summaries of three registration studies, two separate immunogenicity and safety studies and a Phase 3 Stage 2 efficacy and safety study were included within the main body of content. GSK submitted that this information was included to provide background

information so that business analysts would be able to understand the relative efficacy compared to other Covid vaccines and how this might impact the share price and the like.

The Panel noted GSK's submission that communications about Covid-19 issued by the media, medical organisations and government bodies at the relevant time expressed vaccine efficacy in similar terms to those used within the press release to ensure information was easy for the audience to understand and not misleading. GSK submitted that RRR was the value most used and considered when discussing vaccine efficacy as it evaluated the risk of infection irrespective of the transmission setting.

Whilst noting GlaxoSmithKline's rationale for its use of relative risk reduction for vaccinations and that scientific opinion was divided on how to report vaccine efficacy, the Panel considered that the supplementary information to Clause 6.1, 'reference to absolute and relative risk', and compliance with it, should be interpreted in the light of its associated clause, which required that materials etc should not be, amongst other things, misleading and material must be sufficiently complete to enable the recipient to form their own opinion of the therapeutic values of the medicine.

The Panel considered the statement 'The results showed a 64.7% efficacy against symptomatic SARS-CoV-2 infection in adults, regardless of their SARS-CoV-2 infection status prior to vaccination, and 75.1% efficacy in participants previously infected with SARS-CoV-2' made no reference to the comparative arm. The Panel considered that the inclusion of additional information such as the number of subjects in each arm would have helped readers to interpret the study results.

In the Panel's view, noting the omission of absolute risk data, and without any further trial detail or explanation to contextualise the relative risk reduction rates cited, some readers might have assumed that the efficacy rate was, in effect, an absolute rate and that was not so. The Panel therefore ruled a **breach of Clause 6.1**.

With regard to the allegation that GSK had failed to learn from previous cases involving press releases about Covid-19 vaccines and thus had failed to maintain high standards, the Panel considered there were differences between the previous cases and the current one.

The Panel noted GSK's submission that it had in place a specific framework for the review, approval and issue of global press releases where materials were intended for global media and/or financial analysts and that this had been followed in relation to the press release at issue.

In the particular circumstances of this case, the Panel did not consider the complainant had established that GSK took 'little interest in PMCPA decisions' or had 'little incentive to learn from them' and based on the narrow allegations, ruled **no breach of Clause 5.1**.

Complaint received **4 April 2023**

Case completed **5 June 2024**