CASE AUTH/3781/6/23

COMPLAINANT v GSK

Alleged misleading claim about Trelegy on GSK's website

CASE SUMMARY

This case was in relation to the promotion of Trelegy on a GSK website.

The outcome under the 2021 Code was:

Breach of Clause 6.1	**Making a misleading claim**
Breach of Clause 6.2	**Making an unsubstantiated claim**
Breach of Clause 5.1	**Failing to maintain high standards**

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce the confidence in, the pharmaceutical industry**

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

FULL CASE REPORT

A complaint was received from an anonymous, contactable complainant who described themselves as a health professional, about GSK.

COMPLAINT

The complaint wording is reproduced below with some typographical errors corrected:

> "A claim misled audience into clinical data outcomes with reference to Trelegy. The misleading claim was housed on [website link provided]. At the origin of the webpage, the following misleading claim was listed: Trelegy demonstrated greater annualised moderate/severe exacerbation reduction vs. another COPD single-inhaler triple therapy1. The reference 1 was to a meta-analysis reference where the meta-analysis had failed to show statistical significance of Trelegy versus one other single inhaler triple therapy for exacerbation reduction and achieved significance vs another single inhaler triple therapy for exacerbation reduction. As the claim in question referenced another single therapy inhaler the claim should have been explicitly clear about which inhaler this was in reference to considering there were 2 separate single inhaler triple therapies (Trixeo and Trimbow). The claim was deliberately misleading without reference to the exact single inhaler triple therapy the exacerbation reduction had occurred vs Trelegy and did not meet the parameters of the code. GSK had breached clauses 6.1, 6.2, 5.1, 2."

When writing to GSK, the Authority asked it to consider the requirements of Clauses 2, 5.1, 6.1 and 6.2 of the Code as cited by the complainant.

GSK's RESPONSE

The response from GSK is reproduced below with certain text related to specific individuals removed:

> "The complainant states that the claim in question, which was on the promotional webpage [website link provided] misled the audience because, in a comparison of Trelegy vs another COPD (Chronic Obstructive Pulmonary Disease) single-inhaler triple therapy (SITT), the comparator single inhaler therapy was not explicitly named. The complainant has suggested breaches of Clauses 6.1, 6.2, 5.1 and 2 of the 2021 ABPI Code of Practice.
>
> GSK is strongly committed to following both the letter and the spirit of the ABPI code of practice and all other relevant regulations. We have reviewed the claim and related materials as well as conducted an urgent internal investigation. Regrettably, GSK agrees that the claim is misleading and acknowledges breaches of clauses 6.1, 6.2 and 5.1 for the reasons set out below. GSK does however deny breaching clause 2, for the reasons also stated below.
>
> **Background**
>
> The webpage referred to is part of a more extensive promotional website called GSK.pro which contains promotional information about all GSK products currently marketed in the UK. Within the website, there is a section dedicated entirely to the product Trelegy. The webpage in question is one of the sections within this.
>
> The claim at issue refers to the results of a network meta-analysis (NMA) conducted by GSK looking at, among other things, a comparison of the three currently available SITTs in the UK – Trelegy, Trimbow (Chiesi) and Trixeo (AstraZeneca). The NMA was conducted to provide additional information to HCPs [health professionals] in the absence of head-to-head trials being available. Several different clinically meaningful endpoints were analysed of which one was the annualised rate of exacerbation reduction. Trelegy was found to have a statistically significant difference against Trixeo but not to Trimbow.
>
> The claim states that *"Trelegy demonstrated greater annualised moderate/severe exacerbation reduction vs another COPD single-inhaler triple therapy."* A visual representation of the data for Trelegy against both Trixeo and Trimbow was presented below the claim, showing the statistically significant data versus Trixeo and the numerical (but not statistically significant) difference versus Trimbow, along with a video featuring one of the main authors, an eminent UK Professor in Respiratory medicine, describing the NMA, it's methodology and outcomes.
>
> The claim at issue is similar to a claim in material that was the subject of Case AUTH/3719/12/22 raised by Chiesi. The PMCPA has not yet ruled on Case AUTH/3719/12/22, however, in our response to the PMCPA in that case, GSK

acknowledged that: *"the claim should have been worded more clearly as improvement is significant for comparison to Trixeo but the improvement vs Trimbow is not significant."* The claim was subsequently changed, substituting "...vs. other..." with "vs. another..." and presenting related data on the same page in more detail, but not immediately adjacent to the claim.

Having re-assessed the claim in light of the current complaint, we acknowledge that the claim as presented is still not to the standard that we would expect it to be. GSK agree that it should have been made explicitly clear that Trelegy only had statistically significant annualised exacerbation reduction in COPD patients versus Trixeo by mentioning it specifically. Indeed, whilst the changes to this claim were being considered following our response to Case AUTH/3719/12/22, [senior medical employee] consulted with [another senior medical employee], an experienced signatory, who gave a view that the claim should be explicit that the difference was only significant versus Trixeo. GSK are disappointed that this advice was not followed.

Immediate and follow up actions taken by GSK in Case AUTH/3781/6/23

The complaint was received late afternoon on Wed 21st June. On Thursday 22nd June, a senior team review involving [senior medical and commercial employees] identified the need to take down the website and halt the use of all material containing the specific claim, to prevent any further exposure of HCPs to the claim in question. Instructions to achieve this were issued on the evening of Thursday 22nd June and action initiated Friday 23rd June. Confirmation of the website being disabled was received on Monday 26th June, with delay only due to the intervening weekend. Confirmation of the cessation of use of other material was also received on 26th June.

GSK immediately recognised the seriousness of this complaint, given the potential for a breach of undertaking and the similarity with the claim at issue in Case/AUTH/3719/12/22 (notwithstanding the fact this case has yet to be ruled upon). At 0930 on Friday 23rd June, an urgent meeting was held between [senior leader and senior medical, commercial, compliance and legal employees]. In this meeting, all agreed that the claim at issue was not appropriate and should not have been used. It was also decided that an investigation should be conducted to determine why the claim was used as it stood. It was decided that the outcome of the investigation should be brought back to the same senior leaders to agree corrective and preventive actions and to then decide on the details for the response to the PMCPA.

At 0930 on the 29th of June [employees referred to above] met again to receive an update. In this meeting it was reported that an initial review suggested we have all relevant systems and processes in place to control promotional materials. The investigation also reported that [a senior medical employee] had previously advised the Trelegy team to be clear that the comparison was versus Trixeo, and that despite this direction, the team had together, made a decision to take a different course of action, amending the claim from *"...vs other single inhaler triple therapy..."* to *"...vs another single inhaler triple therapy..."* with business rules in place alongside this core claim to ensure that the data which qualified the claim was shown immediately below the claim. It was also reported that at the time decisions were being made about the claim, there were few internal GSK permanent employee final medical signatories in the Trelegy team. Following receipt of this report, the decision was made to acknowledge the breach

of the Code with regard to the claim itself, but to explore if the systems and processes we have in place are sufficient to suggest that we have not breached clause 2 of the Code.

Subsequent GSK Actions

Following the review and decisions by the senior team on the morning of the 29th of June, GSK received a further complaint at 1224hrs the same day about another promotional claim on the Trelegy promotional website (Case AUTH/3785/6/23). This complaint was about a different claim, and a separate response will be provided, however when this complaint was received an urgent meeting was convened again at 1630 hrs with [senior leader and senior medical, commercial, compliance and legal employees], whereby the claim at issue in the new complaint was immediately acknowledged as being in breach of some of the clauses as alleged, and the seriousness of this alongside Case AUTH/3781/6/23 was immediately realised. Whilst both are different complaints with specific nuances in operational detail, it is important to note that it was the same team, working on the same product, that were involved, and from this point on, GSK managed both cases together (rather than maintaining an artificial separation by nature of PMCPA case number). Whilst there are some differences in how key decisions were made in the activity that resulted in each complaint, the overarching root cause and remediation requirements are the same, and so we will cross reference to actions taken in response to Case/AUTH/3785 in this response.

Given the gravity of the two cases taken together, a decision was made to immediately suspend **all** promotional pages on the GSKPro HCP Trelegy promotional website, regardless of whether it contained the claims at issue or not, and this was actioned and confirmed by the close of the same day, preventing any further potential for HCPs to be exposed to the claims at issue, and to allow GSK time to look for any further potential, but as yet unidentified, issues.

Acknowledging the seriousness of the wider issue in hand, a decision was made to form what GSK call an Incident Management Team, to manage the further investigation, corrective actions and preventive measures in both cases and ensure senior management leadership and oversight. The IMT were convened at 0900 on Friday 30th June. The IMT consisted of [senior leader and senior medical, commercial, compliance and legal employees]. The IMT further required the withdrawal of all promotional material, beyond the GSKPro website, containing the additional claims at issue and appointed [a senior medical employee] as an independent lead for the IMT investigation and actions. The IMT asked [this senior medical employee] to form a team to ensure the following:

1. Conduct an assessment of any remaining Trelegy materials that had not yet been identified as being at issue, to reassure the IMT that this was an isolated issue and that there were no further claims to cause concern.
2. Conduct a thorough root cause analysis and identify Corrective and Preventive Actions.
3. Manage the responses to the PMCPA.
4. Consider if any action was required to confirm that this issue does not extend into teams outside of the Trelegy team.

5. Consider how to approach business continuity and provide signatory resource to allow some business continuity without relying on the signatories who approved the claims at issue, until investigation and remediation is in place.

On Monday, 3rd July, the following workstreams were initiated and briefed:

1. Management of Immediate Response:

    - A senior GSK employed signatory from outside of the business unit and who was not involved in the complaints, to review remaining materials in circulation and confirm no additional risk / misleading claims were in circulation

2. Root Cause Analysis: Review of the Internal Control Framework (ICF):

    - Thorough review of the ICF that governs promotional materials
    - Assess the effectiveness of the ICF across the business:
        - confirm that training and validation of signatories had been conducted as required in the ICF
        - review core promotional campaign for each priority product in all other business units (for speed, this was limited to a review of claims, not a review of technical aspects of code compliance or materials execution), specifically to identify any similarly misleading or un-substantiable claims and in their absence, reassure GSK that the issue was limited to the Trelegy team.

3. Root Cause Analysis: Deep Dive on Judgement and Decision Making in the Trelegy Team

    - Understand Decision making and judgement – conducting a deep dive on timelines for decision making and judgement in both cases: understand who made what decisions, who else was involved, identify any disagreement and how it was dealt with and understand any escalations made / not made.

The out-put of these workstreams is detailed below. However, it is of note that a further complaint, Case AUTH/3792/7/23, was received by GSK on the 5th July at 1032hrs concerning a GSK Trelegy payor / commissioner promotional website (Value.gsk) and at 1430hrs, the review of remaining Trelegy promotional materials flagged a further use of a misleading claim *"...vs an ICS/LABA..."* that was inappropriate and should not be in use. Whilst Case/AUTH/3792/7/23 was not concerning similarly misleading or un-substantiated claims, taken together with the finding of further claims of concern in remaining materials, [a senior commercial employee] made an immediate decision to require the suspension of the value.gsk website (this was actioned and confirmed by the close of the same day) and to discuss next steps with the [senior leader]. By 0930 on Thursday 6th July, the [senior commercial employee] and [senior leader] had concluded that GSK no longer had confidence in the full set of respiratory promotional materials, and so requested the recall of **all** active materials utilised throughout the wider respiratory team, recognising the significant business impact of such a severe action, but also recognising the need to ensure control of our promotional compliance with the Code. Whilst Case AUTH/3792/7/23 will be the subject of a separate response, it is

important to note that all further actions taken by GSK take account of the broader impact of that case, case AUTH/3781/6/23 and case AUTH/3785/6/23.

On Friday 7th July, the findings of the work-streams were reported back and these were then discussed at a further meeting of the IMT on Monday 10th July, to agree further remediation activities and how to respond to the PMCPA. The findings of the root cause analysis and the agreed remediation activities are detailed below.

GSK root cause analysis – Framework of Controls

As mentioned above, GSK has worked urgently and diligently to thoroughly review all relevant existing procedures and controls that are in place: the ICF. GSK believes the ICF to be robust and industry leading in its comprehensive approach. We also attach the GSK UK copy approval SOP (a part of the ICF) which all signatories must follow. The copy approval SOP has been updated several times and incorporates findings of breaches from previous complaints where possible. GSK do recognise that Copy Approval Management Monitoring (CA MM) was reduced in the time leading up to certification and release of the materials at issue. The decisions relating to the reduced CA MM, as discussed in [the ICF], were made on the basis of no findings for some time, and so GSK believe that at the time, this was a reasonable use of resource. GSK acknowledge that CA MM may have caught the claims at issue in this complaint, however we also recognise that they may not (only a percentage of work is ever reviewed in any management monitoring). GSK also recognise that MM is not a requirement of the Code, but a step over and above usual requirements, and so do not believe that the temporary reduction in CA MM detracts from the comprehensive nature of our ICF nor constitutes a breach of the Code.

GSK was also reassured to find that our review of leading campaign materials from other business units, whilst highlighting some areas for improvement, did not identify any claims of a similarly misleading or un-substantiable nature. We were also reassured to find that the medical signatories who certified the promotional material that was subject to the complaint had undertaken all required training, validation, and continuing development through attendance at the required Code update forums.

GSK believe that the findings of our thorough review of the existence and operation of the ICF provides reassurance that the ICF is working as intended and that the issues that have led to the current complaints are isolated within a particular team, in the presence of a set of unique circumstances, as explained below.

GSK root cause analysis - Understanding Decision Making and Judgement in the Trelegy Team

GSK acknowledges that the decision to allow the use of this claim was misguided in the face of commercial pressure and a very competitive marketplace. We believe that the team were let down by their judgement and communication. In our investigation, GSK has identified the following reasons for this:

- Delays and difficulties in communication, especially with interactions involving a previous senior commercial employee

- Lack of in-house ABPI Code experience: heavy reliance on contingent worker signatories and no ABPI code experience in the medical leadership-line supervising them
- Unclear framework for decision making: no clear, single final decision maker (notwithstanding the role of the final medical signatory as the certifier of final form); decisions taken as a group; unclear accountability for final decisions concerning medical input and a belief that [a senior medical employee's] input was advisory and not mandatory.
- The usual core claims approach for sign off of materials was ineffective in this case – the core claim as documented was flawed, and the final claim which was operationalised in this material was different from the core claim.
- Mixed knowledge in the team of the previous complaint and undertaking, and poor understanding of its implication (despite the fact that our ICF includes provision of a share-point site which details all GSK complaints, findings and undertakings and which signatories and commercial reviewers must acknowledge their awareness of when they validate)
- A 'group-think' approach provided a false sense of reassurance that all were aligned and a belief that emails to stakeholders provided implied agreement, without a formal check to confirm accurate understanding of how the claim needed to change in light of Case AUTH/3719/12/22.

Corrective and Preventative Actions

[GSK provided detailed corrective and preventative actions, which have been removed from the case report].

Given the actions above, GSK is confident that the issues highlighted by the claim resulting in the complaint is due to an isolated situation within a specific team (the respiratory team) due to a unique set of circumstances rather than a widespread occurrence across the UK affiliate. The team in question has had massive upheaval recently with changes in personnel, with inadequate signatory support leading to a forced reliance on multiple short-term contractors for sign off. The commercial team has also had recent personnel changes adding further to the disruption.

While GSK acknowledges that this does not absolve it of blame and that it is responsible for the actions of all its' staff, we believe that the overall standard of materials in GSK is of as high a standard as can be expected, as evidenced by some recent PMCPA cases where we have been able to successfully defend ourselves. Despite this, GSK takes its responsibility extremely seriously when we are made aware of any issues and have acted urgently, proactively, and ethically to investigate and rectify them. We believe our actions as described above demonstrate this.

We are also confident that the processes and internal structure within GSK are robust enough to maintain a high standard of compliance and governance with respect to the ABPI code of practice, UK regulations and the law as evidenced by the actions we have undertaken.

GSK believes that a breach of clause 2 is and should be reserved for special sanction when fundamental flaws in the inner workings of a company, including deliberately deceptive behaviour or actions are identified or, crucially, when there is a significant risk

to patient safety which we strongly do not believe to be the case here. While acknowledging that the claim in the complaint is not up to what we would consider a high enough standard, GSK firmly believes that we do not have a fundamental issue with our processes and controls. We therefore deny a breach of clause 2.

Summary
Given the findings of our root cause analysis detailed above, GSK is confident that the issues highlighted by the claim resulting in the complaint is due to an isolated situation within a particular team (the General Medicines Respiratory team) due to a unique set of circumstances, rather than a widespread occurrence across the UK affiliate. The team in question has had significant upheaval recently, with changes in personnel and inadequate internal (GSK employee) signatory support, leading to a forced reliance on multiple short-term contractors for medical certification. The commercial team has also had recent personnel changes adding further to the disruption. However, GSK is clear that this does not absolve it of blame and that it is responsible for the actions of all its' staff. We take our responsibility extremely seriously and when we were made aware of issues, have acted urgently, proactively, and ethically to remove the risk, investigate, and rectify the issue. We believe our actions as described above clearly demonstrate this.

We are also confident that the processes and internal structure within GSK are robust and as far as any company can put procedures in place, we believe that we have done all we can to maintain a high standard of compliance and governance with respect to the ABPI code of practice, UK regulations and the law. GSK believes that a breach of clause 2 is and should be reserved for special sanction when fundamental flaws in the inner workings of a company are identified or, crucially, when there is a significant risk to patient safety. While acknowledging that the claim in the complaint is not of the high standard we would expect, GSK contends that we have not brought the industry into disrepute but have been let down by the judgement and decision making of one team. We therefore deny a breach of clause 2."

PANEL RULING

GSK referred to two complaints (Case AUTH/3785/6/23 and Case AUTH/3792/7/23) received following receipt of the complaint at issue (Case AUTH/3781/6/23). The Panel noted that the three complaints were three separate cases and therefore the Panel would only consider the evidence in relation to Case AUTH/3781/6/23 and it would make no comment in relation to Cases AUTH/3785/6/23 and AUTH/3792/7/23.

GSK referred to Case AUTH/3719/12/22 and the 'potential for a breach of undertaking'. However, the Panel noted that the complaint at issue (Case AUTH/3781/6/23) was received prior to the Panel making its ruling for Case AUTH/3719/12/22. Furthermore, there was no allegation in relation to a breach of undertaking. Therefore, the matter in relation to the undertaking provided by GSK for Case AUTH/3719/12/22 was not considered by the Panel.

The Panel noted the promotional webpage at issue (PM-GB-FVU-WCNT-200013 (V8.0)) was part of the Trelegy Ellipta (fluticasone furoate, umeclidinium, vilanterol) section of the GSK.pro website. The Panel took account of the screenshot of the webpage taken by the case preparation manager from the link provided by the complainant.

The Panel noted that the Trelegy Ellipta section contained subsections accessed by tabs at the top of the webpage which were labelled “Home”, “Clinical Data”, “Trelegy Patient”, “Molecules”, “Dosing and Device”, “Cost” and “Safety Data”. The allegations appeared to concern a webpage in the clinical data subsection.

The complainant alleged that the claim ‘Trelegy demonstrated greater annualised moderate/severe exacerbation reduction vs. another COPD single-inhaler triple therapy’ was misleading as there were two other single inhaler triple therapies (Trixeo and Trimbow) and the claim did not state the exact one it was referring to.

The Panel considered the layout of the page. At the top of the page, in a box and in large prominent font, was the claim ‘Trelegy demonstrated greater annualised moderate/severe exacerbation reduction vs. another COPD single-inhaler triple therapy.’ The claim was referenced to Ismaila *et al*. (2022). Immediately below the claim, in smaller font, was the statement ‘In a network meta-analysis (NMA) of 23 randomised controlled trials (RCTs) involving adult COPD patients eligible for triple therapy, 17 of which reported moderate/severe exacerbation endpoint. Analysis based on a Frequentist Fixed Effect (FE) model.’ Beneath this was a section titled ‘New data - Single Inhaler Triple Therapies compared in a NMA.’ There was an embedded video which was said to provide an overview of what a network meta-analysis was and how they sit in the evidence hierarchy, how this particular network meta-analysis was structured and its limitations and an overview of the key conclusions from this network meta-analysis. Beneath the video was the statement ‘Other NMAs exist which differ in their methodology and study inclusion which do not show any statistical differences between SITTs [single inhaler triple therapies]. No head-to-head randomised control clinical trials exist for single inhaler triple therapies.’

Beneath this was a graphic titled ‘Difference in annualised exacerbation incidence of Trelegy vs. other COPD single inhaler triple therapies.’ The graphic showed two downward arrows of equal size and prominence, positioned next to each other, denoting reductions in annualised exacerbation incidence. The green arrow on the left showed Trelegy Ellipta vs Trixeo Aerosphere at 12 and 24 weeks. It stated 38% in large green text followed by in much smaller text ‘significantly fewer exacerbations IRR:0.62 (95% CI: 0.45, 0.86); p=0.0044’. The grey arrow on the right showed Trelegy Ellipta vs Trimbow pMDI at 12 weeks. It stated 27% in large grey text followed by in much smaller text ‘numerically fewer exacerbations IRR: 0.73 (95% CI: 0.51, 1.04) p =0.0774 (not significant).’ Below appeared the statement ‘In a network meta-analysis (NMA) of 23 randomised controlled trials (RCTs) involving adult COPD patients eligible for triple therapy, 17 of which reported moderate/severe exacerbation endpoint. 10 studies contributed to the network at 24 weeks. Analysis based on a Frequentist Fixed Effect (FE) model. This methodology is aligned with the Cochrane principles.’ More Trelegy Ellipta data in relation to exacerbation reduction followed.

The Panel did not have a copy of Ismaila *et al*. (2022) as it was not provided by either party. GSK submitted that the network meta-analysis was conducted to provide additional information to health professionals in the absence of head-to head studies and that several different clinically meaningful end points were analysed, of which one was the annualised rate of exacerbation reduction. GSK further submitted that Trelegy had a statistically significant difference versus Trixeo and numerical difference (but not statistically significant) versus Trimbow.

The Panel noted that Clause 6.1 required, among other things, that comparative information must be sufficiently complete and unambiguous and the supplementary information to Clause 6.1 concerned the need for particular care when presenting comparisons based on statistical information to ensure that differences which did not reach statistical significance were not presented in such a way as to mislead.

The Panel considered the immediate and overall impression created by the webpage to a busy health professional. The Panel noted the claim at issue 'Trelegy demonstrated greater annualised moderate/severe exacerbation reduction vs. another COPD single-inhaler triple therapy' appeared in large prominent text at the top of a webpage that was focussed on clinical data. The Panel considered that the impression created by the claim was of a statistically significant difference.

The Panel considered that the claim was ambiguous in relation to which COPD single-inhaler triple therapy was the comparator. The information about the comparator was not in the same visual field as the claim at issue. The reader would have to scroll further down the page to the graphic of the downward arrows depicting the difference in annualised exacerbation incidence of Trelegy vs Trixeo and Trelegy vs Trimbow, which were displayed side-by side with equal size and prominence, however, the difference between Trelegy and Trimbow was not statistically significant.

The supplementary information to Clause 6.1 included that claims must be capable of standing alone. The Panel considered that the headline claim 'Trelegy demonstrated greater annualised moderate/severe exacerbation reduction vs. another COPD single-inhaler triple therapy' on the webpage at issue was ambiguous with regard to the comparator and created a misleading impression that was not capable of substantiation. The Panel therefore ruled **breaches of Clauses 6.1 and 6.2** as acknowledged by GSK.

The Panel took account of GSK's submission that an experienced signatory had previously advised, in connection with a previous complaint, that the claim in question should be revised to be explicit that the difference was only significant versus Trixeo. The Panel noted GSK's submission that the Trelegy team had made the decision not to follow this advice for reasons including "commercial pressure and a very competitive marketplace". In this regard, the Panel considered that GSK's use of the misleading claim in question was such that it had failed to maintain high standards and it ruled a **breach of Clause 5.1,** as acknowledged by GSK.

Clause 2 was a sign of particular censure and was reserved for such use. The Panel recognised that GSK had conducted a thorough investigation in response to this complaint and had put corrective and preventative measures in place. The Panel considered that the matters raised in this complaint were adequately covered by its rulings of breaches of the Code above and did not consider that a breach of Clause 2 was warranted. The Panel therefore ruled **no breach of Clause 2**.

Complaint received **21 June 2023**

Case completed **25 September 2024**