CASE AUTH/3708/11/22

COMPLAINANT v GSK

GSK's activities at the European Respiratory Society meeting

CASE SUMMARY

This case concerned two sponsored presentations at a congress and the appropriateness of the presence of medical science liaison (MSL) staff on a promotional stand at the meeting.

The complainant alleged that the presentations were not fully transparent about the results from a meta-analysis of triple combination products for chronic obstructive pulmonary disease and claims comparing the effects of Trelegy with other single inhaler triple therapies were incorrect and therefore misleading and not capable of substantiation.

The Panel ruled a breach of the following Clauses of the 2021 Code on the basis that overall, and on balance, the slides did not fairly reflect the data and health professionals might be misled as to the clinical relevance of certain results presented such that the presentation created a misleading impression which was incapable of substantiation:

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

The Panel ruled no breach of the following Clauses of the 2021 Code because in its view the complainant had not established that the MSLs had acted in a promotional capacity that required them to take an appropriate examination for representatives or that their activities constituted disguised promotion. The Panel did not consider that in relation to the matters alleged, GSK's actions had brought discredit upon, or reduced confidence in, the pharmaceutical industry.

No Breach of Clause 2 (x2)	**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**
No Breach of Clause 9.4	**Requirement that representatives take an appropriate examination within their first year of employment and pass it within two years**
No Breach of Clause 15.6	**Requirement that promotional material and activities must not be disguised**

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 UK Ltd and the role of its medical science liaison (MSL) staff and the content of two presentations sponsored by GSK at the European Respiratory Society (ERS) meeting.

COMPLAINT

The complainant noted that the European Respiratory Society meeting took place in Barcelona in September 2022, as part of this, GSK had a promotional stand in the exhibition hall at the conference. However, members of the UK GSK medical science liaison team were present on this stand. The complainant alleged that this was inappropriate as none of the GSK UK MSLs had the ABPI exam to be considered a representative. By being on a promotional stand, the UK MSLs, whose job role was strictly only non-promotional, were soliciting questions from health professionals about GSK products, when the role of a MSL was only to act to answer unsolicited questions. As a result, the interactions that the GSK UK MSLs had on the stand were fully promotional. As GSK head offices were based in the UK, the activities at ERS in Barcelona had to abide by the UK Code. This was not the case and the complainant alleged breaches of Clauses 9.4, 5.1, 15.6 and 2.

The complainant further alleged that the GSK evening symposium titled, 'How molecular pharmacology was improving patient outcomes in COPD' had two presentations which were not fully transparent about the results from a meta-analysis of triple combination products for COPD. The first one was titled, 'Are all triple therapies the same? Learning from head-to-head and indirect comparisons', and the second talk was titled 'Real-world evidence on triple therapy: what have we learned?'. The complainant alleged that in the two talks, it was incorrectly stipulated that Trelegy had shown superior exacerbation reduction vs Trimbow as part of a weak meta-analysis data pack. However, this was not correct as the P-value was not statistically significant. Despite this statistical failure, the sessions projected that Trixeo was superior to Trimbow. There was a breach of Clauses 6.1, 6.2, 5.1 and 2.

When writing to GSK, the Authority asked it to consider the requirements of Clauses 2 (x2), 5.1 (x2), 6.1, 6.2, 9.4 and 15.6 of the Code.

RESPONSE

GSK stated that the complainant alleged several breaches against two separate activities which took place at ERS in Barcelona in September 2022. GSK responded to the allegations under each activity below.

1 Interactions of GSK MSLs with health professionals on a promotional stand, specifically soliciting questions on GSK products.

As specifically requested by the PMCPA, in addition to the company's response, GSK provided the following evidence:

- Details of the arrangements for GSK's exhibition stand(s) (copies provided).

- Any briefing(s) provided to company attendees, including for MSLs, at the European Respiratory Society in September 2022 (copies provided).
- Details of the MSL role and whether the MSLs had/required the ABPI representatives' exam (copies provided).

Congress context and how GSK prepared and trained the staff attending.

GSK stated that the ERS was the world's largest respiratory meeting, where over 20,000 delegates came together to present and discuss the latest scientific and clinical advances across the entire field of respiratory medicine. In 2022, the ERS congress was held in Barcelona. GSK had extensive experience participating at ERS congress due to the company's heritage in respiratory disease.

Different GSK therapeutic areas joined to participate at ERS 2022, according to the congress's scientific focus, with UK MSLs attending. All staff, including these MSLs, were briefed on their accountabilities in relation to ERS.

GSK stated that as context for the complainant, it was worth noting that the MSL role at GSK was a non-promotional role. As per the MSL job description, the role of an MSL was to 'foster a more educated healthcare environment by firstly communicating their deep knowledge of GSK data in the context of overall patient care to ensure evidence-based understanding of the science behind GSK medicines and vaccines and secondly gathering valuable insights on GSK products and services, and on medical and scientific information to better understand patient needs and evidence gaps'. All MSLs had a scientific background. GSK MSLs were not required to take the ABPI representatives' examination. GSK MSLs had ongoing and mandatory training to ensure they understood their role and GSK confirmed that the relevant MSLs were up-to-date with their training at the time of ERS.

GSK stated that it went to great lengths to ensure the distinct roles of the MSL and promotional representatives remained separate. In addition to the points raised above, specifically for ERS, GSK did the following:

- GSK sponsored two booths at ERS, one commercial booth and one medical booth. The GSK briefing pack showed the layout of the exhibition hall and relative location of both GSK booths, with a walkway separating the booths. The commercial booth was designed for the promotion of licensed GSK medicines in accordance with the Code and local regulations. The medical booth was designed to facilitate legitimate medical and scientific exchange with health professionals and did not have any branded material or brand names. It was noteworthy that while GSK MSLs had a separate area for scientific exchange, GSK MSLs had access to all areas within the congress, and might have been physically present on the commercial booth. However, as per the briefing detailed below, GSK MSLs were further instructed on the non-promotional nature of their role, how to conduct legitimate scientific exchange and to avoid inappropriate engagements with health professionals in the congress.

- All GSK staff attending ERS were briefed extensively. All briefing slides were distributed to GSK staff attending ERS:

    - **Mandatory GSK global briefing in Barcelona, for all GSK medical and commercial staff**:

- This detailed the appropriate engagement with health professionals.
- The function of the medical booth and role of MSLs in managing unsolicited questions.
- GSK could confirm all MSLs attended.

- **Mandatory UK staff briefing for General Medical**:

  - This contained the medical rota for the medical stand.
  - Governance principles of transparency with health professionals (all GSK medical staff had name badges with 'GSK Medical' on them), activities which MSLs could engage in, where conversations could take place and the avoidance of using the commercial booth or being around commercial colleagues when engaging with health professionals.

- **Severe asthma briefing meeting over teams re Medical Booth** :

  - This covered governance principles of transparency with health professionals (all GSK medical staff had name badges), activities which MSLs could engage in, where conversations could take place and the avoidance of using the commercial booth or being around commercial colleagues when engaging with health professionals.

GSK stated that it had discussed this complaint with the MSLs in question and found no evidence to corroborate the views of the complainant.

In summary, while GSK could not comment on whether GSK MSLs were seen on the commercial stand, the company confirmed that there was no evidence of inappropriate behaviour of GSK MSLs soliciting questions from health professionals about GSK products. GSK UK MSLs in attendance at ERS were extensively trained on the non-promotional nature of their role, and what activities were appropriate for them to conduct, both with regard to their day-to-day activities in the UK and specifically at the 2022 ERS congress in Barcelona. GSK had a clear, separate, non-promotional, non-product-branded medical stand for legitimate MSL activities to take place. GSK noted that the complainant had provided no material evidence that GSK UK MSLs were soliciting questions from health professionals on the GSK promotional stand at ERS. Based on the evidence above and the lack of evidence supplied by the complainant, GSK respectfully and strongly refuted the alleged breaches of Clauses 9.4, 5.1, 15.6 and 2.

2 Health professional challenge on the content of the presentations at the ERS 2022 GSK Industry Symposium – September 2022:

As supporting evidence, GSK noted the PMCPA request and had provided:

- an original or good quality colour copy of the symposium material available to those who were invited;
- a copy of the certificate approving the material in question and

- copies of all references cited in GSK's response and a copy of the relevant summary of product characteristics (SPC).

GSK confirmed that a GSK symposium was held in September 2022 at ERS entitled '**How molecular pharmacology is improving patient outcomes in COPD**'. This was part of the ERS sponsored symposia series and appeared on the ERS programme. It consisted of:

- **Co-chair's introduction** by [first named Professor] and [first named Doctor] (GSK employee).
- **Efficacy by design: from pharmacology to effective therapy** by [second named doctor].
- **Are all triple therapies the same? Learning from head-to-head and indirect comparisons** by [second named Professor].
- **Real-world evidence on triple therapy: what have we learned?** By [third named Professor].
- **Panel discussion and live Q&A**. Facilitated by [first named Professor] and [first named Doctor].

All slides, in their final form, were reviewed and certified in accordance with the ABPI and local requirements by a qualified ABPI signatory. Of note, as per GSK's processes, this material also underwent review as documented on the approval certificate.

The complainant alleged that GSK 'had two presentations which were not fully transparent about the results from a meta-analysis of triple combination products for COPD', citing the talks given by [second named Professor] and the [third named Professor]. Specifically, a claim that 'it was incorrectly stipulated that Trelegy had shown superior exacerbation reduction vs Trimbow as part of a weak meta-analysis data pack. However, this was not correct as the P value was not statistically significant'. The complainant further asserted that 'Despite this statistical failure, the sessions projected that Trixeo was superior to Trimbow'.

GSK stated that it confirmed the talk by [named third Professor] entitled '**Real-world evidence on triple therapy: what have we learned?**' did not include any slides on a network meta-analysis, nor mentioned either medicine Trimbow or Trixeo.

Regarding the talk by the [second named Professor] '**Are all triple therapies the same? Learning from head-to-head and indirect comparisons,**' the first half of this presentation highlighted data from a range of comparator studies, either dual combination therapies or components of other single inhaler triple therapies (SITTs) versus Trelegy (fluticasone furoate (FF)/umeclidinium (UMEC)/vilanterol (VI)). It was explained that despite these data, there remained an evidence gap, with currently no head-to-head data comparing FF/UMEC/VI with other SITT for patients with COPD. The talk then transitioned to discussing data from the 2022 Network Meta analysis (NMA) by Ismaila *et al* within the context of no head-to-head alternatives. The presentation explained the methodology used in conducting an NMA, the design of the Ismaila NMA, results on forest plots taken directly from the source publication, the limitations of the Ismaila NMA and a summary slide.

The NMA in question was originally presented at the 2022 Annual meeting of the American Thoracic Society (ATS) in poster format:

- Network meta-analysis of the efficacy of fluticasone furoate/umeclidinium/vilanterol

(FF/UMEC/VI) versus other triple therapies for the treatment of chronic obstructive pulmonary disease (COPD): A comparison of annual moderate and severe exacerbations (Ismaila A *et al*, ATS 2022, Poster. P478).

- Comparative efficacy of fluticasone furoate/umeclidinium/vilanterol (FF/UMEC/VI) versus other triple therapies for the treatment of chronic obstructive pulmonary disease (COPD): A systematic literature review and network meta-analysis. (Ismaila A *et al*, ATS 2022, Poster. P649).

The NMA was subsequently published containing additional detail in the high index scientific journal: Advances in Therapy (Ismaila AS*et al*. Adv Ther 2022.

All slides were fully referenced, all comparisons were fully substantiated. All slides contained a footer:

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

The limitations of the NMA were discussed by the presenter immediately after the results section.

All results displayed a corresponding p-value, and the summary slide made it clear that the reduced risk of moderate and severe exacerbations on Trelegy (FF/UMEC/VI) versus Trimbow (beclomethasone dipropionate (BDP)/formoterol fumarate dihydrate FOR)/glycopyrronium (GLY)) was not statistically significant. 'Numerically greater reduction' and NS (Not Significant) were adjacent to the data.

Excerpt from summary slide:

- 'Compared with other SITT, FF/UMEC/VI SITT showed.....
  Reduced risk of moderate and severe exacerbations ...
  …
  Numerically greater reduction vs BDP/FOR/GLY160/6/12.5 (IRR was 0.73, NS, p=0.0774).'

The reduced risk of moderate and severe exacerbations on Trelegy (FF/UMEC/VI) versus Trixeo (budesonide BUD)/ glycopyrronium bromide (GLY)/formoterol fumarate dihydrate (FOR)) at two different doses was statistically significant.

Excerpt from summary slide:

- 'Compared with other SITT, FF/UMEC/VI SITT showed ...
  Significantly greater reduction in annualised exacerbation rate, compared with BUD/GLY/FOR 320/18/9.6 (IRR was 0.62, p=0.0044) and BUD/GLY/FOR 160/18/9.6 (IRR was 0.61, p=0.0034)'

There was no comparison made directly between Trimbow (BDP/FOR/GLY) and Trixeo (BUD/GLY/FOR) as the complainant suggested.

As further evidence and reassurance of GSK's balanced tone in comparator data presentation, GSK provided the transcript of the [second named Professor's] presentation with the relevant NMA-related statements highlighted and the downloaded videos footage of the symposium talk given by the [second named Professor] which was available to ERS-registered health professionals on the 2022 ERS platform.

The transcript associated with the NMA results demonstrated in various places (text in bold below) the presenter's careful presentation of the data:

- 'So these are the forest plots that now show you the trough FEV1 if you want values on the left side at Week 12, and on the right side at Week 24, Going through from top to bottom, you see there are comparisons with other triple treatments but also with dual treatments and also with tiotropium alone. So, this is the line of identity: on this side this would favour triple treatment with comparisons, 12 weeks and at 24 weeks, triple treatment with FF/UMEC/VI **seems to** be superior versus alternative therapies'.

- 'Similar analysis was performed regarding exacerbation. So here you see the combination of moderate and severe exacerbation: on the left side all studies, on the right side the studies with at least 24 weeks of follow identity FF/UMEC/VI **seems to be** superior; **the right side would favour comparator**. And as you can see for **most of these comparisons**, it **looks like** FF/UMEC/VI **gets to a better** exacerbation prevention signal than the comparators'.

This was reiterated in the summary slide, where the results were individualised to one or other of the alternate single inhaler triple therapies licensed.

- 'Now let me summarise what I've shown to you. This Network Meta Analysis that I've shared with you showed, compared with other as SITTs, the combination FF/UMEC/VI **seems to be** superior, statistically superior regarding trough FEV1 at 12 weeks and 24 weeks compared to **two other comparators** for 12 weeks. And at 24 weeks **for one comparator** with two different doses of the ICS. In addition to that, there was a reduced risk of moderate and severe exacerbations regarding the annualised exacerbation rate compared with **another triple** with two different doses of ICS'.

Based on the evidence presented, GSK strongly refuted the alleged breaches of Clauses 6.1, 6.2, 5.1 and 2.

In summary, GSK denied any breaches of the Code in respect of this case.

PANEL RULING

The Panel noted that the complaint concerned two separate matters, firstly, the conduct of the GSK UK MSL team at the European Respiratory Society meeting held in Barcelona in September 2022, and secondly, allegedly misleading and unsubstantiated claims made during a GSK sponsored symposium at that meeting.

1 MSL interactions with health professionals on a promotional stand

The Panel noted that the complainant alleged that the presence of the MSLs on the promotional booth amounted to soliciting enquiries from health professionals and was thus disguised promotion which constituted a breach of Clause 15.6. It further noted that a breach of Clause 9.4 was alleged on the basis that the presence of the MSLs on the promotional stand was inappropriate as none of them had taken the ABPI examination for representatives.

The Panel noted GSK's submission that it went to great lengths to ensure that the distinct roles of non-promotional MSLs and promotional representatives were kept separate and confirmed that the role of MSLs at GSK was entirely non-promotional. The Panel noted that, according to GSK, the individuals concerned were up-to-date with their mandatory training to ensure that they understood their role.

The Panel noted that GSK did not dispute that the UK MSLs might have been present on the commercial stand as they had access to all areas of the congress. It also noted GSK's submission that when discussing the complaint with the MSLs in question it found no evidence to corroborate the allegations. The Panel noted that all GSK medical staff had name badges with 'GSK Medical' on them, but further considered that, irrespective of the name badges, any substantive interactions with health professionals that took place as an integral part of a commercial stand might be considered promotional and have to comply with the relevant requirements of the Code.

The Panel noted GSK's submission that it had two separate booths at ERS, a large promotional booth and a smaller medical one designed to facilitate legitimate medical and scientific exchange with health professionals and which did not have any branded materials or display any brand names. The Panel noted that the two booths were adjacent to each other but were separated by a walkway in between.

The Panel noted that the GSK MSLs attending ERS had been briefed on different aspects of the meeting. According to GSK, all MSLs attended the global briefing 'ERS Booth Customer Experience' which stated 'Remember the distinction between promotion and scientific exchange' and slides covered the medical booth detailing the nature of questions within the scope of the medical booth and how to respond. A separate briefing session for UK general medical staff attending ERS was described as mandatory but it appeared that some UK MSLs had not attended this session. This was concerning given that global and UK functions might interpret certain terms differently. For instance, it was unclear whether the reference to legitimate scientific exchange in the global briefing was consistent with the reference to the legitimate exchange of medical and scientific information during the development of a medicine in the supplementary information to Clause 3.1 of the Code. The Panel noted that a slide in the briefing for general medical staff attending ERS stated that the medical team were permitted to have proactive non-promotional meetings/interactions via usual rules of MSL engagement, but must make sure that they did not meet in the promotional area at the congress and that the sales/marketing teams were not present. A further briefing was provided for medical staff working in the severe asthma team but did not mention MSLs specifically or where discussions should and should not take place.

The Panel noted that the Constitution and Procedure stated that the complainant had the burden of proving their complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. GSK had provided some evidence to support its position that its MSLs were trained and clear about the non-promotional nature of their role. In the Panel's view, noting the definition of a representative at Clause 1.19 of the Code, the

complainant had not established that the MSLs had acted in a promotional capacity, as alleged, such that they were required to take an appropriate examination for medical representatives and the Panel, therefore, ruled **no breach of Clause 9.4**. Further, the Panel considered that given its finding above that the complainant had not established that GSK MSLs had acted in a promotional capacity, it therefore could not be established that their activities were disguised in this regard and **no breach of Clause 15.6 was ruled.**

In the light of its rulings of no breaches of the Code above, and whilst noting with concern that it appeared that not all MSLs had attended the mandatory UK briefing, the Panel did not consider that the complainant had established that GSK had failed to maintain high standards in relation to the matters alleged, or that its actions had brought discredit upon, or reduced confidence in, the pharmaceutical industry. The Panel ruled **no breach of Clauses 5.1 and 2**.

2 Alleged misleading and unsubstantiated claims made in a GSK-sponsored symposium

The Panel noted the allegation that two presentations were not fully transparent about the results from a meta-analysis of triple combination products for COPD. The complainant noted that it was incorrectly stipulated that Trelegy had shown superior exacerbation reduction vs Trimbow as part of a weak meta-analysis data pack which was not correct as the P-value was not statistically significant. In addition, despite this statistical failure, two presentations projected that Trixeo was superior to Trimbow. The complainant alleged breaches of Clauses 6.1, 6.2, 5.1 and 2.

The Panel noted that triple therapy for COPD comprised an inhaled corticosteroid (ICS), a long-acting muscarinic antagonist (LAMA) and a long-acting β2 agonist (LABA) and could be delivered via a single device or multiple inhaler devices. At the time of the presentation single inhaler triple therapy products were available as combinations of either FF/UMEC/VI (Trelegy), BUD/GLY/FOR (Trixeo) or BDP/GLY/FOR (Trimbow).

The Panel noted that the symposium was titled 'How molecular pharmacology is improving patient outcomes in COPD' and consisted of three presentations with a Panel discussion and live Q & A. The complainant referred specifically to the second and third presentations. GSK provided the slides for both presentations and the transcript for the second presentation.

The Panel noted that the third presentation 'Real-world evidence on triple therapy: what have we learned?' did not include any slides on a network meta-analysis, nor mentioned either Trimbow or Trixeo. There was mention of Trelegy (FF/UMEC/VI) and reference to the INTREPID trial. However, whilst the complainant mentioned the title of the third presentation, the specific allegation did not appear to be relevant to the content of that presentation and, therefore, the Panel considered that the third presentation was not the subject matter of the complaint.

The Panel noted the second presentation 'Are all triple therapies the same? Learning from head-to-head and indirect comparisons,' provided an overview of the clinical trials underpinning the therapeutic area, including discussion of the ETHOS, IMPACT and INTREPID trials. The speaker highlighted that there was an evidence gap in that there were no head-to-head data comparing single inhaler triple therapies but that potential differences between medicines could be identified by undertaking a network meta-analysis where treatments and healthcare interventions were compared using data from separate studies. The speaker went on to present results from the network meta-analysis, Ismaila *et al*, which was the subject of the complaint.

The Panel noted 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 should 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 readers were given sufficient information to enable them to form their own opinion of the therapeutic value of the comparison.

The Panel noted the limitations of the Ismaila *et al* network meta-analysis; 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.

In relation to the limitations and the definitions of moderate and severe exacerbations in Ismaila *et al*, the Panel noted the study authors' comments 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. Consequently, the results of moderate and severe exacerbations were pooled to reduce the impact of the observed heterogeneity in definitions between trials. 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 noted that the complainant questioned whether the presentations were fully transparent about the results from the network meta-analysis and also GSK's submission that the language and tone of the comparator data presentation were careful and balanced. The Panel questioned whether the slides fairly reflected the caution expressed by the authors.

GSK submitted that all slides about the network meta-analysis contained a footnote, in bold text, that stated, 'Information from an indirect comparison made through a network meta-analysis; the limitations of these studies should be taken into account. Analysis is limited by differences in study design and patient characteristics between trials'. The Panel noted that, in addition, certain slides where the detailed efficacy and safety results were shown stated 'Information from an indirect comparison made through a network meta-analysis; the limitations of these studies should be taken into account. Analysis is limited by differences in study design and patient characteristics between trials. Network meta-analysis of 23 RCTs, informed by 17 trials reporting moderate/severe exacerbation endpoint, 5 trials reporting trough FEV_1 at 24 weeks and 15 trials reporting trough FEV_1 at 12 weeks, in adult COPD patients eligible for triple therapy. The analysis included single- and multiple-inhaler therapies ICS/LABA and LAMA/LABA, and tiotropium monotherapy. Analysis is limited by differences in study design and patient characteristics between trials'. This full footnote did not appear on the summary or conclusions slides which each referred to efficacy but contained the abridged version. The

Panel noted that it was an established principle under the Code that the main body of the material should be capable of standing alone in relation to the requirements of the Code and therefore any qualification required for Code compliance should form part of the main body of the material rather than being relegated to a footnote or similar. The Panel therefore queried whether it was appropriate to relegate certain information about the limitations of the NMA to a footnote in the slides.

The Panel considered that a similar principle applied when considering the slides in light of what was said by the speaker. Whilst comments by the speaker were relevant, in the Panel's view, the slides still needed to be capable of standing alone in relation to Code compliance.

The Panel noted that the slides discussed the NMA in relation to lung function, exacerbations, safety, limitations, summary and conclusions. In the Panel's view, the slides, and particularly those discussing the efficacy results, were text and data heavy such that it was likely that not all viewers would be able to adequately read and understand all the nuances including the footnotes.

The Panel noted that the primary endpoint was defined as the mean change from baseline in trough FEV_1 at 24 weeks and that annualised exacerbation rate was a secondary endpoint. The presentation contained one slide for each endpoint and showed forest plots illustrating the comparators within the scope of the network meta-analysis for each outcome. The slide relating to the exacerbation endpoint headed 'Network meta-analysis: FF/UMEC/VI provided greater improvements in annual rate of combined moderate and severe exacerbations than most comparators' included two forest plots, one showing data for all 18 comparators and the other a subset of 8 comparators with 24 or more weeks of follow-up. Both forest plots included the p-values of the results for each comparison and a vertical line showing the incidence rate ratio of 1.0 which indicated no difference between Trelegy and the comparator. The 95% confidence intervals were shown with those to the left of, and not crossing, the vertical line indicating statistical significance. All data for comparators with 24 weeks or more of follow-up was statistically significant.

On these endpoint slides the longer footnote described above was situated below a prominent blue bar containing either the claim 'FF/UMEC/VI SITT provided significantly greater improvements in trough FEV_1 versus other commonly used therapies, at weeks 12 and 24, suggesting favourable long-term efficacy of FF/UMEC/VI versus alternative therapies' in relation to the FEV endpoint or, in relation to the exacerbations endpoint, the claim 'FF/UMEC/VI SITT provided greater improvements in annual moderate and severe exacerbations versus other commonly used therapies, suggesting favourable long-term efficacy of FF/UMEC/VI'.

A slide headed 'Limitations of this study' summarised four key limitations, three of which the speaker explained the audience had to be aware of; that the network meta-analysis was limited by differences in study designs and patient populations, heterogeneity in the definitions of moderate and severe exacerbations across multiple studies but within acceptable limits to allow study comparisons, the limited number of studies and SITTs available for inclusion and that some comparisons were not feasible and could not be linked to the network of evidence due to the absence of a common comparator and insufficient data. This was followed by a summary slide of the results described above and a slide headed 'Conclusions'.

The Panel noted the allegations that the presentation incorrectly stipulated that Trelegy had shown superior exacerbation reduction versus Trimbow as part of a weak meta-analysis data

pack and that this was not correct as the p-value was not statistically significant, and that despite this statistical failure, the sessions projected that Trixeo was superior to Trimbow. In this regard, the Panel noted that Ismaila *et al* did not compare Trixeo to Trimbow.

The Panel noted the summary slide headed 'Summary of network meta-analysis findings' presented the results for the primary endpoint, the mean change from baseline in trough FEV_1, and the secondary endpoint relating to annualised combined moderate and severe exacerbation rates. The subheading read 'This network meta-analysis suggests that FF/UMEC/VI SITT provides favourable outcomes in comparison with LABA/LAMBA, ICS/LABA, MITT and other SITT'. Beneath in larger, and thus more prominent font size, in black and blue text, a further subheading read 'Compared with other SITT, FF/UMEC/VI SITT showed:'. The slide then used different colours and bold text to draw the readers' immediate attention to unequivocal claims including, in pink font, the sub-heading 'Reduced risk of moderate and severe exacerbations' and in light blue text, results that demonstrated statistical significance. In the Panel's view, attention was not drawn to the final bullet point which used neither emboldened text, nor colour to catch the reader's eye and read 'Numerically greater reductions vs BDP/FOR/GLY 160/6/12.5 (IRR was 0.73, NS, p=0.0774)'. The Panel on balance considered that, given the design of the slide including the eye-catching unequivocal pink subheadings that the primary message of the slide was of superiority. The Panel considered that this implication was potentially misleading and was not negated by the speaker. In addition, the Panel considered that in the event that a reader did note the final bullet point, there might be an implication that the numerical reduction referred to in that bullet point was of clinical significance and therefore that Trelegy was clinically, albeit not statistically, superior to Trimbow. The Panel noted that at the relevant time, and as shown in the presentation, there were only 3 SITTs available. The Panel considered that, in this context, it was particularly important within a slide that implied unequivocal superiority to be abundantly clear that the comparison with BDP/FOR/GLY 160/6/12.5 did not achieve statistical significance.

The Panel, noting its comments above about the SITT market, considered that the initial misleading impression of unequivocal superiority was compounded by the final conclusions slide which stated 'FF/UMEC/VI showed statistically significant improvement in trough FEV_1 and greater improvement in combined annualised moderate and severe exacerbation rates vs alternative therapies'.

Overall, and on balance, the Panel considered that the presentation was not a fair reflection of the study findings and that it did not give sufficient weight to the limitations of the study. Whilst the Panel noted the 'Limitations of this study' slide described above, it noted that slides had to be capable of standing alone in relation to the Code and considered that given the study was a NMA, signposting certain study limitations in footnotes, was not sufficient. 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 noted that it was an established principle under the Code that materials should provide sufficient information to enable recipients to form their own opinion of the therapeutic value of medicines.

The Panel was also concerned that the exacerbation data was not consistently and accurately described across the slides and considered that this was particularly important, given the study authors' comments referred to above about the substantial heterogeneity in the definition of

severe exacerbations and the pooling of moderate and severe exacerbation data to reduce the impact of the observed heterogeneity in definitions between trials. It was not always clear that the endpoint combined moderate and severe exacerbation data, for instance, this was not made clear in the subheading in pink font on the slide, 'Reduced risk of moderate and severe exacerbations'. Similar concerns applied to another slide. The Panel noted that it was not always clear that the exacerbation data related to the annualised exacerbation rate, which the Panel understood to be a fixed measure of exacerbation frequency and, in this regard, again noted the pink subheading on the slide referred to above.

The Panel noted its comments above and considered that, overall, and on balance, the slides did not fairly reflect the data and, in addition, health professionals might be misled as to the clinical relevance of certain results presented. On balance, the Panel considered the presentation created a misleading impression which was incapable of substantiation and therefore ruled **breaches of Clauses 6.1 and 6.2**.

In the light of its comments and rulings above, the Panel considered that GSK had failed to maintain high standards and ruled **a breach of Clause 5.1**.

The Panel noted that Clause 2 was used as a sign of particular censure and reserved for such use. The Panel considered that the rulings of breaches above adequately covered this matter and an additional ruling of a breach of Clause 2 would be disproportionate in the particular circumstances of this case. The Panel, on balance, ruled **no breach of Clause 2**.

The Panel noted that the complainant had alleged that the sessions projected that Trixeo was superior to Trimbow, however, the Panel was unable to identify any instances of direct comparison between Trixeo and Trimbow and made no rulings in this respect.

Complaint received **16 November 2022**

Case completed **15 December 2023**