CASE AUTH/3715/11/22

COMPLAINANT v GSK

Allegations about a European Respiratory Society 2022 symposium video

CASE SUMMARY

This case concerned a video on a GSK promotional website which summarised the content of GSK's symposium at the European Respiratory Society Congress 2022 and included data from a GSK network meta-analysis that investigated the comparative efficacy of Fluticasone Furoate/Umeclidinium/Vilanterol (FF/UMEC/VI) versus other triple and dual therapies for patients with COPD.

Allegations related to misleading comparative claims for GSK's medicine Trelegy (FF/UMEC/VI) versus other therapies and also that health professionals had been paid to make misleading claims.

The outcome under the 2021 Code was:

Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 6.1 (x4)	**Making a misleading claim**
Breach of Clause 6.2 (x2)	**Making a claim incapable of substantiation**
Breach of Clause 14.1 (x4)	**Making a misleading comparison**

No Breach of Clause 2	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 5.1	**Requirement to maintain high standards at all times**
No Breach of Clause 6.6 (x2)	**Requirement that another company's medicines must not be disparaged**

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 about GSK.

COMPLAINT

The complainant alleged a video hosted on the GSK Respiratory promotional website was uncompliant. The video was a ERS 2022 symposium summary with [named professor] and [named GSK employee] and could be identified on the Trelegy Ellipta promotional website. At 4

minutes and 1 second, a slide was shown claiming that Trelegy provided greater improvements in annual rate of combined moderate and severe exacerbations than most comparators. However, this was incorrect as the exacerbation rate vs Trimbow had failed statistical testing. The complainant stated the claim and the speaker should have made clear from the beginning as to this failure of Trelegy but instead had misled by presenting the claim that Trelegy had shown greater exacerbation success against comparators. The speaker had also verbalised a difference vs other single inhaler therapies without any mention of the statistical failure. The complainant further alleged the conclusion slide had a bullet point that said Trelegy showed statistically significant and greater improvement in annualised moderate and severe exacerbations vs alternative therapies and that the speaker did not make clear the failure of Trelegy in direct comparison to Trimbow for this endpoint. The claims were misleading, disparaging and should not have been approved by the review team at GSK for release. The complainant expressed concern that health professionals had been paid to provide misleading claims. Direct breaches of Clauses 6.1, 6.2, 6.6 and 2 were alleged.

When writing to GSK, the Authority asked it to consider the requirements of Clauses 2, 5.1, 6.1, 6.2, 6.6 and 14.1 of the Code.

RESPONSE

GSK stated that it was committed to following both the letter and the spirit of the Code and all other relevant regulations.

GSK noted that the complainant had alleged breaches of Clauses 2, 6.1, 6.2 and 6.6 of the 2021 Code. The case preparation manager had also raised Clauses 5.1 and 14.1.

The complainant had mentioned two materials:

1. Trelegy Ellipta promotional website intended for UK health professionals.

2. European Respiratory Society (ERS) 2022 Symposium Summary video embedded within the aforementioned website.

While the complainant had cited the job code of the website, the specific allegations related to the separately approved embedded video found within the website and GSK's response therefore would focus on this video.

Of note, the video in question was intended to present the highlights of the GSK symposium that had taken place at ERS 2022, as explained verbally by the first speaker [named professor], at timepoint 19 seconds. While the two speakers in the video had co-chaired the symposium, the video was recorded separately prior to the symposium itself.

As the content of the 90-minute symposium was known in advance, GSK chose particular data which summarised the symposium content and which would be useful to be highlighted in a short (under 10 minutes) video recording made available for the benefit of health professionals who were unable to attend or stream the symposium when it took place. [Named professor] stated that the video went over 'some of the important data and insights from the ERS symposia'. The video was certified under the Code and made available on the UK Trelegy Ellipta promotional website.

[Named professor's] involvement in the video recording was contracted as an activity in an amendment to their original External Expert Individual Agreement which was for co-chairing the symposium. The Amendment Agreement added the recording of the 'Symposia Highlight Video' (the subject of the complaint) as an activity covered by the terms of the original Agreement.

The second speaker on the video was a GSK employee, who had the appropriate knowledge and expertise to discuss the data presented in the video. As their participation in the recording of the video fell within the remit of their job, there was no separate agreement for them.

Both speakers in the video were also co-chairs of the symposium, and the data discussed in the video was a summary of the data presented at the symposium. There had been a briefing for all the co-chairs and speakers at the symposium which made clear what the symposium objectives were and emphasised that the content and discussions had to be in line with the Trelegy Ellipta license. GSK believed that the requirements for content laid out in the symposium briefing covered the requirements for content of the video as well. Therefore, no separate briefing had been created for the video, as the speakers in the video were already aware of what they could and could not say based on the symposium briefing. Furthermore, as the video was not recorded at a live meeting, there had been the opportunity to edit it to remove any unsuitable content as part of the review and approval process.

The complainant referred to Single Inhaler Triple Therapies (SITTs) which combine an inhaled corticosteroid (ICS), long-acting β2-agonist (LABA) and long-acting muscarinic antagonist (LAMA) into one delivery device.

Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI)) was GSK's SITT indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who were not adequately treated by a combination of an inhaled corticosteroid and a long-acting β2- agonist or a combination of a long-acting β2-agonist and a long-acting muscarinic antagonist.

Other SITTs licensed in the UK for the same indication were Trimbow (beclometasone dipropionate/formoterol/glycopyrronium bromide (BDP/FOR/GLY)), and Trixeo (budesonide/glycopyrronium bromide/formoterol (BUD/GLY/FOR)).

The complainant had made allegations regarding two slides shown during the video in question. GSK would address the allegations for each slide below.

Moderate and severe exacerbations slide

GSK stated that the complainant alleged that 'At 4 minutes and 1 second, a slide was shown claiming that Trelegy provided greater improvements in annual rate of combined moderate and severe exacerbations than most comparators. However, this was incorrect as the exacerbation rate vs Trimbow had failed statistical testing. The claim and the speaker should have made clear from the beginning as to this failure of Trelegy but instead had misled by presenting the claim that Trelegy had shown greater exacerbation success against comparators. The speaker had also verbalised a difference vs other single inhaler therapies without any mention of the statistical failure'. The complainant later made the overarching allegation 'The claims were misleading, disparaging and should not have been approved by the review team at GSK for release'.

The slide shown at timepoint 4 minutes and 1 second discussed lung function improvement which did not match what the complainant had alleged. For the purposes of this response, GSK assumed that the complainant was referring to the subsequent slide shown from timepoint 4 minutes and 3 seconds until 4 minutes and 15 seconds, which did discuss the annual rate of combined moderate and severe exacerbations.

This slide had the heading 'Trelegy provided greater improvements in annual rate of combined moderate and severe exacerbations than most comparators from a frequentist fixed effect model: all studies'. This was referenced to Ismaila AS *et al*. Adv Ther (2022). Both speakers on the video had the necessary expertise to discuss the paper. This network meta-analysis (NMA) of randomised controlled trials investigated the comparative efficacy of Trelegy Ellipta (FF/UMEC/VI) versus any triple (ICS/LABA/LAMA) combinations and dual therapies in patients with COPD. Outcomes of interest included lung function measured as forced expiratory volume in 1 second (FEV1) (the primary endpoint measured at 24 weeks), and annualized rate of combined moderate and severe exacerbations.

Below the slide heading were two forest plots referenced to Ismaila A *et al*. American Thoracic Society Meeting (2022). The forest plot on the left illustrated a view of 18 comparators within the scope of the NMA for the exacerbation outcome. The forest plot on the right illustrated a subset of these – 8 comparators with ≥24 weeks of follow-up. Both forest plots clearly displayed the p values of the results for each comparison. They also clearly showed visually a vertical line representing the incidence rate ratio (IRR) of 1.0 which indicated no difference between Trelegy Ellipta and the comparator. IRR plotted with their respective 95% confidence intervals wholly on the left of this vertical line indicated a statistically significant favourable outcome for Trelegy vs the comparator. The forest plots showed a clear visual presentation of the data in addition to the p value, so it was immediately clear which results showed statistical significance, and which only showed a numerical difference.

When this slide was displayed on the video, the speaker stated, 'Similarly, when we look at moderate to severe COPD exacerbations, FF/UMEC/VI provided a significantly greater improvement compared with other commonly used triple therapy options, including other SITTs'.

GSK stated that taking the first part of the allegation regarding this slide, the complainant stated that 'a slide was shown claiming that Trelegy provided greater improvements in annual rate of combined moderate and severe exacerbations than most comparators. However, this was incorrect as the exacerbation rate vs Trimbow had failed statistical testing.' The claim in this part of the complainant's allegation was found in the headline of the slide. The forest plot showing the analysis from all studies in the NMA for this endpoint presented on the slide in question showed that Trelegy had demonstrated statistically significant greater improvements in the annual rate of combined moderate and severe exacerbations vs 11 out of 18 comparators. Of the remaining 7 comparators, while statistical significance was not demonstrated, the point estimate of the IRR numerically favoured Trelegy in 6 comparisons, including the comparison with Trimbow (BDP/FOR/GLY), IRR (95% CI) 0.73 (0.51, 1.04), p=0.0774. There was also 1 comparison where the point estimate was exactly 1.00. In total therefore, 17 of the 18 comparisons for this endpoint were numerically favourable to Trelegy, with 11 of these being statistically significant. GSK's position was that the headline statement was therefore correct as most comparisons (11/18) had demonstrated statistical significance in favour of Trelegy for the annual rate of combined moderate and severe exacerbations, while 17/18 comparisons were numerically favourable to Trelegy. Those comparators where statistical significance was not demonstrated, including vs Trimbow (BDP/FOR/GLY) were clearly graphically shown on the

forest plot with confidence intervals crossing the IRR value of 1.0, with accompanying labels showing the p values. On this point GSK believed the headline claim was correct and no competitor product had been disparaged and therefore denied breaches of Clause 6.1 and Clause 6.6. The headline claim was capable of substantiation through the referenced Ismaila *et al* 2022 paper and so GSK denied a breach of Clause 6.2. The claim was not misleading as it related to the outcome of annual rate of combined moderate and severe exacerbations in COPD, which was relevant for all the comparators which were clearly identified in the forest plot. Therefore, GSK denied a breach of Clause 14.1.

The next part of the allegation regarding this slide stated that 'The claim and the speaker should have made clear from the beginning as to this failure of Trelegy but instead had misled by presenting the claim that Trelegy had shown greater exacerbation success against comparators. The speaker had also verbalised a difference vs other single inhaler therapies without any mention of the statistical failure'. The data in the forest plots on the slides clearly showed the combined moderate and severe exacerbation outcomes from the Ismaila NMA comparing Trelegy with 18 comparators. As described above, it was clear which comparisons were statistically significant in favour of Trelegy and which comparisons showed non-statistically significant numerical benefit in favour of Trelegy. Furthermore, a prominent sentence under the forest plots on the slide stated 'Other NMAs exist which differ in their methodology and study inclusion which do not show any statistical differences between SITTs'. This placed the Ismaila study in the wider context of other studies so HCPs could appreciate that different methodologies might lead to different results. GSK believed that the slide itself visually portrayed results from the NMA accurately, the claims as written could be substantiated, they did not disparage a competitor product and were not misleading.

However, GSK acknowledged that the voiceover from the speaker that was heard when this slide was displayed was not accurate with regard to the results for Trelegy versus other SITTs. The speaker stated that 'FF/UMEC/VI provided a significantly greater improvement compared with other commonly used triple therapy options, including other SITTs'. While this was true for the comparison of Trelegy vs Trixeo (IRR (95% CI) 0.62 (0.45, 0.86); p=0.0044), the results were numerically in favour of Trelegy versus Trimbow (IRR (95% CI) 0.73 (0.51, 1.04); p=0.0774), but were not statistically significant. GSK accepted that the voiceover on this slide was not accurate, could not be substantiated and was misleading and therefore accepted that this was in breach of Clauses 6.1, 6.2 and 14.1, respectively. GSK did not believe that a competitor product had been disparaged, as no particular product was mentioned in the voiceover, and the slide visually portrayed the data for both competitor SITTs accurately, and therefore GSK denied a breach of Clause 6.6 on this point.

This was an unintentional and inadvertent slip of the tongue for the speaker to use the word 'significantly' in this context when making the recording, which unfortunately was also not detected by the signatory when the video was reviewed and certified. GSK accepted that high standards were not maintained on this point and therefore acknowledged this was a breach of Clause 5.1.

GSK stated that all its employees who worked on promotional external interactions were trained on the GSK Policy 'Code of Practice for Promotional and Non-promotional External Interactions'. This stated on page 3, in a section titled 'Principles', 'Our verbal, printed and digital information and communications are... accurate, fair, objective and balanced (i.e. we do not overstate efficacy, understate safety or make unsubstantiated comparisons); capable of substantiation (i.e. based on data or other evidence that can be provided or referenced); never

knowingly offensive or disparaging'. The single inadvertent use of the word 'significantly' by the speaker in the voiceover was not a deliberate attempt by GSK to misrepresent the data. GSK believed data presented visually on the slide itself was not in breach of the Code. GSK had clear policies in place to ensure data was portrayed accurately in the appropriate context, and regretted this had not happened on this occasion with the voiceover.

GSK noted the supplementary information to Clause 2 which stated that 'A ruling of a breach of this clause is a sign of particular censure and is reserved for such circumstances'.

The supplementary information also listed examples of activities which were likely to breach Clause 2, none of which were similar to the breaches described above. In this case, an unfortunate, isolated error was made with the inadvertent use of the word 'significantly' in the voiceover. The video as a whole, including the content of the slides and the rest of the voiceover, was fair and balanced and would have enabled an HCP to make an informed judgement about the NMA results. GSK did not believe the breaches described above had led to discredit being brought upon or confidence being reduced in the pharmaceutical industry. Therefore, GSK denied a breach of Clause 2 on this point.

Conclusion slide

The complaint alleged that the conclusion slide had a bullet point that said Trelegy showed statistically significant and greater improvement in annualised moderate and severe exacerbations vs alternative therapies and that the speaker had not made clear the failure of Trelegy in direct comparison to Trimbow for this endpoint. The complainant also made the overarching allegation 'The claims were misleading, disparaging and should not have been approved by the review team at GSK for release'.

The conclusion slide had a number of bullet points which appeared as a build. The particular bullet point in question was discussed by the speaker for 16 seconds. The bullet point stated 'Trelegy (FF/UMEC/VI) shows statistically significant improvement in trough FEV_1 and greater improvement in combined annualised moderate and severe exacerbation vs alternative therapies'.

It was clear from the phrasing that there were two different claims being made in this bullet point. The first was regarding 'statistically significant improvements in trough FEV_1... vs alternative therapies'. The second was regarding 'greater improvement in combined annualised moderate and severe exacerbation vs alternative therapies', which did not state any statistical significance.

The voiceover from the speaker regarding this bullet point stated 'Based on a recent network meta-analysis the triple Trelegy Ellipta showed significantly greater benefits on lung function than most comparators, including other single inhaler triple therapies. Likewise, we are seeing greater improvements in exacerbation reduction'.

Again, it was clear from the voiceover that the data around lung function (trough FEV_1) showed 'significantly' greater benefits for Trelegy vs most comparators, whereas the data around exacerbation reduction showed greater improvements without implying statistical significance.

The complainant was therefore incorrect in their assertion that the claim stated 'statistically significant and greater improvement in annualised moderate and severe exacerbations vs

alternative therapies' as the 'significant' aspect applies only to lung function (trough FEV_1), not to exacerbations.

The data regarding lung function (trough FEV_1) was based on the reference Ismaila A *et al*. American Thoracic Society Meeting (2022). This data had been shown in more detail earlier in the video although the complainant had made no allegations regarding that earlier slide or the lung function data. In summary, the lung function data was derived from the same NMA as described above. This showed statistically significant differences in FEV_1 in favour of Trelegy versus 11 out 14 comparators at the 12-week timepoint, and versus 7 out of 8 comparators at the 24-week timepoint. At 12 weeks, Trelegy showed statistically significant lung function improvement versus both competitor SITTs, Trimbow and Trixeo. At 24 weeks, competitor SITT comparisons were only available for Trixeo, and this again showed a statistically significant difference in favour of Trelegy. While the first part of the bullet point in question on the conclusions slide was not the subject of the complaint, it should be noted that GSK believed that the claims regarding the lung function results from the NMA had been portrayed appropriately in line with Code requirements.

Regarding the second part of the bullet point in question on the conclusions slide which was the subject of the complaint, GSK asserted that neither the content of the conclusion slide, nor the voiceover discussing the conclusion slide stated that Trelegy showed statistically significant improvement in annualised moderate and severe exacerbations vs alternative therapies. The bullet point did state Trelegy showed 'greater improvement' in this endpoint vs alternative therapies, and the speaker had said that 'greater improvements' in exacerbation reduction were being seen (when referring to Trelegy vs most comparators). This claim related back to the data shown on the slide discussed above and referenced to the Ismaila poster.

To summarise this had shown greater improvements in the annual rate of combined moderate and severe exacerbations for Trelegy vs 17 out of 18 comparators (ie most comparators), including Trimbow (BDP/FOR/GLY), as the point estimate of the IRR was less than 1.0. As it had not been stated on the conclusion slide that these improvements were statistically significant, GSK believed the claim was accurate, capable of substantiation and not misleading, so denied breaches of Clauses 6.1, 6.2 and 14.1, respectively. No competitor product had been mentioned on the conclusion slide so GSK denied that the claim was disparaging a competitor product and therefore denied a breach of Clause 6.6. As GSK denied these allegations regarding the conclusions slide, GSK believed that high standards had been maintained and therefore denied a breach of Clause 5.1. Consequently, GSK also denied a breach of Clause 2 regarding the conclusions slide.

Allegation regarding paying HCPs to provide misleading claims

The complainant alleged 'Concern that HCPs had been paid to provide misleading claims', although no evidence for this had been provided. GSK denied this allegation.

GSK stated that it had provided the agreement and amendment agreement with the first speaker [named professor], showing their rate of remuneration and allocated time for recording the video. There was no suggestion or allegation that [named professor] made any misleading claims.

The second speaker was an employee of GSK and so was not specifically paid additionally for the production of this video, but rather this fell into the remit of their role. While GSK

acknowledged that the employee did make an inadvertent mention of the word 'significantly' in regard to an outcome of the NMA which was misleading, this was not a deliberate attempt to mislead, and was an unfortunate spoken error made once in the course of the video. GSK had provided as an enclosure a Policy document assigned as training to all staff involved in external promotional interactions, including the speaker, which made clear GSK's position that communications must be accurate, fair, objective and balanced.

GSK stated that it denied that HCPs had been paid to provide misleading claims. GSK consequently denied breaches of Clauses 5.1 and Clause 2 in this regard.

Actions taken by GSK

GSK stated that it acknowledged that the voiceover in the video when the exacerbation data from the NMA was being discussed had been in breach of the Code. This version of the video had been withdrawn and was no longer available on the Trelegy promotional website. GSK might in future edit the video to remove the non-compliant part of the voiceover and certify and distribute a new version of the video for UK HCPs. GSK was also checking other materials to ensure there were no similar non-compliant claims made.

Conclusion

In conclusion, GSK acknowledged breaches of Clause 6.1, 6.2, 14.1 and 5.1 relating to the single unintentional and inadvertent use of the word 'significantly' in the spoken claim 'FF/UMEC/VI provided a significantly greater improvement compared with other commonly used triple therapy options, including other SITTs'.

GSK stated that it denied all other breaches of these Clauses in relation to other allegations made by the complainant. GSK also denied all allegations of breaches of Clauses 6.6 and Clause 2.

PANEL RULING

The Panel noted the complainant referred to a video hosted on the GSK respiratory promotional website which was the European Respiratory Society (ERS) 2022 GSK symposium highlights with a Professor and GSK employee, entitled, 'How molecular pharmacology translated into patient benefits in COPD'.

The Panel noted that the complainant had set out their concerns regarding claims which were associated with two specific slides shown within the video highlights. The complainant alleged that the claims regarding GSK's medicine Trelegy Ellipta were misleading, disparaging and should not have been approved; there were also concerns that HCPs had been paid to provide misleading claims.

Trelegy Ellipta (fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI)) was GSK's Single Inhaler Triple Therapy (SITT), a combination of an inhaled corticosteroid (ICS), long-acting β2-agonist (LABA) and long-acting muscarinic antagonist (LAMA) in one delivery device; Trelegy was indicated as a maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who were not adequately treated by a combination of an inhaled corticosteroid and a long-acting β2- agonist or a combination of a long-acting β2-agonist and a long-acting muscarinic antagonist.

GSK submitted that other SITTs licensed in the UK for the same indication were Trimbow (beclometasone dipropionate/formoterol/glycopyrronium bromide (BDP/FOR/GLY)), and Trixeo (budesonide/glycopyrronium bromide/formoterol (BUD/GLY/FOR)).

The Panel noted the symposium in question presented data from a GSK network meta-analysis (Ismaila *et al*). In its view, a network meta-analysis (NMA) was a useful technique of combining both direct and indirect treatment comparisons across a network of studies to provide a comparison of interventions within a single analysis. Whilst NMAs were an established and valid methodology, particularly in the absence of head-to-head trials, the Panel noted their validity relied amongst other things upon several assumptions being met including that studies in the network were sufficiently homogenous and thus care had to be taken when interpreting the results and drawing conclusions from an NMA. The Panel noted that NMAs were more statistically complex than meta-analyses with which health professionals might be more familiar and thus it was particularly important that the nature of the analysis was made clear and that recipients of the data were given sufficient information to enable them to form their own opinion of the therapeutic value of the comparison.

The Panel noted that the primary endpoint of the Ismaila *et al*. network meta-analysis was defined as the mean change from baseline in trough FEV_1 at 24 weeks and that annualised exacerbation rate was a secondary endpoint. It also noted the limitations; differences in study design, definitions of moderate and severe exacerbations and the patient inclusion/exclusion criteria of the trials included in the analysis, and clinical heterogeneity between the participants included in each study. The limited number of studies on SITTs available for inclusion was another limitation, while the lack of a common comparator in the network meant that some comparisons were not possible and, modelled estimates were used as input if available in the publications, and if they were not available estimates were modelled from the raw data.

The Panel noted that there was substantial heterogeneity in the definition of severe exacerbations ie with respect to hospitalisation across multiple studies and that the analysis of severe exacerbations alone was not deemed robust and therefore was not published. The results of moderate and severe exacerbations were therefore pooled to reduce the impact of the observed heterogeneity in definitions between trials. Noting that the authors of the network meta-analysis had concluded that while the findings of this network meta-analysis suggested favourable efficacy with single inhaler therapy comprising FF/UMEC/VI further analysis was required as additional evidence became available. The Panel questioned whether the presentation fairly reflected the caution expressed by the authors.

The Panel noted the complainant's allegation that Trelegy was claimed to provide greater improvements in annual rate of combined moderate and severe exacerbations than most comparators which was incorrect as the exacerbation rate had failed statistical testing when compared to Trimbow. The complainant stated this should have been made clear from the beginning and that the speaker did not make clear the failure of Trelegy in the direct comparison; in this regard, whilst the Panel noted the complainant referred to a webpage on the GSK pro website, the allegations related to two slides shown in the GSK ERS symposium highlights video and the Panel made its rulings accordingly.

Moderate and severe exacerbations slide

The Panel noted the first slide at issue highlighted by the complainant was headed 'Trelegy provided greater improvements in annual rate of combined moderate and severe exacerbations than most comparators from a frequentist fixed effects model: all studies' and was referenced to the network meta-analysis (NMA), Ismaila *et al*. 2022. The slide displayed two forest plots titled 'All studies' and 'Studies with ≥24 week follow up' which were positioned side by side and referenced to Ismaila A *et al*. American Thoracic Society Meeting (2022). The 'all studies' forest plot set out the annualised moderate – severe exacerbation rates of 18 comparators versus Trelegy Ellipta within the scope of the NMA; a subset of these were illustrated in a forest plot to the right with 8 comparators with 'studies with ≥24 week follow up' this provided data, where available, to account for heterogeneity induced by differences in length of follow up.

The Panel noted that the forest plots set out data from the NMA for both triple and dual therapies; in setting up this section the speakers gave the impression that the data was only versus other single inhalation triple therapies SITTs. Prior to this slide the speakers set up the data which followed and stated, amongst other things:

- 'Even though we have seen head-to-head evidence between the dual or monotherapies in COPD, there remains an evidence gap in our understanding of the relative efficacy between triple therapy options for patients, including the available single-inhaler triple therapies or SITTs' and
- 'To help address this evidence gap, GSK has performed a rigorous network meta-analysis of data from the literature with different triple therapies, including studies with common characteristics as described here and within that analysis, we identified 23 studies for inclusion.'

The Panel noted GSK's submission that the forest plot showing the analysis from all studies in the NMA showed 17 of the 18 comparisons for the endpoint were numerically favourable to Trelegy, including the comparison with Trimbow (BDP/FOR/GLY), IRR (95% CI) 0.73 (0.51, 1.04), p=0.0774; 11 out of 18 comparators demonstrated **statistically significant** greater improvements (emphasis added by Panel).

The Panel noted that below the two forest plots was a prominent blue bar containing the prominent bold text:

> 'Trelegy SITT provided greater improvements in annual moderate and severe exacerbations versus other commonly used therapies, suggesting favourable long-term efficacy of Trelegy' and
>
> 'Other NMAs exist which differ in their methodology and study inclusion which do not show any statistical differences between SITTs.'

The Panel queried the appropriateness of the inclusion of disclaimers on NMAs, as below, in very small font in the footer of the slide:

> 'Information from an indirect comparison made through a network meta-analysis; the limitation of these studies should be taken into account. Analysis is limited by differences in study design and patient characteristics between trials.'

The Panel noted the slide was shown for approximately 12 seconds during which time the speaker stated: 'Similarly, when we look at moderate to severe exacerbations FF/UMEC/VI

provided a significantly greater improvement compared with other commonly used triple therapy options, including other SITTs'.

In relation to the allegation that the speaker had verbalised a difference compared to other SITTs without any mention of the statistical failure, GSK acknowledged that the voiceover from the speaker that was heard when this slide was displayed was not accurate. GSK submitted that whilst 'FF/UMEC/VI provided a significantly greater improvement compared with other commonly used triple therapy options, including other SITTs' was true for the comparison of Trelegy vs Trixeo (IRR (95% CI) 0.62 (0.45, 0.86); p=0.0044), the results for Trelegy versus Trimbow (IRR (95% CI) 0.73 (0.51, 1.04); p=0.0774) were not statistically significant.

The Panel considered incorrect reference to Trelegy providing **significantly** greater improvement compared with other SITT options (emphasis by Panel), which was not so, meant the speaker's claim was such that it was misleading as acknowledged by GSK; the Panel ruled **a breach of Clauses 6.1 and 14.1** accordingly, as acknowledged by GSK.

With regard to the written slide itself, the Panel noted GSK's position that the headline statement 'Trelegy provided greater improvements in annual rate of combined moderate and severe exacerbations than most comparators' was correct as most comparisons (11/18) did demonstrate statistical significance in favour of Trelegy for the annual rate of combined moderate and severe exacerbations, while 17/18 comparisons were numerically favourable to Trelegy.

The Panel noted its views outlined above that care should be taken when interpreting the results and drawing conclusions from NMAs, and thus considered it was particularly important that claims were based on statistical significance, rather than numerically favourable results.

The Panel noted the voiceover preceding the slide and noted it included the statement 'GSK has performed a rigorous network meta-analysis of data from the literature with different **triple therapies** (emphasis added), including studies with common characteristics as described here and within that analysis, we identified 23 studies for inclusion'.

The Panel considered the overall impression of the slide to a health professional. Whilst the Panel noted that 61% of comparisons (11/18) were associated with statistical significance, the Panel considered the overall impression to a viewer might be that a higher percentage of studies would have reached statistical significance. In the Panel's view, the forest plots failed to clearly illustrate the studies with statistical significance. The Panel noted that the slide was only displayed for 12 seconds and was very text and data heavy, with no attempt to highlight which comparisons did not achieve statistical significance. Further, no attention had been drawn to the results that achieved statistical significance to differentiate.

The Panel noted Clause 6.1 stated 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.

In the Panel's view, the claim, on balance, was one that misleadingly implied statistical superiority and clinical relevance for Trelegy compared to 'most comparators', which would likely have been interpreted as other triple therapies including Trimbow. The Panel did not

consider the forest plots which showed the significance of each study negated this misleading impression, particularly noting the preceding narrative and during the slide and the inadequate time that the slide was shown. In the Panel's view, noting its comments above and that the claim was ambiguous, it was unlikely those viewing the video were presented with sufficient information to enable them to form their own opinion of the therapeutic value of the medicine. The Panel therefore ruled a **breach of Clauses 6.1 and 14.1**.

With regard to substantiation, whilst the Panel noted the wording of the headline claim, 'Trelegy provided greater improvements in annual rate of combined moderate and severe exacerbations than **most** comparators' (emphasis added by Panel), might have technically been capable of substantiation, it considered its finding above that the overall impression of the claim and associated voiceover. The Panel, noting GSK acknowledged a breach of Clause 6.2 in relation to the speaker's narrative, considered the overall impression was nonetheless that Trelegy provided statistically significant improvements compared with other SITT options, which could not be substantiated. The Panel therefore considered the 12 second section of the video containing this information, was incapable of substantiation and the Panel ruled a **breach of Clause 6.2** in this regard.

Clause 6.6 stated the medicines, amongst other things, of other pharmaceutical companies must not be disparaged. Whilst the Panel considered the slide and how it was presented meant viewers might have been misled to believe that Trelegy provided significantly greater improvement compared to Trimbow, albeit that Trimbow was not mentioned by name, as ruled in breach of the Code above, the Panel considered there was a fine line between stating a positive outcome of one medicine and disparaging another. The Panel did not consider, on balance, that the albeit inaccurate comparative claim presented was such that it disparaged the alternative inhalers, including Trimbow, and **no breach of Clause 6.6 was ruled**.

Conclusions slide

The Panel noted the second slide at issue highlighted by the complainant was the Conclusions slide which included, among other things, the bullet point 'Trelegy (FF/UMEC/VI) shows statistically significant improvement in trough FEV_1 and greater improvement in combined annualised moderate and severe exacerbations vs alternative therapies' which was referenced to Ismaila *et al* 2022. The voiceover for this bullet point stated 'Based on a recent network meta-analysis the triple Trelegy Ellipta showed significantly greater benefits on lung function than most comparators, including other single inhaler triple therapies. Likewise, we are seeing greater improvements in exacerbation reduction'.

The Panel noted the complainant's allegation that the claim stated Trelegy showed statistically significant and greater improvement in annualised moderate and severe exacerbations compared to alternative therapies but the speaker did not make clear the failure of Trelegy in direct comparison to Trimbow for this endpoint; the claims were allegedly misleading, disparaging and should not have been approved for use.

In the Panel's view, noting the conclusions slide was presented a considerable time after the results slide and that information unconnected to the NMA had been presented in between, it was important that care was taken to ensure the key take home messages were sufficiently complete and portrayed unambiguously.

Whilst the Panel noted GSK submitted there were two different claims being made in this bullet point, the first regarding 'statistically significant improvements in trough FEV_1 vs alternative therapies' and the second was regarding 'greater improvement in combined annualised moderate and severe exacerbation vs alternative therapies', the latter of which did not state any statistical significance, the Panel considered the overall impression to the recipient.

In the Panel's view, there was no clear separation between the two claims, which formed part of the same sentence of the bullet point; the Panel noted its view on NMAs as set out above and considered it was particularly important that claims substantiated by NMAs were clearly based on statistical significance. In the Panel's view, the viewer would likely have been led to believe the combined annualised moderate and severe exacerbation compared to all alternative therapies was statistically significant, and in particular other triple therapies, which was not so. The Panel therefore **ruled a breach of Clause 6.1 and 14.1** in relation to the contents of the slide.

The Panel further noted the contents of the voiceover and considered the misleading impression was not negated by the speaker; in the Panel's view, reference to 'statistically greater benefits on lung function' followed by 'greater improvements in exacerbation' reduction gave the misleading impression that the exacerbations reduction was statistically significant for Trelegy compared to all comparators, which was not so. A **breach of Clause 6.1 and 14.1** was therefore ruled for the voiceover.

The Panel noted its comments above in relation to the conclusion slide and associated voiceover which in the Panel's view, misleadingly implied that Trelegy showed statistically significant improvement in combined annualised moderate and severe exacerbations compared to all alternative therapies which was not so; the Panel considered the misleading impression that Trelegy had statistically greater benefits than all comparators was not capable of substantiation and therefore ruled **a breach of Clause 6.2**.

However, the Panel did not consider it had been established that Trimbow had been disparaged as alleged and **no breach of Clause 6.6 was ruled**.

Payment to HCPs

In relation to the complainant's allegation that HCPs had been paid to provide misleading claims, the Panel noted the speaker agreement stated the rationale and objective of the symposium was:

> 'education of HCPs [health professionals] attending ERS on the science of our molecules that make up TRELEGY (FF/UMEC/VI), the clinical benefits our RCT head-to-head studies and our newest indirect comparison data, as well as share our Real World Evidence we have generated to support the body of evidence for our FF/UMEC/VI combination. Ability for HCPs to ask questions of an expert panel on the use of Trelegy (FF/UMEC/VI)/Anoro (UMEC/VI) in COPD patients.'

GSK submitted there was a briefing which emphasised that the content and discussions must be in line with the Trelegy Ellipta license and both speakers were aware of what they could and could not say; the Panel noted the briefing document was closely aligned to the objectives as above in the speaker agreement.

Noting the above, the Panel considered that the complainant, who bore the burden of proof, had not established that HCPs had been paid to provide misleading claims as alleged and **no breach of Clause 5.1** of the Code was ruled.

Overall

The Panel, noting its rulings above, considered viewers of the highlights video would likely have been misled to believe exacerbation results for Trelegy were statistically or clinically significant where that was not the case. In this regard, the Panel considered high standards had not been maintained and **a breach of Clause 5.1** was ruled.

Clause 2 was a sign of particular censure and was reserved for such use. Whilst the Panel was concerned with the narrative and misleading information, on balance, taking account all the circumstances of this case, the Panel did not consider that the circumstances of the case meant that GSK had brought discredit upon the industry. The Panel, on balance, ruled **no breach of Clause 2**.

Complaint received **28 November 2022**

Case completed **18 December 2023**