CASE AUTH/3916/5/24

EX-EMPLOYEE v ANGELINI

Allegations about company activities at a number of promotional meetings in the UK and internationally

CASE SUMMARY

This complaint consisted of numerous allegations relating to three promotional meetings and associated activities for Angelini's epilepsy medication, Ontozry (cenobamate).

In relation to the "Southern Epilepsy Forum Meeting", the complainant alleged that:

- **There was discussion at the meeting that was inconsistent with the marketing authorisation for cenobamate – specifically, "questions relating to the use of cenobamate in unlicensed patient groups were asked by a HCP attendee, and a response detailing such use was provided by a contracted HCP speaker".**
- **The meeting slides were not certified prior to the start of the meeting.**
- **These concerns were raised with senior leaders following the meeting but the actions taken did not specifically address the concerns raised around company culture and the importance of adherence to company SOPs and the Code.**

In relation to the "Southern Epilepsy Forum Meeting", the outcome under the 2021 Code was:

Breach of Clause 11.2	**Promoting a medicine for an unlicensed indication**

No Breach of Clause 5.1	**Requirement to maintain high standards at all times**
No Breach of Clause 8.1	**Requirement to certify promotional material**

In relation to one of a series of "Cenobamate Roadshow" meetings, the complainant alleged that:

- **Cenobamate was promoted outside of its marketing authorisation: the use of cenobamate as a monotherapy (rather than as an adjunctive, as licensed) was discussed in the Q&A section of the meeting.**
- **There were no attempts to report mentioned off-label use as adverse events, in line with SOPs and one of the key principles of the Code.**
- **The meeting slides had not been certified.**
- **These concerns were raised with senior employees following the meeting but no action was taken to mitigate such actions at subsequent meetings, or to address the concerns raised around company culture and the importance of adherence to company SOPs and the Code.**

In relation to the "Cenobamate Roadshow" meeting, the outcome under the 2021 Code was:

No Breach of Clause 5.1 (x2)	**Requirement to maintain high standards at all times**
No Breach of Clause 8.1	**Requirement to certify promotional material**
No Breach of Clause 11.2	**Requirement not to promote a medicine for an unlicensed indication**

The complainant made numerous allegations about the "From Now ON" meeting and its associated online platform.

In relation to two on-street banners, the complainant alleged that:

- **By placing these banners outside the meeting venue, Ontozry had been promoted to the public.**
- **The two banners had not been certified for use.**

In relation to the on-street banners, the outcome under the 2021 Code was:

Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 8.1 (x2)	**Failing to certify promotional material**

No Breach of Clause 3.2 (x2)	**Requirement not to advertise prescription only medicines to the public**
No Breach of Clause 3.4 (x2)	**Requirement that companies must comply with all applicable codes, laws and regulations to which they are subject**
No Breach of Clause 26.1 (x2)	**Requirement not to advertise prescription only medicines to the public**

In relation to a presentation on the first day of the "From Now ON" meeting, the complainant alleged that:

- **The speaker advocated for the use of cenobamate as a monotherapy.**
- **The speaker disparaged the European Medicines Agency (EMA) and questioned the competence of the organisation when it came to granting the appropriate marketing authorisation for a medicine.**
- **Reference to the EMA, as the licensing authority, was a breach of the Code.**
- **For a pharmaceutical company to disparage and undermine the competence of a licensing authority in a promotional meeting to a group of UK health professionals brought discredit upon, and reduced confidence in, the pharmaceutical industry.**
- **Inadequate briefing of speakers meant that high standards had not been maintained.**
- **No action was taken to correct the statements made by the speaker, which also meant that high standards had not been maintained.**
- **These allegations also applied to the video recording of the presentation, made available via the online platform.**

In relation to this presentation on the first day of the "From Now ON" meeting, the outcome under the 2021 Code was:

Breach of Clause 2 (x2)	**Bringing discredit upon, and reducing confidence in, the pharmaceutical industry**
Breach of Clause 5.1 (x2)	**Failing to maintain high standards**
Breach of Clause 11.2 (x2)	**Promoting a medicine for an unlicensed indication**
Breach of Clause 15.2 (x2)	**Including a reference to the licensing authority when this was not specifically required by the licensing authority**

In relation to a "social sharing session" on the second day of the "From Now ON" meeting, the complainant alleged that:

- **The speakers were briefed verbally and were told that, while their slides should be consistent with the marketing authorisation for cenobamate, they would not be stopped from speaking about their experience with cenobamate that was inconsistent with the marketing authorisation**
- **When attendees asked questions relating to use of cenobamate outside of its marketing authorisation, Angelini employees gave verbal approval for the speakers to respond. The speakers told the five groups of attendees about their use of cenobamate in ways that were inconsistent with the marketing authorisation, specifically:**
  - **in paediatric patients**
  - **as a monotherapy treatment**
  - **in pregnant patients**
- **Important safety information from section 4.6 of the summary of product characteristics ("Fertility, Pregnancy and Lactation") was not provided to attendees while discussing the use of cenobamate in these patient groups.**
- **There were no attempts to collect adverse event reports from either the health professionals in attendance or speakers discussing such use. This was not in line with company SOPs or the ABPI principles, and prejudiced patient safety.**

In relation to the "social sharing session" of the "From Now ON" meeting, the outcome under the 2021 Code was:

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 at all times**
No Breach of Clause 6.1	**Requirement that information, claims and comparisons must be accurate, balanced, fair, objective, up-to-date and unambiguous**
No Breach of Clause 11.2	**Requirement not to promote a medicine for an unlicensed indication**

In relation to the "From Now ON" online platform, the complainant alleged that:

- **The videos and slide sets had not been certified in line with the requirements of Clause 8.1.**
- **They did not have an adverse event reporting statement.**
- **The slides did not have UK prescribing information.**

In relation to the "From Now ON" online platform, which included 18 downloadable sets of slides and two viewable videos, the outcome under the 2021 Code was:

Breach of Clause 5.1	**Failing to maintain high standards**
Breach of Clause 8.1 (x15)	**Failing to certify promotional material**
Breach of Clause 12.1 (x13)	**Failing to include prescribing information**
Breach of Clause 12.9 (x13)	**Failing to include the adverse event reporting statement**

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 8.1 (x4)	**Requirement to certify promotional material**
No Breach of Clause 12.1 (x5)	**Requirement to include prescribing information**
No Breach of Clause 12.9 (x5)	**Requirement that all promotional material must include the adverse event reporting statement**

In relation to the "From Now ON" meeting, the complainant alleged that:

- **They had raised their concerns "with senior members of the Angelini Pharma UK-I leadership team at the event" and with a senior medical employee and a global senior compliance employee following the event.**
- **Whilst there is a policy in place at Angelini Pharma with regards to whistleblowing and speaking up, in practice when this policy is exercised, concerns are denied and corrective and preventative actions cannot be considered.**

In relation to these allegations, the outcome under the 2021 Code was:

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**

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 about Angelini Pharma UK-I Limited was received from a contactable complainant who described themselves as a former employee.

COMPLAINT

The complaint wording is reproduced below:

"**Introduction**

I would like to report a series of breaches of the ABPI code of practice from a UK based Pharmaceutical Company, namely Angelini Pharma UK-I. The breaches are in relation to the activity of the company at a number of promotional meetings that took place in the UK, and internationally in 2023. The meetings pertain to the promotion of Ontozry (cenobamate), which has the following licensed indication:

*Ontozry is indicated for the **adjunctive treatment** of focal-onset seizures with or without secondary generalisation in **adult patients** with epilepsy who have not been adequately controlled despite treatment with at least 2 anti-epileptic medicinal products.*

The meetings in question were organised and funded by Angelini Pharma UK-I, and involved UK HCP speakers, and UK HCP attendees, and therefore the 2021 ABPI code of practice (henceforth referred to as the 'the code') applies to these activities.

At and following these events, Angelini Pharma UK-I breached the following clauses:

Clause 2 (x5)
Clause 3.2 (x2)
Clause 3.4 (x2)
Clause 5.1 (x10)
Clause 6.1 (x5)
Clause 8.1 (x24)
Clause 11.2 (x12)
Clause 12.1 (x18)
Clause 15.2 (x2)
Clause 26.1 (x2)

Following attempts to raise very serious breaches of the code within the organisation, and the failure of the organisation to address or acknowledge them, they have been brought for consideration to the PMCPA.

Please find the full details of the complaint below.

Background

A meeting titled the 'Southern Epilepsy Forum Meeting' was a promotional meeting, organised and funded by Angelini Pharma UK-I that took place on 21st April, 2023 in the UK. At this meeting, there was discussion that was inconsistent with the marketing

authorisation for cenobamate. Specifically, questions relating to the use of cenobamate in unlicensed patient groups were asked by a HCP attendee, and a response detailing such use was provided by a contracted HCP speaker. Additionally, the meeting slides were not certified prior to the start of the meeting. **This is a breach of clause 8.1 of the code.**

These concerns were raised to [two senior UK employees] following the meeting. The action taken was to update SOPs and produce a briefing document for HCP speakers at UK meetings, and not specifically address the concerns raised around company culture and the importance of adherence to company SOPs and the code.

The cenobamate 'Road Show' was a series of promotional meetings in the UK, organised and funded by Angelini Pharma UK-I that took place in June, 2023. They involved the use of international HCPs involved in the clinical development of the drug cenobamate. They were contracted as speakers to a UK HCP audience.

As in the 'Southern Epilepsy Forum Meeting' described above, promotion outside of marketing authorisation took place for cenobamate in the London stage of the promotional meeting. This was again in the Q&A section of the meeting, where the use of cenobamate as a monotherapy, rather than an adjunctive as is licensed, was discussed. This was despite the briefing documents being available for use with external HCP speakers. There were more than 10 Angelini Pharma UK-I members of staff present in this meeting, including members of the UK leadership team. None of which intervened to halt, discourage or redirect the discussion that was inconsistent with the product marketing authorisation to the medical affairs team, or to clarify the license of cenobamate at any stage. Additionally, no attempts to report mentioned off-label use as adverse events, in line with SOPs and one of the key principles of the code. The use of meeting slides that had not been certified were once again used in the meeting. **This is a breach of clause 8.1 of the code.**

This meeting was recorded, and an unedited video recording of the meeting can be provided by Angelini Pharma UK-I.

Again, these concerns were raised with the [two senior UK employees] following the meeting. No action was taken to prevent or mitigate such actions at subsequent meetings, or to address the concerns raised around company culture and the importance of adherence to company SOPs and the code.

The 'From Now ON' Meeting

The 'From Now ON' promotional meeting took place in Milan in November 2023, and was organised and funded by Angelini Pharma. The UK affiliate was involved in the organisation and development of the meeting, as it involved UK HCPs, as both speakers and attendees. The meeting took place over a number of days and travel and accommodation was organised and funded by Angelini Pharma for both UK HCP attendees and UK HCP speakers.

Promotion to the Public

There were a number of banners used to promote the event, and to direct the HCPs from the hotel to the venue. These were placed in areas that were accessible to the

general public, including directly outside of the meeting venue on a busy public street in an international business district. The banners state: ‘From Now ON: Charting a different course in epilepsy care’. Angelini Pharma UK-I have images of at least two of these banners in situ, which they will be able to provide. Please also see [attached file] for this image.

The banners identify the brand name ‘Ontozry’ by the use of ‘ON’ as an abbreviation for the brand name, and additionally have the Ontozry brand logo placed in the centre of the ‘O’ in the ‘ON’ in ‘From Now ON’. Ontozry is licensed for use in adult patients with epilepsy. These banners therefore promoted Ontozry, and were located on a busy street accessible to and in view of the general public. None of these banners were certified for use in line with ABPI code requirements. The use of these banners in this way is promotion of a prescription only medicine to the public, and a breach of the ABPI, EFPIA and Italian Farmaindustria Code, and therefore breaches the following clauses of the ABPI code:

Clause 26.1 (x2)
Clause 5.1 (x2)
Clause 8.1 (x2)
Clause 3.2 (x2)
Clause 3.4 (x2)

Disparaging the EMA and promotion inconsistent with Marketing Authorisation
During the promotional meeting, in a session relating to access to medicines, a contracted HCP speaker disparages the European Medicines Agency (EMA), and questions the competence of the organisation when it comes to granting the appropriate marketing authorisation for a medicine. The HCP speaker in question states ‘I do not like the European Medicines Agency’. [They continue], and refers to the EMA as ‘stupid’ because they approved cenobamate (the drug being promoted at the promotional meeting), as only being licensed as an ‘adjunctive’ to other treatments, rather than as a ‘monotherapy’ treatment. The contracted HCP speaker continues to say that ‘monotherapy was prevented by the EMA’ and continues to make a case that it is unjust, and an outlier amongst similar anti-seizure medications, and implies that its use as a monotherapy is acceptable for use. They then conclude that all anti-seizure medications are ‘predestined’ for monotherapy use, further advocating for its use as a monotherapy to the audience with UK HCPs.

Clause 11.2 of the code states that *‘The promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics…’*

This approval by the EMA is consistent with its use in randomised-controlled trials, the results of which were used for the licensing submission of the product. As cenobamate is licensed for use only as an adjunctive treatment, rather than as a monotherapy in the treatment of epilepsy, this is promotion of cenobamate that is inconsistent with the particulars listed in its summary of product characteristics. **Therefore, this is a breach of Clause 11.2 of the code.**

Clause 15.2 states: *‘Promotional material must not include any reference to…or the licensing authority…’*. As the EMA is the licensing authority for cenobamate in Northern

Ireland, and other European countries, any reference to this is a breach of the code. **Therefore, this is a breach of Clause 15.2 of the code.**

For a pharmaceutical company to disparage and to undermine the competence of a licensing authority, in the granting of a marketing authorisation, in a promotional meeting to a group of UK HCPs, is of particular censure. This brings discredit upon, and reduces confidence in the pharmaceutical industry. **This is a breach of Clause 2 of the code.**

As high standards were not maintained through inadequate briefing of HCP speakers, and no action taken to correct the statements made by the speaker, this is also a breach of **Clause 5.1 (x2)**.

This meeting was recorded, and as of January 2024 is available for UK HCPs to view on an online platform for the meeting. The clause breaches cited above also apply to their respective references in the videos on the online platform, and therefore further breaches of **Clauses 11.2, 15.2 and 2** apply. The video recording can be provided by Angelini Pharma as evidence to support the above code breaches.

Promotion inconsistent with Marketing Authorisation for cenobamate
On the second day of the 'From Now ON' promotional meeting between 9.30am and 12.00pm, there was a 'social sharing' session whereby HCP speakers shared their experience with cenobamate in an informal group session. There were 5 groups, where HCP speakers rotated and discussed their experience. The HCP speakers were briefed verbally to share their experience. They were told that whilst their presentation slides should be consistent with the marketing authorisation for cenobamate, they would not be stopped from speaking on their experience with cenobamate that is inconsistent with the marketing authorisation for cenobamate, even if it is not reflected in their meeting slides.

There were a number of questions from individual HCP attendees in relation to use of cenobamate outside of its marketing authorisation. The HCP speakers looked to the Angelini Pharma Employees that had briefed them for the meeting for an acknowledgement of approval, which they verbally received, and proceeded to inform UK HCP attendees of their use in patient groups that were inconsistent with the marketing authorisation of the product. Specifically, this was in relation to their use of cenobamate in paediatric patients, and as a monotherapy treatment. Additionally, experience of the use of cenobamate in pregnant patients was discussed. This was verbalised on five different occasions, amongst five different groups each of around 20 HCPs, including those from the UK. HCPs that were in attendance also shared their experience of the use of cenobamate in these patient groups. I suspect that these sessions were deliberately not made available on the online platform by Angelini Pharma due to the promotion of the use of cenobamate in the manner described above. However, recordings are likely to be available.

This is a breach of clause 11.2 (x5)

The SPC for cenobamate states under section 4.6 Fertility, Pregnancy and Lactation:

*'**Women of childbearing potential and contraception in males and females***

Cenobamate is not recommended in women of childbearing potential not using contraception. Women of reproductive potential concomitantly using oral contraceptives should practice additional or alternative non-hormonal measures of birth control during treatment with cenobamate and until 4 weeks after treatment discontinuation (see section 4.5).

Pregnancy

Risk related to epilepsy and antiepileptic medicinal products in general

It has been shown that in the offspring of treated women with epilepsy, the prevalence of malformations is two to three times greater than the rate of approximately 3% in the general population. In the treated population, an increase in malformations has been noted with polytherapy; however, the extent to which the treatment and/or the underlying condition is responsible has not been elucidated. Discontinuation of anti-epileptic treatments may result in exacerbation of the disease which could be harmful to the mother and the foetus.

Risk related to cenobamate

There are no adequate data from the use of Ontozry in pregnant women.

Animal studies have shown that cenobamate crosses the placenta of rats. Studies in animals have shown reproductive toxicity at levels below clinical exposure (see section 5.3). Ontozry should not be used during pregnancy unless the clinical condition of the woman requires treatment with cenobamate. Women of childbearing potential must use effective contraception during use of cenobamate and until 4 weeks after treatment discontinuation (see section 4.5).

Breast-feeding

It is unknown whether cenobamate or its metabolites are excreted in human milk. Studies in rats showed excretion of cenobamate in the maternal milk (see section 5.3). A risk to the suckling child cannot be excluded. As a precautionary measure, breast-feeding should be discontinued during treatment with Ontozry.

Fertility

The effects of cenobamate on human fertility are unknown. Animal data are insufficient due to exposure below clinical levels (see section 5.3).'

This important safety information was not provided or presented to attendees of the meeting whilst discussing the use of cenobamate in these patient groups. This resulted in an unbalanced presentation of the data for the product in this patient group, and doesn't reflect the clinical evidence documented in the SPC for the product, whilst also

prejudicing patient safety in a particularly vulnerable patient group. **This is a breach of clauses 5.1 (x5), 6.1 (x5) and 2 of the code**.

Additionally, this promotion is inconsistent with the marketing authorisation for the product. **This is a breach of clause 11.2 (x5)**

There were no attempts to collect adverse event reports from either the HCPs in attendance, or speakers discussing such use.

One of the key principles of the ABPI code of practice states: *'We act promptly when advised of adverse events and encourage the use of the MHRA Yellow Card Scheme to support patient safety.'* As this was not followed in line with their own company SOPs, and has prejudiced patient safety, this is of particular censure and **therefore a breach of clause 2 of the code**.

The 'From Now ON' Online Platform
Immediately following the meeting there were 2 videos, and 18 slide sets from the 'From Now ON' meeting available on an online platform for UK HCPs to view, and to download in the case of the slides. As of January 2024, these have not been certified in line with the requirements of clause 8.1, or have an adverse event reporting statement as required in clause 12.9. Additionally, the slides do not have UK prescribing information with them despite being promotional or associated with a promotional meeting, as required in clause 12.1.

Angelini Pharma UK-I has therefore breached clause 8.1 (x20), clause 12.1 (x18), and clause 12.9 (x18) of the code.

Internal Reporting of Non-Compliance

The breaches of the ABPI code that were identified at this meeting, were raised with senior members of the Angelini Pharma UK-I leadership team at the event, who expressed no concern. There was a belief amongst the leadership team that such practice during meetings is acceptable, as they believed that they were attending an international congress meeting, and such activity is acceptable at an international congress meeting. There was also a belief that such activity was acceptable in Italy. None of which is correct.

The concerns around the activity were raised again with the [senior UK medical employee] following the event, who after some consideration recommended that a subordinate should raise the code breaches to the [global senior compliance employee]. Reporting of non-compliance to the [global senior compliance employee] is consistent with the Angelini Pharma Whistleblowing policy. Certain breaches of the ABPI code that were identified at the meeting, that would also be breaches of the EFPIA code of conduct and the Italian Farmaindustria Code, were highlighted to the [global senior compliance employee], in the hope that these concerns would be more likely to resonate with an Italy based colleague. This included the image [provided] that clearly shows promotion of a prescription only medicine to the public. The [global senior compliance employee] responded by indicating that after investigating internally, it was found that there was no non-compliance at the event. This was simply not the case, as can be seen in the [photograph provided].

The email raising this concern to the [global senior compliance employee] and their subsequent response, in addition to the Whistleblowing Policy can be provided by Angelini Pharma UK-I. The email can be seen [in the attached file].

Following the response from the [global senior compliance employee], the senior leadership team of the UK organisation considered the activity at the 'From Now ON' meeting to be acceptable, and plan to continue to fund, organise and contribute UK HCPs to this and other such meetings and activities in future.

The PMCPA's 'Guidelines on Company Procedures Relating to the ABPI Code of Practice for the Pharmaceutical Industry' states:

Companies should strongly encourage a speak up culture and ensure that staff are confident to speak up and encouraged to do so. In addition to informal conversations, access to confidential resources should be available and regularly communicated to staff including details of the company whistleblowing policy.

c Correction: When a compliance issue is identified, (whether reported informally, via a speak up line, through monitoring activity (as above) etc) it should be responded to quickly and thoroughly. Corrective actions should be developed, implemented, and tracked to confirm they have been effective and should, as far as possible, ensure similar issues do not happen in the future. Corrective actions implemented should be documented and held on record.

Whilst there is a policy in place at Angelini Pharma with regards to whistleblowing and speaking up, in practice when this policy is exercised, concerns are denied and corrective and preventative actions cannot be considered. Every level of management in an organisation choosing to overlook the intentional code breaches documented in this report, despite observing them and receiving internal reports regarding them, is conduct falling far short of the standards expected in the pharmaceutical industry, is not in the spirit of the code and drastically reduces confidence in the industry. **This is a breach of clauses 5.1 and 2 of the code.**

Conclusion

The activity of Angelini Pharma UK-I at, and following a series of meetings in 2023, has resulted in the following breaches of the code:

Clause 2 (x5)
Clause 3.2 (x2)
Clause 3.4 (x2)
Clause 5.1 (x10)
Clause 6.1 (x5)
Clause 8.1 (x24)
Clause 11.2 (x12)
Clause 12.1 (x18)
Clause 15.2 (x2)
Clause 26.1 (x2)

> Angelini Pharma UK-I has a culture of proactive non-compliance, which persistently attempts to subvert the code and their own SOPs, to gain a competitive advantage, at the detriment of patient safety and discredit of the industry. Following the attempts to escalate these many very serious breaches of the ABPI code within the organisation as cited in this report, and the failure of the organisation to address or acknowledge them, they have been brought for consideration to the PMCPA."

When writing to Angelini, the PMCPA asked it to consider the requirements of Clauses 2, 3.2, 3.4, 5.1, 6.1, 8.1, 9.2, 11.2, 12.1, 12.9, 15.2, and 26.1 of the 2021 Code.

ANGELINI'S RESPONSE

The response from Angelini is reproduced below:

> "Thank you for your letter of 5th July 2024 in respect of **Case AUTH/3916/5/24: Allegations about company activities at a number of promotional meetings in the UK and internationally in 2023.** I would additionally like to thank you for the extension granted to the normal reply timelines, given the scale of allegations and the international nature of some, the time of year and the fact that some international colleagues are on summer break.
>
> We note this complaint is from a (well regarded) former employee and while the detail provided clearly identifies the individual in question, that fact has not changed the nature of our reply. We have the greatest of respect for the individual concerned and their views, but respectfully disagree with many of their comments on this occasion.
>
> Angelini is a strong supporter of the ABPI Code welcomes all opportunities to learn from and to correct potential shortfalls in our processes. That said, the right of an individual to raise concerns or to have a different perspective to a pharmaceutical company does not necessarily equate to a breach of the Code by said company.
>
> Angelini denies the vast majority of alleged breaches. Our explanations are set out below.
>
> **Background to Epilepsy**
>
> Epilepsy is a difficult-to-treat therapy area. Patients with uncontrolled Epilepsy are commonly treated with multiple products, with newer treatments being used as 'add-on' to the existing regime.
>
> However, when adding more recently authorised efficacious medications like cenobamate that could potentially add to the burden of polytherapy on patients and increase the chances of drug-drug interactions. Thus, existing drugs are often down-titrated or even removed from a patient's regimen if the patient is responding well to the last added medication, so as to reduce side effects and improve quality of life. This may mean reducing the pill burden from 4-7 product to 1-3, meaning a patient may eventually end up on Monotherapy.
>
> Balancing the various combination doses across multiple treatments can often be an art rather than a science to ensure balance between efficacy and safety.

Angelini's licensed product for epilepsy is Ontozry (cenobamate).

Adopting early use of adjunctive cenobamate after the failure of at least two other antiseizure medications in the treatment pathway as authorised by the regulatory bodies could help in reducing this burden of polytherapy on patients. This should not be seen in any way as advocating for mono therapy treatment with Cenobamate,

Background to product

Ontozry (cenobamate) was launched in the UK in late 2021.

Ontozry is authorised by the MHRA in Great Britain as an adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite treatment with at least 2 anti-epileptic medicinal products.

In Northern Ireland and also for the Republic of Ireland the EMA indication is for the adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite a history of treatment with at least 2 anti-epileptic medicinal products.

Note: the three-word difference between the two licences in Great Britain and Northern Ireland is highlighted above in in italics: 'a history of'.

The recommended starting dose of cenobamate is 12.5 mg per day, titrated gradually to the recommended target dose of 200 mg per day. Based on clinical response, dose may be increased to a maximum of 400 mg per day.

In clinical practice, 100mg cenobamate may be used clinically as an assessment point to determine the best doses of each treatment when used in combination. This is why some slides and speakers refer to 100mg cenobamate.

The recommended titration schedule is provided in table 1 of the SPC, which should not be exceeded because of the potential for serious adverse reactions (see section 4.8).

There is a reduced dosage and titration in elderly patients and in all forms of renal and hepatic impairment. Warnings include severe hepatic impairment; and end-stage renal impairment and dialysis.

Drug-drug Interactions include clobazam usage. Pharmacometric analyses of data from healthy subjects and patients predict that clobazam slightly increases cenobamate exposures (by 24%). No dose adjustment of cenobamate is required. Due to a possible increase in exposure of the active metabolite of clobazam (N-desmethylclobazam), related to the induction of CYP3A4 (formation) and the inhibition of CYP2C19 (elimination), the dose of clobazam may need to be reduced.

Like many epilepsy products, there is a registry for patients with concomitant pregnancy.

Background to Angelini approval systems
Angelini uses a proprietary platform called 'Appian' to approve material and activities (similar to Veeva but a different platform).
Of importance is that the actual certification stage is a manual upload of a UK-specific Certificate – this is because the system is designed for international use and is not UK-specific. In practice, it means that while review is noted within Appian, the Certificate must be generated by the Signatory in Word and then saved and manually uploaded into the Appian system.

Where enhanced compliance or budgetary approval is required by someone who is not a registered Final Signatory, the Certified document is subsequently entered into DocuSign for an additional round of approval. This might be the case, for example, when the General Manager is required to approve SOPs or significant budget spend.

In particular, all Need Assessment Forms (Effectively Project initiation documents) must be signed in DocuSign.

It may be important to note that in practice many Events are subject to multiple rounds of approval as additional information is added and confirmed over time, from early concept to final details.

Please also note that a timestamp does not appear on the actual Certificate; but is visible in the Appian system. For additional background, the time clock is set to Central European Time (CET).

Background to cross border activities
Whenever there is an intention for a UK resident to attend an international event, a needs Assessment process is followed. An example of this can be seen in the From Now On event. The Global team raises a 'Cross Border Activity' which includes details of the event and agenda; and includes proposed fees for speakers and appropriate hospitality (etc) for speakers and delegates. This is reviewed by members of the UK medical or compliance teams. A new Needs Assessment Form is then raised in the UK Appian approval system which is Certified by a UK Final Signatory.

Background to speaker briefing.
As noted above, a speaker briefing document was already in place for the Southern Epilepsy Meeting. Following that event, as part of the UK's continuous improvement programme, the [compliance employee] worked with the [senior medical employee] to create additional speaker briefing slides that are now used by members of the medical and compliance team to personally brief all speakers prior to each event. A copy of the new briefing slide deck is provided. Amongst other requirements, this deck specifically draws attention to the need to stay on label, to avoid references to the regulatory bodies and to refrain from disparagement.

General comments about the complaint
Angelini has provided all documentation requested and wider supporting material as appended files in the electronic transfer.

The documentation requested would seem to extend beyond the boundaries of the complaint and has caused considerable workload within the company. For example,

the PMCPA required us to provide multiple documents that are not subject to the complaint and will not add additional context, such as:

- Invitations to meetings
- Copies of material used at or after meetings that it is not subject to the complaint.
- Selection criteria for delegates
- Selection criteria for speakers
- Payment of the speakers
- A list of staff trained in AE reporting when the training is not part of the complaint.
- Copies of SOPs when there is no challenge to the SOP content:
    - A copy of the AE reporting SOP when the existence of the SOP is not part of the complaint.
    - Copy of the whistle-blowing SOP when the existence of the SOP is not part of the complaint.

Further, we do not feel that the addition of Clauses by the PMCPA is appropriate in this instance. The complainant is clearly experienced with the Code of practice and was very precise in the clause numbers cited. For the PMCPA to add clauses beyond 5.1 or 2 would seem to extend the scope of the original complaint. We understand this is appropriate when the complainant is external to the industry or not familiar with the Code, but in this instance, we feel it is unnecessary and inappropriate. We have responded to the additional clauses cited by the case Preparation Manager but feel they have extended their reasonable authority in this regard.

Complaint Part A: Southern Epilepsy Forum Meeting 21 April 2023 in the UK

This is a standalone meeting organised by Angelini UK. It ran over two days from 21st-22nd April 2023 and was held at the [hotel in the UK]. It was attended by 71 UK HCPs (in including 4 Faculty), all invited by Angelini UK.

All speakers were specifically engaged by Angelini UK, appropriately briefed and contracted.

All speaker slides were Certified prior to use as can be seen in the screenshot and appended files.

[Screenshot of ‘Final Signatory Certificate’ for UK17609P April 2023, titled ‘Southern Epilepsy Forum slide deck’. Date signed off: 21/04/2023]

The commercial objective of the event was to position our product Ontozry (cenobamate) appropriately for use in Epilepsy. The agenda reflects that objective.

All speakers were briefed to remain within the licensed indication and to submit slides in good time for Certification. Speaker contracts are provided. As can clearly be seen from the contracts, immediately after indicating the nature of the services to be provided the very next comment (paragraph 1(b) is a clear statement of the standards expected:

> *When performing the Services, Consultant will act in a professional manner and in accordance with (i) industry standards, (ii) the standard of care and diligence*

normally practiced when providing services of a similar nature and (iii) all relevant regulatory and ethical guidelines and all applicable laws and regulations.

The contract then details those standards in paragraph 7, including a requirement (7(j) to report adverse events.

As noted above, following this event, as part of the UK's continuous improvement programme, the [compliance employee] worked with the [senior medical employee] to create additional speaker briefing slides that were used by members of the medical and compliance team to personally brief all speakers at subsequent events. A copy of the new briefing slide deck is provided as it is relevant to the other events raised in the complaint.

Some delegates did receive travel and accommodation support to enable their attendance at this national meeting. Details are provided in the appended material.

All presented slides were within the licensed indication for Ontozry. Prescribing information was presented at the end of every product presentation and appropriate safety data was highlighted at key points on relevant slides.

After an initial company overview from our [senior UK employee], the first presentation by [named speaker] focused completely on Ontozry, provided a clear overview of the capabilities and limitations of the product, and set the scene for the subsequent presentations.

A key element of any meeting is the opportunity for the audience to ask questions of the presenters. On occasions those questions pertain to difficult-to-treat patients, which might be outside the licensed indication for the product. The Code notes the potential for such queries and allows for legitimate medical discussion on such matters so long as they are not promotional in tone and style. Answering a question with succinct, clear answers is not regarded as promotion; indeed, to avoid providing answers to such questions could risk inappropriate prescribing.

Angelini did not proactively initiate discussion on topics outside the licensed indication for the product.

It will be seen from the video that when a member of the audience asks an off-label question, the Angelini [medical employee] advises the audience that it is an off-label topic.

Please note that there is no specific clause referenced within the Complaint in relation to allegations of off-label promotion, but we hope we have addressed any concerns you may have in this regard. Indeed, the complainant's own text clearly indicates the discussion was prompted by audience members:

Specifically, questions relating to the use of cenobamate in unlicensed patient groups were asked by a HCP attendee, and a response detailing such use was provided by a contracted HCP speaker. Additionally, the meeting slides were not certified prior to the start of the meeting.

We note that the sole Clause referenced in relation to this event is Clause 8.1 (Certification). **Accordingly, we deny allegations related to clause 8.1 as we Certified all slides and as we did not proactively initiate conversation beyond the scope of the slides, i.e. all content was Certified.**

It may be relevant to note that the slides were Certified [redacted comment] on the day of the meeting immediately prior to the slides being presented. In fact, we delayed the start of the meeting to ensure the approval process was complete prior to presentations starting. The last-minute approval was owing to some speakers wishing to make final tweaks – this is an often annoying but typical element of any meeting and is why many companies ensure that a Signatory is present at the event itself. However, it also demonstrates the importance we place on compliance matters, especially such as Certification.

We note that the complainant highlights that improvements were made to company SOPs as a direct result of the meeting. The recommendation from the [compliance employee] was to update the and the briefing document used with speakers (and to update the SOP accordingly). This was agreed and completed by the [compliance employee] (please see updated SOPs briefing documents).

We believe that amendments such as this are in line with standard compliance and quality approaches, such as the Quality Circle, to implement continuous improvements in processes and documentation. I.E. updates are a foundational aspect of any compliance programme and do not see any issues in making enhancements based on experience and learning.

Complaint Part B: Cenobamate 'Road Show'

This description applies to a series of meetings in different towns during 12-15 June 2023: [named city] on 12th; [named city 2] on 13th; [named cities 3 and 4] satellite meeting on 14th; and [named city 5] on 15th. The agenda varied slightly on each occasion with different speakers, but all were built around a core presentation: *Assess learnings from US and Germany long term experience with Ontozry*; typically, with local speakers sharing case studies to show local experience.

All speakers were briefed (using the updated briefing slide deck created by the [compliance employee]) to remain within the licensed indication and to submit slides in good time for Certification (Briefing slides are included).

As previously indicated, since late April 2023, a member of the medical or compliance teams personally briefs each speaker using the provided briefing deck. Amongst other requirements, this deck specifically draws attention to the need to stay on label, to avoid references to the regulatory bodies and to refrain from disparagement.

Thus, all speakers were briefed to remain within the licensed indication and to submit slides in good time for Certification.

All speaker slides were Certified prior to use as can be seen in the screenshot and appended files). In fact, the slides were Certified [redacted comment] on the day of the meeting - immediately prior to the slides being presented. The near-event approval was owing to some speakers wishing to make final tweaks – this is an often annoying but

typical element of any meeting and is why many companies ensure that a Signatory is present at the event itself.

[Screenshot of 'Final Signatory Certificate' for UK18386P June 2023, titled 'June 2023 Roadshow (14-15th June 2023'. Date signed off: 14/06/2023]

Speaker contracts and briefings are provided to the PMCPA with the appended material.

As can clearly be seen from the contracts, immediately after indicating the nature of the services to be provided the very next comment (paragraph 1(b) is a clear statement of the standards expected:

> *When performing the Services, Consultant will act in a professional manner and in accordance with (i) industry standards, (ii) the standard of care and diligence normally practiced when providing services of a similar nature and (iii) all relevant regulatory and ethical guidelines and all applicable laws and regulations.*

The contract then details those standards in paragraph 7, including a requirement (7(j) to report adverse events.

All presented slides were within the licensed indication for Ontozry. Prescribing information was presented at the end of every product presentation and appropriate safety data was highlighted at key points on relevant slides.

As the complainant indicates, the meeting included a Q&A session:

> *promotion outside of marketing authorisation took place for cenobamate in the London stage of the promotional meeting. This was again in the Q&A section of the meeting, where the use of cenobamate as a monotherapy, rather than an adjunctive as is licensed, was discussed.*

As mentioned previously, a key element of any meeting is the opportunity for the audience to ask questions of the presenters. On occasions those questions pertain to difficult-to-treat patients, which might be outside the licensed indication for the product. The Code notes the potential for such queries and allows for legitimate medical discussion on such matters so long as they are not promotional in tone and style. Answering a question with succinct, clear answers is not regarded as promotion; indeed, to avoid providing answers to such questions could risk inappropriate prescribing.

Angelini did not proactively initiate discussion on topics outside the licensed indication for the product.

We note that the sole Clause raised in relation to this event is Clause 8.1 (Certification). **Accordingly, we deny allegations related to clause 8.1 as we Certified all slides and as we did not proactively initiate conversation beyond the scope of the slides, i.e. all content was Certified.**

We note comments from the complainant in respect of the collation of AE reports; however, the clause raised is 8.1, which does not address AE reporting. Accordingly, we are unclear what the complaint actually is (AE reports do not fall within the scope of

Clause 8.1 and are not certified). As previously mentioned, speaker contracts include specific references to AE reporting requirements in paragraph 7(j). However, we have no evidence that any attendee at the meeting actually said anything that would constitute a reportable adverse event – the asking of a question about a topic is a statement of a patient experience in the sense that it constitutes a reportable Adverse Event.

It should also be noted that the required MHRA AE reporting statement appears prominently and frequently throughout the slide decks. Additionally, the Angelini PV Lead was actually present at this event. Angelini trains (and tests) all staff in AE recognition and reporting on an annual basis. PV training materials and relevant training records are included in the Appended materials to this Response.

PV training materials are included in the Appended materials to this Response.

Comments were made by the complainant in relation to [their] 'raising of concerns' but the specific concerns are not provided in the complaint. Nor are we aware of changes to procedure that needed to be made following this event. Nor does this appear to be an actual Code-related complaint.

Complaint Part C: From Now On meeting

Background context
From Now On was an Angelini standalone meeting organised by the Angelini Global team for an international audience and was held in Milan on 28-29 November 2023.

The UK hosted 13 delegates to attend, providing accommodation, subsistence and travel support. In addition, two UK speakers ([named]) were engaged to present at the event, said individuals receiving a fee and associated accommodation travel and subsistence support.

Because of the differences in acceptable content across Europe, Angelini UK worked with the Global team to ensure the event was suitable for UK HCP attendance. Indeed, [compliance employee] was part of the UK team and was assigned to partner with the Global team to ensure UK compliance considerations were taken into account in the months leading up to the event; and was personally responsible for approving relevant materials from a UK perspective and in fact attended the event in person in their UK compliance capacity.

As previously indicated, whenever there is an intention for a UK resident to attend an international event, a needs Assessment process is followed. An example of this can be seen in the From Now On event. The Global team raises a 'Cross Border Activity' which includes details of the event and agenda; and includes proposed fees for speakers and hospitality (etc) for speakers and delegates. This is reviewed by members of the UK medical or compliance teams. A new Needs Assessment Form is then raised in the UK Appian approval system which is Certified by a UK Final Signatory. [Redacted comment].

As previously indicated, since late April 2023, speaker briefing slides are used by members of the medical and compliance team to personally brief all speakers prior to

each event. A copy of the new briefing slide deck is provided. Amongst other requirements, this deck specifically draws attention to the need to stay on label, to avoid references to the regulatory bodies and to refrain from disparagement. As [compliance employee] personally created this briefing deck and was specifically assigned to ensuring UK compliance considerations were taken into account for the From Now On meeting, it is highly likely that [they] personally ensured that all global speakers were briefed using this deck or now similar (although we cannot categorically confirm that).

As indicated, the two UK speakers were [named speaker] and [named speaker], who were joint presenters for one 35-minute session on Day 1. Technically, according to the UK Code, the slides presented by [named speaker] and [named speaker] are the only slides presented at this meeting where Certification is mandated by the UK Code, however, the UK Certified the entire slide deck, [redacted details about the signatory].

The provided Certificate (screenshot and appended file) clarify that the slides were Certified on 28th November. The initial documentation was an email from the Signatory (owing to an IT issue) which was then supplemented by an upload of the actual Certificate when the online system was functional again.

The second screenshot – from the Appian system shows that the file name indicates the intention to additionally use the deck within the portal 'slides for upload'. I.e. the slides were Certified to be used on the day and with the intention for their future use in digital materials such as the portal mentioned in the complaint.

[Screenshot of 'Final Signatory Certificate' for UK20841P November 2023, titled 'From Now ON Slides'. Date signed off: 28/11/2023]

[Screenshot from Appian system for UK20841P, showing (among other things) – Use Start Date: 23-11-2023, Description: "From Now ON Speaker Decks", Notes: "Speaker presentation decks for From Now ON Meeting in Milan 28th-29th November 2023. These presentations are created at global level but will be approved at local level. A placeholder will be uploaded first to get a job code to add to the decks.", Material Type: "Others", Channel: "Others", Document: All slides FNO for upload.pptx, Uploaded on: 28/11/2023]

Part C (1): Promotion to the public

It is alleged that external banners advertising the event outside the meeting venue constituted promotion to the public. It can clearly be seen from the photograph provided that the only link between the banner and the drug is an image incorporated within the 'O' in the meeting title.

The complainant alleges a breach of Clause 26.1 for promotion to the public for each banner. The public will not associate the image with the product. There is no other mention of the product on the banners. Accordingly, the banners are not promoting to the public and **Angelini rejects allegations relating to clause 26.1 of the ABPI Code**.

Since the allegation relates to promotion to the *public*, Certification is not appropriate under clause 8.1 of the Code. Accordingly, **Angelini rejects allegations relating to clause 8.1 of the ABPI Code**.

Since the allegation relates to promotion to the public and no product is identifiable to the public, there cannot have been any off-label promotion to the public. Accordingly, **Angelini rejects allegations relating to clause 3.2 of the ABPI Code**.

Since the allegation relates to promotion to the public and no product is identifiable to the public, there cannot have been any associated breaches of the Code in this regard. Accordingly, **Angelini rejects allegations relating to clause 3.4 of the ABPI Code**.

Since the allegation relates to promotion to the public and no product is identifiable to the public, there cannot have been any associated breaches of the Code in this regard. Standards were maintained. Accordingly, **Angelini also rejects allegations relating to clause 5.1 of the ABPI Code**.

Part C (2): Disparaging the EMA

The *From Now On* meeting covered a wide range of topics, including that of exploring barriers to the uptake of new medicines in epilepsy. This is a key area of debate amongst epilepsy specialists and a highly relevant topic. [Named speaker 1] leads this discussion (Timepoint 42:08 on video Angelini 28 Nov 23_pt03) and provides an international and US perspective, which includes reference to areas of potential improvement. For example, [Named speaker 1] highlights the need for improvements in industry/ academia interactions and industry/FDA Medical Education programmes.

[Named speaker 2] then gives a European perspective and focuses on the regulatory pathway approval of new medicines. It is at this point that the EMA is mentioned (Timepoint 58:15 on video Angelini 28 Nov 23_pt03).

[Named speaker 2] highlights the fact that the regulatory approval process mandates combination use in regulatory studies but will only approve medicines for uses tested in those studies, subsequently meaning that new drugs can only be licensed for combination use. [The speaker] expresses dissatisfaction with this scenario and goes on to explain how one of the main problems in epilepsy management and patient care is drug-drug interactions; said interactions arising directly from the regulatory-enforced combination use of new products.

[The speaker's] choice of phraseology is unfortunate and one borne out of frustration:

> *'There is one organisation I do not like and I will tell you why. "If the drug is successful and better than placebo …you get a labelling (sic) and the European Medicines Agency is stupid enough just to allow the labelling for add-on therapy only - no mono therapy licence because they say you get the licence only for what the studies showed. So, if you get a new treatment, the first line mono therapy approach is prevented by the European Medicines Agency*'.

At this point European Medicines Agency is actually named on the slide. (@58:30)
[Named speaker 2] (@1:00:51) goes on to say that:

> '*A drug like cenobamate in my eyes is a perfect monotherapy drug but we are not allowed to apply that*'.

It is important to note that the specific phrases highlighted by the complainant were not used by the speaker - although we accept that the comments that were expressed were not appropriate and were heard by an audience that included UK HCPs.

However, we categorically deny that this is a breach of Clause 2.

The comments were made in the context of the Regulatory approach to medicines approval and were not directed at any individual within the organisation. We note that Clauses related to disparagement, such as Clause 6.7 were not raised by the Case Preparation Manager; and in any even Clause 6.7 would not apply as the EMA is an organisation, not an individual.

We would also like to highlight that [named speaker 2] is not English and is not a native English speaker. Whilst English is widely used in professional medical presentations, this situation requires many academics to learn English as a second, third or even fourth language. It is widely recognised that non-English speakers of the English language do not always understand the perfect use of grammar or sentence syntax.

Consider the similar sentences below in their use of similar words and phrases:

- The way the EMA approve epilepsy medicines is silly.
- The way the EMA approve epilepsy medicines is stupid.
- It is stupid of the EMA to approve medicines in the way they do.
- The EMA is stupid to approve medicines in the way they do.

The various forms and words mean very different things to a native English speaker but are clearly addressing the same point – that the speaker disagrees with the regulatory approach.

It can clearly be seen from [named speaker 2]'s sentence structure and grammar that, whilst good enough to present to an international audience of medical specialists in a language foreign to [them], [their] mastery of the English language is not perfect.

The difficulty in foreigners speaking English is widely recognised and studied academically as it is a major consideration in business, in social cohesion and in immigration, to name but some areas. Even a quick search on Wikipedia identifies how common the issue is:

> ***Difficulties for learners***
> *Language teaching practice often assumes that most of the difficulties that learners face in the study of English are the consequence of the degree to which their native language differs from English (a contrastive analysis approach). A native speaker of Chinese, for example, may face many more difficulties than a native speaker of German, because German is more closely related to English than Chinese. This may be true for anyone of any mother tongue (also called the first language, normally abbreviated L1) setting out to learn any other language (called a target language, second language or L2). See also second-language acquisition (SLA) for mixed evidence from linguistic research.*
>
> *Language learners often produce errors of syntax, vocabulary, and pronunciation thought to result from the influence of their L1, such as mapping its grammatical*

patterns inappropriately onto the L2, pronouncing certain sounds incorrectly or with difficulty, and confusing items of vocabulary known as false friends. This is known as L1 transfer or 'language interference'. However, these transfer effects are typically stronger for beginners' language production, and SLA research has highlighted many errors which cannot be attributed to the L1, as they are attested in learners of many language backgrounds (for example, failure to apply 3rd person present singular -s to verbs, as in 'he make' not 'he makes').

Some students may have problems due to certain words being usable, unchanged, as different parts of speech. For example, the word 'suffering' in 'I am suffering terribly' is a verb, but in 'My suffering is terrible' is a noun — and confounding matters is the fact that both of these sentences express the same idea, using the same words. Other students might have problems due to the prescribing and proscribing nature of rules in the language formulated by amateur grammarians rather than ascribing to the functional and descriptive nature of languages evidenced from distribution. For example, a cleric, Robert Lowth, introduced the rule to never end a sentence with a preposition, inspired by Latin grammar, through his book A Short Introduction to English Grammar.[13] The inconsistencies brought from Latin language standardization of English language led to classifying and sub-classifying an otherwise simple language structure. Like many alphabetic writing systems, English also has incorporated the principle that graphemic units should correspond to the phonemic units; however, the fidelity to the principle is compromised, compared to an exemplar language like the Finnish language. This is evident in the Oxford English Dictionary; for many years it experimented with various spellings of 'SIGN' to attain a fidelity with the said principle, among which were SINE, SEGN, and SYNE, and through the diachronic mutations eventually settled on SIGN.[14] Cultural differences in communication styles and preferences are also significant. For example, a study among Chinese ESL students revealed that preference for not using the tense marking on verb present in the morphology of their mother tongue made it difficult for them to express time-related sentences in English.[15] Another study looked at Chinese ESL students and British teachers and found that the Chinese learners did not see classroom 'discussion and interaction' type of communication for learning as important but placed a heavy emphasis on teacher-directed lectures.[16]

Angelini agrees that it was silly of the speaker to have used the word 'stupid'.
Angelini agrees that it was stupid of the speaker to have used the word 'stupid'.
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It was stupid/silly/unfortunate to have referred to the regulatory body in such a manner.

As indicated, while we recognise that the phraseology used by the speaker was not appropriate - and might be regarded as not achieving the standards that Angelini or the PMCPA would expect, however, we do not believe that in context the single-word 'stupid' by a non-native English speaker in an international symposium held outside the UK is something that brings the industry into disrepute in the context of a measured scientific discussion.

Indeed, to make such a ruling might be regarded as elitist; or discriminatory.

Few native *English* HCPs could even make the same presentation (let alone perfectly) in Dutch, French, German, Spanish, Italian or Greek.

Further, this was an isolated instance of a highly respected internationally recognised epilepsy specialist and academic expressing frustration with the limitations of a regulatory process to a small audience of other specialists. Angelini could not foresee that the specific words would be used; and, indeed, the speaker contract specifically highlights the need to behave appropriately and professionally (Paragraph 1(b) of the speaker contract).

The speakers had been specifically briefed and contracted to act professionally and we believe were specifically briefed by the UK [compliance employee] not to be disparaging and not to refer to the regulatory bodies at all. [Named speaker 2] did not intend to disparage the EMA; [they] simply used inappropriate spoken sentence structure.

Please also note that the comments about the EMA were edited out of the version of the video that was uploaded into the portal that UK HCPs could access after the event.

Typically, Clause 2 is reserved for matters such as risks to patient safety, financial impropriety, etc. Recent cases considered by the Appeal Board have determined, for example, that raising awareness of prescription medicines to the entire general public on social media (even by a senior company official) is not a Clause 2 activity. To regard a single use of a single word in the same category as matters of bribery and patient safety would be to undermine the very point of Clause 2.

Accordingly, Angelini denies a breach of clause 2.

The complainant makes the point that the speaker's reference to the European Medicines Agency is, in itself, a breach of the Code. In context, we do not think that it should be – it is unreasonable that naming the regulatory body is banned in a scientific discussion just because the discussion is about the medicine (and therefore defined as promotional). But, of course, we recognise the current wording of Clause 15.2.

Accordingly, Angelini accepts a breach of clause 15.2.

<u>Part C (3): Promotion inconsistent with Marketing Authorisation during the main presentation</u>
Angelini has reviewed the entire slide deck and the recordings of the various presentations. We can confirm that at no point did the speakers present information about the unlicensed use of our product. Indeed, when matters relating to the limits of the licence were raised, the speakers were careful to highlight the relevant boundaries.

For example, on several occasions, the audience was encouraged to start patients on low doses and to titrate to higher doses for refractory patients.

For example, at time-point 1615 in Nov 23 pt02, session leads discuss difficult patients and mention the necessary low doses of clobazam.

Additionally, Video 1 @ 29 mins highlights with a question about pregnancy and a brief discussion re the definition of 'child-bearing' (whole adult life or when not on contraception).

Part C (4): Promotion inconsistent with Marketing Authorisation during the breakout sessions

This section of the complaint specifically addresses the morning of Day 2, the 'Social Sharing sessions'. These were effectively breakout Q&A sessions promoted by short presentations from the faculty who rotated between the 5 mentioned groups.

Contrary to the complainant's allegation, Speakers were most definitely not briefed to share experience outside the product licence; the exact opposite is true (as can be seen from the contracts and briefing slides mentioned previously). We believe that during a verbal briefing speakers were told to answer questions honestly, even if the question related to off-label use, but to clarify the product licence should such an instance arise. Angelini has no evidence that anything inappropriate occurred in this regard. During these breakout sessions, we do not believe that speakers proactively raised issues related to monotherapy use.

We note the multiple allegations in respect of the breakout sessions. The complainant is correct that these sessions were not recorded as they were deliberately designed to be opportunities for discussion rather than plenary presentations.

Part C (4)(a): general allegations relating to off-label promotion during the breakout sessions

As previously indicated, all speakers were briefed to remain within the licensed indication and to submit slides in good time for Certification.

All presented slides were within the licensed indication for Ontozry. Prescribing information was presented at the end of every product presentation and appropriate safety data was highlighted at key points on relevant slides.

A key element of any meeting is the opportunity for the audience to ask questions of the presenters. On occasions those questions pertain to difficult-to-treat patients, which might be outside the licensed indication for the product. The Code notes the potential for such queries and allows for legitimate medical discussion on such matters so long as they are not promotional in tone and style. Answering a question with succinct, clear answers is not regarded as promotion; indeed, to avoid providing answers to such questions could risk inappropriate prescribing.

We note that the complainant raised concerns related to paediatric patients; the use of cenobamate as a monotherapy treatment; and the use of cenobamate in pregnant patients. We further note that no evidence was provided by the complainant.

Angelini did not proactively initiate discussion on topics outside the licensed indication for the product. If questions were asked about the topics listed by the complainant, we would expect that the HCPs were referred to the SPC; however, we cannot categorically confirm that as there is no recording of these sessions to confirm either the questions asked, or the answers given.

Angelini categorically denies all allegations in relation to clause 11.2 of the Code.

Part C (4)(b): allegations relating to Pregnancy and fertility considerations during the breakout sessions

The complainant raises concerns that no specific attention was paid to matters relating to pregnancy and fertility treatment, etc, during the breakout sessions in the section of the complaint labelled ***Promotion inconsistent with Marketing Authorisation for cenobamate***. Angelini does not consider that the complainant as expressing a view as to the wider meeting but is limiting the concerns to the breakout sessions.

In other parts of the meeting, pregnancy was mentioned. For example, slide 181 by [named speaker] (UK speaker) specifically mentions these topics and it clearly declares that pregnancy is a contraindication.

Please note Specialists in epilepsy are very familiar with the risks associated with epilepsy treatments in specialist populations - and the profile of our product is not meaningfully different from existing products in this regard. In fact, owing to the lack of data with our product, specifically, and in line with all epilepsy treatments, effective contraception is necessary in women of child-bearing age taking epilepsy medication. It may be helpful to note that Angelini also funds a registry of occurrences of pregnancy when using *cenobamate* so that advice can be updated in the future.

However, an expectation that all epileptic females will refrain from having children is unrealistic and therefore interest in pregnancy (and related) data is high amongst epilepsy specialists. For example, in Video 1 @ 29 mins there is a question about pregnancy and a discussion re definition of 'childbearing' (whole adult life or when not on contraception) in the context of effective contraception. But there is definitely no encouragement for the audience to use *cenobamate* (or any product) in pregnancy.

Given that the complainant raises 5 different allegations related to Clauses 6.1; 5.1 and 2 of the Code, we believe the allegations regarding these clauses refer specifically to the breakout sessions. We can confirm that no recording exists of these discussions. We can only assume that the concerns relate to questions posed to speakers during the workshop (Q&A) sessions.

Regardless, Angelini believes that appropriate information was provided at the appropriate time to the audience of epilepsy specialists.

Accordingly, Angelini categorically denies all allegations concerning clauses 6.1; 11.2; 5.1 and 2 of the Code in relation to the Q&A Breakout sessions.

Part C (4)(c): allegations relating to AE collation during the breakout sessions

In the section of the complaint labelled ***Promotion inconsistent with Marketing Authorisation for cenobamate,*** the complainant raises concerns that Adverse Events identified during the breakout sessions of the meeting. Angelini does not consider that the complainant is expressing a view as to the wider meeting but is limiting the concerns to the breakout sessions.

Angelini is not aware of any AE reports made at any point in the meeting, including during the breakout sessions. Note: q*uestions* from the audience pertaining to use in specialist populations are typically not reportable Adverse Event *declarations* (of pregnancy, side effects (etc)).

Angelini cannot confirm the nature of the discussions in the breakout sessions. We cannot accept (and have no evidence) that Angelini speakers initiated conversation about off-label topics or that any reportable adverse events were discussed. Not [*sic*] do we have any records of which HCPs asked which questions and therefore we cannot know the nationality of questions raised by individual HCPs. (Obviously only AEs related to UK HCPs would fall within the scope of the ABPI Code of Practice).

Angelini can confirm that the contract signed by all speakers includes a very clear refence to AE reporting in paragraph 7(j).

We note that the PMCPA added Clause 9.2 to the list of clauses to be considered; and that a request was made for confirmation that all UK staff attending the From Now On meeting in Milan had been appropriately trained; and that the UK SOP related to AE reporting be provided. We have provided this information and documentation; however, we object to this specific area of the PMCPA attention. The complainant alleged that AEs were not reported and that a failure to report AEs was not in line with our SOP. There is no complaint about the SOP, per se; and no complaint that staff had not been trained.

For the record, **we categorically deny allegations related to Clause 9.2** but do not agree this clause is even within scope of the original complaint.

Angelini trains and tests all staff in AE recognition and reporting on an annual basis. All UK staff in attendance in Milan had been AE trained. PV training materials and relevant training records are included in the Appended materials to this Response.

We are not aware of any UK HCPs identifying reportable Adverse Events; accordingly, **Angelini categorically denies all such allegations in relation to Clause 2 of the Code**.

Complaint Part D: From Now On Online Platform (Portal)

All attendees at the From Now On meeting were given access to a portal from which they could download copies of the slides presented at the meeting. The portal can be accessed from: [URL provided].

For clarity, the portal required log-in with an Angelini ID and password and could only be accessed by those that attended the event itself (please see screenshot below). For additional clarity, access was limited to those that attended the From Now On event.

It can be clearly seen from the screenshots that a UK-specific version of the portal was created for UK delegates attending the event. It contained a version of the slide deck that was specifically Certified by [compliance employee] for the purpose of upload into the portal. It specifically includes clear and prominent links to UK PI and AE reporting.

[Screenshot of the top portion of the From Now ON portal, showing a section for registration, a section inviting the user to “Discover the steering committee” and a section inviting the user to “Discover our international faculty”]

As can be seen from the screenshot (below), the portal contained two videos; the first containing the recording of day 1; and the second containing the recording of day two. It also contains every presentation from the two days (18 presentations in total). The slide content is exactly as presented on the day (including the text that named the EMA). The videos were edited after review by the UK Signatory to ensure removal of the verbal comments about the EMA.

Because all these documents were contained in the same portal, Angelini regards the portal itself as the item of promotional material that required Certification. Regrettably, the portal (including its contents) was not Certified by a UK Signatory.

We understand that the UK [compliance employee] apparently advised the UK marketing team in January 2024 that the portal and its content did *not* require specific Certification as the delegates had ‘already seen the live presentations’. Obviously, this is incorrect. [Redacted comment about staffing changes] and it may be that this was overlooked in the handover, although we are unable to clarify further why the portal was not Certified as it should have been.

The portal was definitely informally assessed by the UK [compliance employee] as they made sure that only the edited version of the videos were uploaded and they made sure the portal was specific to UK HCPs and contained UK PI and the MHRA AE reporting statement. However, the portal as a standalone item of promotional material was not Certified.

Accordingly, Angelini accepts a single breach of Clause 8.1 for a failure to certify the portal containing the videos and slides.

Note: We do not think it appropriate to rule Angelini in breach for each *individual* video or each individual slide deck because the ***portal*** is the item of material that should be Certified. The videos and slides only as elements within that portal as records of the overall meeting in video and slide format; they were neither considered nor approved as standalone items for use in any other way.

If the PMCPA thinks otherwise, we would ask that the breach is seen in relation to each material type. For example, it would be a failure to Certify the edited videos (plural), rather than regarding it as a breach for each of the two daily video files.

We would also like to highlight again that the slides *were* Certified as previously indicated and we therefore deny any allegations of non-Certification in relation to the slides within the portal.

As previously indicated and as can be seen from the screenshot below, the entire set of slides was Certified prior to use, for presentation and upload. In fact, the slides shown in the portal bear a UK-specific Job bag Code.

As can be seen from careful scrutiny of the Appian screenshot, the name of the file is 'All slides for upload'. This clearly implies the slide deck was to be approved for upload into the Portal.

[Screenshot from Appian system for UK20841P, showing (among other things) – Use Start Date: 23-11-2023, Description: "From Now ON Speaker Decks", Notes: "Speaker presentation decks for From Now ON Meeting in Milan 28th-29th November 2023. These presentations are created at global level but will be approved at local level. A placeholder will be uploaded first to get a job code to add to the decks.", Material Type: "Others", Channel: "Others", Document: All slides FNO for upload.pptx, Uploaded on: 28/11/2023]

Thus while the portal was not Certified, the slides were.

Even if the PMCPA disagrees and decides the slides should have been specifically Certified for the Portal, where the single deck was displayed as 18 viewable slide files (for ease of viewing) we would ask that PMCPA regards it as a failure to Certify the edited version of the slides (plural) rather than a failure to certify each of the 18 individual *presentations* and that the PMCPA uses its discretion in this regard.

To confirm, **Angelini denies 18 breaches of Clause 8.1 in relation to the slides**.

As can clearly be seen from the screenshot below, a clear and obvious link is provided for UK HCPs within the portal itself to UK PI and UK AE reporting. Accordingly, **Angelini denies 18 breaches in relation to Clause 12.1** and **Angelini denies 18 breaches in relation to Clause 12.9.**

[Screenshot of a portion of the portal, showing (among other things) a box titled "Agenda" with, in larger all caps font, "FOR UK & IRELAND ATTENDEES: AGENDA, PRESCRIBING INFORMATION AND ADVERSE EVENT REPORTING"]

<u>Complaint Part E:</u> Internal reporting of non-compliance

The complainant drew specific attention to the Angelini Whistleblowing SOP. As part of a comprehensive management of compliance issues, we welcome comments and concerns for all our staff; the complainant was not an exception to that position when they worked for us.

However, we are under no obligation to agree with their concerns.

As correctly indicated by the complainant, the Global team did investigate the concerns raised by the complainant at the time. The Global team confirmed that they had investigated concerns raised but did not find anything to be non-compliant from a Global perspective.

We have reconsidered the concerns raised by the complainant as part of this case and would like to offer the following observations.

- This was a professional interaction between two [employees], in the context of feedback following the event; rather than a 'whistleblowing' concern

expressed through the Speak Up channels. It was responded to in that manner, [employee] to [employee].

- We would also like to add that the specific concerns raised with the Global team were discussed with the [senior UK medical employee] beforehand, who was copied on the email to the Global Team, thus reinforcing the position that this was professional feedback rather than 'whistleblowing'.
- The global team did consider the professional concerns properly. The timeline associated with their response as provided by the Global Team is:
    - *December 5, 2023, [complainant]'s message was received by the Global Compliance; December 5, 2023, a message was sent from Global Compliance to the Global Medical and Global Regulatory aimed at scheduling a meeting on the matter with the purpose to gather all the relevant elements.*
    - *December 18, 2023, the topic was discussed with Global Compliance, Global Medical and Global Regulatory and it was confirmed that all materials were approved by Global Medical and Global Regulatory according to the local regulation in addition to the internal policies and procedures.*
    - *December 20, 2023, the reply was sent from Global Compliance to the [complainant] Cc'd Global Regulatory, UK-I GM and UK-I Medical*
    - *December 20, 2023, the informative was forwarded for alignments' purpose to Global Marketing, General Counsel, International Operations*
- As discussed elsewhere in this response, the specific concerns raised are subjective and to an extent, concerned with internal company procedure. Angelini UK does not agree that there was any actual Code breach.
    - The banners outside the venue were not non-compliant.
    - Non-product Signage does not require certification.
    - The UK speaker's slides were appropriately certified in advance; we have no evidence they were changed following Certification.
    - Last-minute changes to the final deck are inevitable; however, the deck was Certified by a UK Signatory, even though the majority of the deck did not actually require Certification (as most speakers were not from the UK)
    - We cannot confirm the nature of the discussions in the breakout sessions and have no evidence that Angelini initiated conversation about off-label topics or that any reportable adverse events were discussed, or by which nationality of HCP.

To turn to the specific wording of the complainant:

> *Whilst there is a policy in place at Angelini Pharma with regards to whistleblowing and speaking up, in practice when this policy is exercised, concerns are denied and corrective and preventative actions cannot be considered. Every level of management in an organisation choosing to overlook the intentional code breaches documented in this report, despite observing them and receiving internal reports regarding them, is conduct falling far short of the standards expected in the pharmaceutical industry, is not in the spirit of the code and drastically reduces confidence in the industry*

Angelini did investigate. Appropriate levels of management were aware. They simply did not agree with the complainant's interpretations and did not agree that breaches of the Code had occurred.

Accordingly, **Angelini UK categorically denies any breaches of Clauses 5.1 or 2 specifically in connection with the 'internal reporting' issues**.

Complainant concluding remarks.
Angelini would also like to take the opportunity to comment to address the concluding remarks of the complainant.

Together with the current management team and our external compliance support, the complainant was a key contributor to the raising and maintenance of compliance standards. Angelini is proud of its approach to compliance and will continue to welcome feedback and scrutiny.

It is always disappointing when a former employee raises concerns, especially one so highly thought of as the individual in this instance. We hope that the professional differences of opinion in relation to the matters raised in this complaint will not detract from the positive experiences that we otherwise hope the individual enjoyed in their time with Angelini.

Angelini Conclusion
Angelini hopes that we have addressed any concerns that the PMCPA may have had on receipt of this complaint. We welcome any questions on any aspect of our approach to compliance."

FURTHER RESPONSE FROM ANGELINI

After giving preliminary consideration to this case, the Panel requested further information from Angelini before making its ruling:

- Screenshots from the approval system showing the time of certification and any relevant metadata for:
  - The slides presented at the Southern Epilepsy Forum meeting
  - The slides presented at the Cenobamate Roadshow London meeting
- Clarification regarding the statement (relating to "From Now ON") that "the comments about the EMA were edited out of the version of the video that was uploaded into the portal that UK HCPs could access after the event" – the "edited" video provided to the Panel by Angelini appeared to include the same version of the presentation as the "unedited" version
- Clarification regarding the following in relation to the "From Now ON" portal:
  - Was there a separate version of the portal for UK attendees?
  - Was the full slide deck certified once for use both as an in-person presentation and within the portal? Or was it certified for each use separately?
  - Were prescribing information and the AE reporting statement included on any of the 18 individual presentation slide sets available to download from the portal? The Panel noted that the final slide of the full deck showed prescribing information but it is not clear what happened once the slide deck was split for upload to the portal.
  - Were the two videos downloadable from the portal?

- What was the user journey to prescribing information and the AE reporting statement within the portal?

The response from Angelini is reproduced below:

> "Thank you for your letter dated 22nd August 2025 requesting further information to case 3916, following our original response to you over twelve months ago on 5th August 2025. Obviously, we are concerned that the matter is not yet resolved after such a lengthy period of time.
>
> We had previously provided an extremely comprehensive response to the issues were raised by a former employee. The passage of time means that personnel have changed in the business [redacted].
>
> The nature of the additional queries leads us to believe that the PMCPA may be focusing on fine detail, rather than the substance of the complaint. [Redacted comment about the complainant]; we hope that you will make your rulings with that context in mind.
>
> <u>Screenshots of Certification for the Southern Epilepsy Forum and Cenobamate Roadshow London meeting.</u>
>
> We provide the screenshots here.
>
> [Screenshots from Appian system for UK17609P, showing (among other things) – Description: "Southern Epilepsy Forum slide deck", Use Start Date: 21-04-2023, Final signatory approval: "21-04-2023 13:52:41]
>
> [Screenshots from Appian system for UK18336P, showing (among other things) – Description: "June 2023 Roadshow Local Speaker slides 14th June", Use Start Date: 12-06-2023, Final signatory approval: "12-06-2023 15:24:16]
>
> [Screenshots from Appian system for UK18386P, showing (among other things) – Description: "June 2023 Roadshow 14-15th June 2023", Use Start Date: 14-06-2023, Final signatory approval: "14-06-2023 18:01:40]
>
> As previously indicated, the start of both these meetings were delayed until the Signatory had approved minor last-minute amendments to the slides. It is possible that the paperwork was completed after a lavatory break or well-earned for the Signatory, but they definitely completed the assessment prior to the two events starting. Please note that date and time of our approval system was configured to our Global headquarters' Central European Time (CET)
>
> We have reviewed the videos from the meetings and note that they do not show time stamps for the actual start. Therefore we cannot provide evidence that the meetings started after actual certification was completed, but we also note that the burden of proof lies with the complainant.

Part C(2) From Now on meeting

In the element of our response labelled Part 2(2) regarding the From Now On meeting, we addressed the aspersion that the speaker disparaged the MHRA. In our response, we included the following paragraph:

> *Please also note that the comments about the EMA were edited out of the version of the video that was uploaded into the portal that UK HCPs could access after the event.*

We are grateful for the opportunity to address this erroneous statement. We had believed that the comments were edited out of the video; in fact, they were not. The only editing that occurred was in relation to formatting of the events into chapters to make the content more easily accessible.

We would like to apologise for this error in our previous submission.

From Now On Portal

In the part of our Response labelled Part D, we address the allegations in response to the Portal accessible to delegates at the meeting.

We had previously indicated that all the slide decks were individually Certified for presentation as Speaker Decks and “for upload”. We had previously provided the screenshot showing the metadata for the complete deck. We accept that the Appian layout and its metadata is not perfect, but we contend that the intent is clear that the Signatory was Certifying for presentation and upload (into a portal).

We further accept that the portal itself was not Certified as an individual promotional asset and had indicated that we would accept a single breach of Clause 8.1 for failing to Certify the portal.

We would also like to clarify, again, that each individual speaker slide deck was certified prior to the meeting.

As requested, we are including a video showing the user journey to access the slides within the portal. It clearly shows prominent signposts to the PI and AE as is acceptable in most digital formats. Therefore, there is no requirement for each slide deck to contain PI and AE reporting statements as they are provided within the portal as a reference for delegates who may wish to consolidate their learning after the event; not as promotional content, *per se*.

However, if the slide decks are to be treated as individual items of material, it should be noted that six make no reference at all to cenobamate and as such are not promotional and do not require PI or AE statements when viewed as standalone items. These include:

- The importance of brain health and the burden of neurological disorders ([speaker name])
- **Emotional and social burden of uncontrolled epilepsy (**[speaker name]**)**

- **Impact of delayed treatment or medication switch in Epilepsy (**[speaker name]**)**
- **Failure to use new breakthrough treatments for epilepsy:** potential additional European drawbacks ([speaker name])
- **Do we still need new treatments for epilepsy? (**[speaker name]**)**
- **Psychiatric comorbidities (**[speaker name]**)**

A seventh deck makes only passing reference to cenobamate and as such we would not regard it as promotional in isolation.

- Here and now: overview of the current guidelines and literature update ([speaker name])

Of the remaining 18 decks that mention cenobamate one does contain PI and one includes the AE statement immediately after the title slide.

- Use of cenobamate: is sooner better? The place of cenobamate in antiseizure medicine sequencing ([speaker name])
    - This deck includes the licensed indication and the AE statement immediately after the title slide
- Clinical case (post-traumatic epilepsy) ([speaker name])
    - Note that this deck contains both the prescribing information and the AE reporting statement on the final slide

For complete clarity, the videos cannot be downloaded.

Conclusion

We trust that this additional information will allow the PMCPA to come to a conclusion in the near future."

PANEL RULING

This complaint from a former employee of Angelini consisted of numerous allegations relating to three promotional meetings and associated activities for Angelini's epilepsy medication, Ontozry (cenobamate).

Ontozry was indicated for the adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite treatment with at least 2 anti-epileptic medicinal products.

The Panel noted Angelini's concern that the case preparation manager identified clauses to be addressed by the company in addition to those cited by the complainant. The Panel observed that it was standard practice for the case preparation manager to identify the relevant clauses of the Code to ensure that the Panel was able to appropriately adjudicate on all allegations. The Panel referred to Paragraph 5.2 of the 2021 PMCPA Constitution and Procedure, under which the complaint was taken up, which included:

"… To assist companies in ensuring that a complete response is submitted the case preparation manager may suggest relevant supporting material to be supplied. It is nonetheless the responsibility of the respondent to ensure that a full response is submitted. If the complainant is not a pharmaceutical company, the case preparation manager may suggest the clauses of the Code to be addressed. …"

Southern Epilepsy Forum Meeting – 21 April 2023

The complainant made allegations about the "Southern Epilepsy Forum Meeting", a promotional meeting, organised and funded by Angelini Pharma UK-I that took place in the UK on 21 April 2023. Angelini confirmed that this was the first day of a two-day standalone meeting organised by Angelini UK that was attended by 71 UK health professionals, all invited by Angelini UK. The speakers were engaged, briefed and contracted by Angelini UK.

The complainant alleged that:

- There was discussion at the meeting that was inconsistent with the marketing authorisation for cenobamate – specifically, "questions relating to the use of cenobamate in unlicensed patient groups were asked by a HCP attendee, and a response detailing such use was provided by a contracted HCP speaker".
- The meeting slides were not certified prior to the start of the meeting.
- These concerns were raised with senior leaders following the meeting but the actions taken (updating SOPs and producing a briefing document for health professional speakers at UK meetings) did not specifically address the concerns raised around company culture and the importance of adherence to company SOPs and the Code.

In relation to the first allegation, the Panel noted that the complainant did not specify which unlicensed patient groups had been referred to or which speaker had answered the question from the audience. As part of its response to the complaint, Angelini provided the Panel with a video recording of the first day of the meeting and a copy of the slides used. While the PMCPA was not an investigatory body and a full assessment of the content of the day-long meeting was not feasible, the Panel considered that promotion of a medicine outside the terms of its marketing authorisation was a serious matter and it had a responsibility to address the complainant's concerns. Noting the complainant's reference to questions being asked by an attendee, the Panel therefore limited its consideration to the question-and-answer sections of the video recording.

The Panel identified the following six exchanges between speakers and the audience during the meeting as being of relevance to this allegation:

1. Video timestamp [00:56:39] – a question relating to use of cenobamate in children

Attendee: *"Have you used it [cenobamate] off licence at all – on children or, sort of, teenagers?"*

Speaker 1: *"I am not at liberty to say but my seat is next to yours and so I could tell you about where I would like to use it, were the licence to expand. It has a different licence in the States and if you spoke to people there, you might hear their experience. And there are published cases of people using it differently."*

2. Video timestamp [00:59:04] – a question about patients with short QT syndrome

Chair: *"How often do you encounter a patient in whom you cannot prescribe [cenobamate] because of short QTc?"*

Speaker 1: *"Oh no. No, no, no, no. I'm told that the short QT families are so rare that you will write them up if you see them. But again, it's not a bad thing to be picking up an ECG of somebody with refractory epilepsy – it's probably long overdue."*

Chair: *"I had one case."*

Speaker 1: *"You've had one!"*

Chair: *"But not familial. Just ECG showed very short QTc and I did not prescribe – but that was one."*

3. Video timestamp [00:59:35] – a question about administration via a feeding tube

Attendee: *"Can it [cenobamate] be administered via a PEG?"*

Speaker 1: *"Now that's a good question. So currently there's not a liquid formulation: it's tablet only. I'm not sure how the company would feel for me to answer this question, but I'll tell you what we do. We do crush it and we do put it down the PEG. And we know parents who have managed to do it that way for their young people and it seems to have a similar efficacy that way. So it's not recommended, but I can tell you through practice that is something we have done."*

Attendee: *"It is a water-soluble drug as well, isn't it – and there is some data out there […inaudible on recording…]"*

Speaker 1: *"The comment was important for the room. So it's water soluble, which will probably help to give you additional advice when it comes to how much water to stick in with the crushed or dissolved tablet in the PEG."*

4. Video timestamp [02:01:55] – a question about generalised epilepsy and diagnostic doubt

Attendee: *"I was just thinking we sometimes have real diagnostic doubt – whether it's a focal epilepsy or a primary generalised. If you have a patient with that doubt, would you try cenobamate?"*

Speaker 2: *"Um… I'm just trying to think if I've got anybody like that. I mean usually – I think, you know because I'm quite lucky with, you know, I report EEG and things like that – so usually I've seen the EEG and things like that which does often – and, you know, and I get people in for prolonged monitoring. So I probably don't have that same amount of diagnostic doubt. I'm certainly not using it for generalised epilepsies. I'm hopeful that those studies are going to happen – but I guess it's a little bit like using brivaracetam – you know, we use that quite flexibly between the different epilepsy types – I think over time it's probably just going to… but… we will see what happens with time. But I am not at the moment using it at all for the generalised epilepsies."*

5. Video timestamp [03:40:04] – questions about patients with swallowing difficulties

Attendee 1: *"This is a question for all of you, but with the drug company too. [Speaker 3], you mentioned that a third of your patients had learning disabilities that you put on cenobamate. How did you get around the people who can't swallow tablets? Is there a liquid formulation on its way any time soon?"*

Speaker 3: *"As far as I'm aware, none of our patients that had learning disabilities had swallowing difficulties – so I can't think of any time where that problem emerged. So I'm not quite sure."*

Speaker 2: *"We've certainly got a couple who are using it through PEG tubes. It's just been. The pharmacy have sorted out mixing it up with water."*

Chair: *"It's more a question about the patient who doesn't like taking tablets but has no dysphagia as such. [Named speaker], do you have any experience with that? Yoghurt? Spoonful of yoghurt?"*

Speaker 5: *"Yes, if they've got some safe swallow – but I haven't got anybody that we've prescribed for that have PEG feeds I don't think. Have you [addressing an audience member]? You've got one, have you?"*

Attendee 2: *"They just dissolve it in some water and put down the PEG tube with lunch."*

Chair: *"Yes, that's PEG – but the question was without the PEG – person who doesn't like taking tablets – and there is no liquid alternative."*

Attendee 2: *"Just want a little bit of food."*

Chair: *"Yeah."*

Speaker 5: *"Yeah, something like a yoghurt or something that…"*

Attendee 1: *"The lady I'm thinking of chews her tablets – so she either has it in liquid form or else she'll chew them – which isn't very pleasant. She's the first person we're thinking of with learning disabilities to prescribe it [cenobamate] for."*

Angelini Medical employee: *"Hi there. Thank you for the question. My name is [name], I work in the Medical team. So in terms of formulations currently there's only the tablet authorised. So that's the only preparation there. There are plans for a liquid formulation – part of the regulatory approvals ongoing – but there's no plans for it to be… it's not going to be here anytime soon. So, yeah, unfortunately there's no timelines on that. It's in line with the paediatric licence in investigation first in the licence. So, you know, it's going to be some time."*

Attendee 3: *"Ok so without [inaudible] prescriber and without understanding the licensing rules and what have you… what can consultants do? What can they advise their patients? Could they use it off licence?"*

Attendee 4: *"Crushing and dissolving is off licence."*

Angelini Medical employee: *"It's off label; yeah, it's off licence. Part of my role, I have to advise you that if that's something you're doing, it should be reported as an adverse event through the MHRA yellowcard reporting."*

[Moderator moves on to next question]

Attendee 5: *"Can I just ask on the subject of the learning disability community then? So really it limits the use of cenobamate if we've got people who have got swallowing difficulties or who are PEG-fed – it reduces their change of going onto the medication, doesn't it?"*

Moderator: *"I think that's probably a statement rather than a question – but if there is no alternate licence preparation at the present time, then we will have to wait for the liquid preparation."*

Angelini Medical employee: *"So just to add – if there are any patients that are PEG-fed, or you are looking at off-label use, if you could contact the Angelini Pharma medical department, they may be able to share some information with yourself."*

6. Video timestamp [03:49:25] – a question about cenobamate's position in the treatment pathway

Attendee 1: *"Should we be considering cenobamate sooner rather than going through the BNF before ending up at cenobamate? Should we consider it after the first failed add-on?"*

Speaker 2: *"I would say that's probably what I'm moving to. So the patients who I'm seeing sort of fairly early on, so sort of lamotrigine, levetiracetam, use them together – if that doesn't work then I will start using it and I'll just see what happens with that and whether, you know, it turns to be like lacosamide or whatever and it just becomes one in a number but I don't see a reason, as you suggest, to go through lots and lots of different medications before that. I might do brivaracetam before cenobamate but I suspect it'll be one that I use quite high up the list."*

Speaker 3: *"Yeah, I agree – I think it's heading that way."*

Chair: *"I think that there is another interesting niche for this drug and that is patients with tonic-clonic seizures because, especially those who have history of neuropsychiatric problems and perampanel, which is my favourite drug in this situation, might be risky. Then cenobamate may offer a better side effects profile."*

Attendee 2: *"So would you ideal combination by lamotrigine, levetiracetam, and then cenobamate? Is that how you'd progress? We don't have the availability, unfortunately, in [named county] of cenobamate but we're working hard towards improving on that. And we have a lot of patients on a combination of levetiracetam and lamotrigine and they are doing relatively well, but you still get the occasional seizure breakthrough and I just wonder whether cenobamate would be the next drug to add to that combination or whether you have, as we just said, whether it needs to be going through what NICE recommends and where cenobamate now will sit from the NICE point of view."*

Speaker 2: *"Yeah, certainly for the SMC in Scotland, it's your second adjuvant and that's the restriction on it. I think it's the same for NICE, isn't it?"*

Speaker 4: *"Yeah."*

Speaker 5: *"But I think your own confidence grows, doesn't it, when you try when drugs are new and you start to see really positive effects and which is sort of sustained across several of your patients. So it gives you that confidence to think of it probably a little sooner than you may have done before."*

Speaker 6: *"If you take the historical perspective, levetiracetam wasn't the next – wasn't the first-line adjunctive therapy historically, but it probably is now and even sooner – but times change with experience."*

The Panel took into account the following points from the Ontozry (cenobamate) summary of product characteristics:

- Section 4.1 Therapeutic indications: "Ontozry is indicated for the adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite treatment with at least 2 anti-

epileptic medicinal products."

- Section 4.2 Posology and method of administration: "… Oral use. Cenobamate should typically be taken once daily as single oral dose at any time. However, it should preferably be taken at the same time each day. It may be taken with or without food (see section 5.2). The tablet should be swallowed with a glass of water. The tablets cannot be split accurately as there is no break line and the accuracy of the dose cannot be ensured."

- Section 4.3 Contraindications: "… Familial Short-QT syndrome …"

The Panel considered it unlikely that the complainant was referring to the question about patients with short QT syndrome (exchange number 2, above). This question had been asked by the Chair of the meeting, rather than an audience member and the speakers confirmed that they had not prescribed cenobamate in this patient group. The Panel took account of the relevant sections of the summary of product characteristics, including section 4.4, and did not consider the limited discussion was inconsistent with the summary of product characteristics in this regard.

Regarding use in children and teenagers, the Panel noted that cenobamate was licensed only for use in adult patients. An audience member asked whether one of the speakers had used cenobamate in children or teenagers (exchange number 1, above). The Panel considered that it was clear from the question and the speaker's answer that such use would be off licence but noted that the speaker went on to state they could say where they "would like to use it, were the licence to expand", referring to the licence in the US and that there were published cases. The Panel also noted that exchange number 3 (above) included reference by a speaker to parents administering cenobamate to "their young people" and, in exchange number 5 (above), the company's medical employee made reference to a future paediatric licence.

Noting that cenobamate was indicated for treatment of focal-onset seizures with or without secondary generalisation, the Panel considered the question about diagnostic doubt in relation to primary generalised epilepsy (exchange number 4, above). In answering this question, the speaker suggested that in the future it might be possible to use cenobamate for generalised epilepsies but did not reiterate the licensed indication. The speaker did confirm that they were not currently using cenobamate in generalised epilepsies.

The Panel also noted with concern that in exchange number 6, a speaker referred to the use of cenobamate in patients with tonic-clonic seizures and cited it as an alternative to perampanel in individuals with a "history of neuropsychiatric problems". According to Section 4.1 of the perampanel summary of product characteristics, accessed on 5 August 2025 by the Panel, the relevant licensed indication related to primary generalised tonic-clonic seizures. The Panel considered that use of cenobamate in this way would be off licence.

The Panel's primary concern related to the discussion of administration of cenobamate via PEG (percutaneous endoscopic gastrostomy) feeding tubes (exchanges 3 and 5, above). In exchange number 3, while acknowledging it was not recommended, a speaker described their own practice of crushing the tablets and administering via PEG tubes, stating that it "seems to have a similar efficacy that way". The Panel observed this comment was not addressed by the company. In the later exchange, multiple speakers shared their experiences of PEG tube administration. An Angelini medical employee followed by confirming that crushing and

dissolving the tablets was off-licence and that the tablet was the only authorised formulation. The employee went on to volunteer additional information about a forthcoming liquid formulation linked to a future paediatric licence which was “not going to be here anytime soon”.

The Panel took into account Angelini’s submission that all presented slides were within the licensed indication for Ontozry and that it did not proactively initiate discussion on topics outside the licensed indication for the product. Angelini submitted that, on occasions, the audience at meetings asks questions about difficult-to-treat patients, which might be outside the licensed indication for the product. In the Panel’s view, enquiries relating to off-label use should be treated with care, particularly when made in the presence of a group of health professionals. Those responding on behalf of the company should not suggest or presume that others might be interested in the answer and the answer to the question should not go beyond the specific question asked. The licensed indication should be made clear.

In this case, the Panel considered that, while the complainant’s allegation was broad and non-specific, there was evidence that Ontozry (cenobamate) had been promoted outside the terms of its marketing authorisation – for example, by discussion of its administration by crushing and dissolving the tablet. The Panel therefore ruled a **breach of Clause 11.2**.

With regard to the allegation that the meeting slides were not certified prior to the start of the meeting, Angelini provided a copy of the certificate for the slides, dated 21 April 2023, the date of the meeting. The time of final signatory approval was 13:52 CET (equivalent to 12:52 in the UK). The Panel noted that the agenda for the event showed a networking brunch from 11:30–12:30 with the first presentation scheduled to start at 12:30. Angelini submitted that the slides were certified on the day of the meeting, immediately before being presented and that the start of the meeting was delayed to ensure the approval process was complete. Angelini submitted that this was due to some speakers wishing to make “final tweaks” to their slides. The Panel noted that the speaker briefing included a deadline for the submission of slides that was a month before the meeting date, and stated that “when slides have been approved by Angelini Pharma, no changes can be made”.

The Panel was concerned that the slides had not been certified until the very last minute before the meeting – indeed that the start of the meeting had to be delayed to enable this – and the consequent pressure that this could put on the signatory to approve the slides when all arrangements were already in place. It was important that signatories must be free to decline to certify material if, in their opinion, it did not meet the requirements of the Code. The Panel queried what would have happened if the signatory identified issues that meant they were not able to approve the slides on the morning of the meeting.

Nonetheless, the Panel noted that the complainant bore the burden of proof and took account of Angelini’s submission that the start time of the meeting had been delayed. The Panel considered, on the evidence before it, it had not been established that the slides had not been certified prior to the start of the meeting as alleged. The Panel therefore, on balance, ruled **no breach of Clause 8.1**.

In relation to the third allegation in this section, that the complainant had raised their concerns with senior employees following the meeting but was dissatisfied with the action taken, the Panel had no evidence before it of such concerns having been raised. The Panel noted that the complainant bore the burden of proof. In the absence of any evidence, it had not been

established that Angelini had failed to maintain high standards and in this regard, the Panel ruled **no breach of Clause 5.1**.

Cenobamate Road Show – June 2023

The complainant made allegations about the "Cenobamate Roadshow", a series of promotional meetings in the UK, organised and funded by Angelini Pharma UK-I that took place in June 2023. The complainant referred specifically to the London meeting. Angelini explained that there were four meetings, one of which was a combined London/Manchester satellite meeting, and that the agenda varied slightly on each occasion with different speakers, but all the meetings were built around a core presentation.

The complainant alleged that:

- Cenobamate was promoted outside of its marketing authorisation at the London meeting: the use of cenobamate as a monotherapy (rather than as an adjunctive, as licensed) was discussed in the Q&A section of the meeting. There was no intervention from the Angelini staff present.
- There were no attempts to report mentioned off-label use as adverse events, in line with SOPs and one of the key principles of the Code.
- The meeting slides had not been certified.
- These concerns were raised with senior employees following the meeting but no action was taken to mitigate such actions at subsequent meetings, or to address the concerns raised around company culture and the importance of adherence to company SOPs and the Code.

Angelini provided the Panel with a video recording of the London meeting and a copy of the slides used. In relation to the first allegation, the Panel limited its consideration to the question-and-answer session as referenced by the complainant. The Panel identified the following exchange between two speakers and a member of the audience (video timepoint 54:07) as being of relevance to this allegation:

> Attendee: *"I was just wondering with all your experience, have any of you had any pregnancies?"*
>
> Speaker 1: *"Well I had number 3 pregnancy in the world and things turned out well. The first four pregnancies, two persons terminated the pregnancy – that was actually advised in the protocol, though it wasn't required. Two patients had successful live births without complications. And I don't think we really have significant number of patients reported with monotherapy outcomes at this point."*
>
> Speaker 2: *"I think that this brings, it's a very, very important issue because, you know, it looks like the take-up of this drug is going to be another levetiracetam. And it won't be long before it will move down to monotherapy. So the earliest we get the data – so that will allow us to advise our patients – the better. And I think that we should always be registering with the registries for pregnancies, our patients that we come across – because it's very important and, you know, we should not waste any opportunity – as soon as we hear this, we should make sure that they are included in the registries."*

Section 4.1 of the Ontozry (cenobamate) summary of product characteristics stated that Ontozry was indicated for the adjunctive treatment of focal-onset seizures with or without secondary

generalisation in adult patients with epilepsy who have not been adequately controlled despite treatment with at least two anti-epileptic medicinal products.

The Panel took into account Angelini's submission that all presented slides were within the licensed indication for Ontozry and that it did not proactively initiate discussion on topics outside the licensed indication for the product. Angelini submitted that, on occasions, the audience at meetings asks questions about difficult-to-treat patients, which might be outside the licensed indication for the product.

The Panel reiterated its view that enquiries relating to off-label use should be treated with care, particularly when made in the presence of a group of health professionals. Those responding on behalf of a company should not suggest or presume that others might be interested in the answer and the answer to the question should not go beyond the specific question asked. The licensed indication should be made clear.

The Panel noted that the relevant exchange began with an audience question about pregnancy experience with cenobamate. In response, one speaker stated there were not a significant number of patients reported with monotherapy outcomes and the other stated it won't be long before it will move down to monotherapy.

While the question did not refer to monotherapy specifically, the Panel consider it reasonable to interpret the response in the established context to use monotherapy in pregnancy, where possible, at the lowest effective dose.

The Panel observed that Ontozry was indicated for use as an adjunctive treatment only. Section 4.6 of the SPC stated, among other things, that it should not be used during pregnancy unless the clinical condition of the woman requires treatment with cenobamate; women of childbearing potential must use effective contraception during use of cenobamate and until 4 weeks after treatment discontinuation.

In the Panel's view, "I don't think we really have significant number of patients reported with monotherapy outcomes at this point" indicated the limited data relating to monotherapy. The second speaker's statement, "it won't be long until [cenobamate] will move down to monotherapy", while not well qualified and seemingly speculative of a potential future indication, nonetheless implied that such use was not part of the terms of its current marketing authorisation.

On balance, noting the comments were in response to an unsolicited question by a member of the audience, the Panel did not consider that the complainant had established that Ontozry had been promoted outside the terms of its marketing authorisation. The Panel therefore ruled **no breach of Clause 11.2**.

The complainant's second allegation in this section was that there were no attempts to report off-label use as adverse events. The complainant provided no information about the particular example(s) of off-label use they were referring to.

Angelini submitted that:

- there was no evidence that any attendee at the meeting said anything that would constitute a reportable adverse event,

- the required adverse event reporting statement appeared prominently and frequently throughout the slide decks,
- Angelini trains and tests all staff in adverse events recognition and reporting on an annual basis, and
- the Angelini pharmacovigilance lead was present at the meeting at issue
- the speaker contracts included specific references to adverse event reporting.

The Panel noted that the complainant bore the burden of proof and it was not for the Panel to make out the complaint. The Panel considered that the complainant had not established, on the balance of probabilities, that Angelini had failed to report adverse events as alleged. The Panel considered there was no evidence before it that Angelini had failed to maintain high standards in this regard. The Panel therefore ruled **no breach of Clause 5.1**.

The Panel noted that while the case preparation manager had raised Clause 9.2, there did not appear to be an allegation that Angelini personnel were not fully conversant with pharmacovigilance requirements relevant to their work; the complaint was limited to reporting adverse events. The Panel therefore made no ruling in relation to Clause 9.2.

With regard to the complainant's allegation that the meeting slides were not certified, Angelini submitted that the slides were certified on the day of the meeting, immediately prior to their use. Angelini submitted that the near-event approval was due to some speakers wishing to make "final tweaks" to their slides. The Panel noted that the speaker briefing included a deadline for submission of slides of three weeks in advance of the meeting, and stated that "changes to slides on the day will not be possible".

Angelini provided a copy of the certificates for the slides. The certificate for the local speakers' slides was dated 13 June 2023 (the day before the meeting) and the time of final signatory approval was 15:24 CET (equivalent to 14:24 in the UK). The certificate for the main slide deck was dated 14 June 2023 (the day of the meeting) and the time of final signatory approval was 18:01 CET (equivalent to 17:01 in the UK). The Panel noted that the invite for the event showed a start time of 18:00, with the first presentations starting at 18:45.

The Panel reiterated its concerns (above) about not certifying slides until the day of the meeting. The Panel noted it was apparent that this was not an isolated incident and that such circumstances put pressure on the signatory to certify material at very short notice when arrangements were already in place. However, the matter before the Panel related to the meeting slides not allegedly having been certified. Noting that both slide decks had been certified before their use at this meeting, the Panel ruled **no breach of Clause 8.1**.

In relation to the fourth allegation in this section, that the complainant had raised their concerns with senior employees following the meeting but no action had been taken, the Panel once again had no evidence before of such concerns having been raised. The Panel noted that the complainant bore the burden of proof. In the absence of any evidence, it had not been established that Angelini had failed to maintain high standards and in this regard, the Panel ruled **no breach of Clause 5.1**.

'From Now ON' Meeting – November 2023

The complainant made allegations about the "From Now ON" meeting, which took place in Italy in November 2023.

Angelini submitted that this was a standalone meeting organised by the Angelini Global team for an international audience and that Angelini UK worked to ensure the event was suitable for UK health professionals. Two UK speakers were engaged to present at the event, and the UK team hosted 13 delegates to attend, providing accommodation, subsistence and travel support.

The Panel noted that the email invitation to the meeting, "intended for UK and Irish healthcare professionals", described it as a promotional meeting. The email referred to it being "the first international Ontozry-focused event" and "a great opportunity to share updates and experiences in the treatment of epilepsy with Ontozry and to better understand its safety and efficacy and the potential benefits to your daily clinical practice." This was followed by the faculty of experts along with a link to a promotional registration website and agenda.

Whether the ABPI Code applied to materials and activities organised by a non-UK company, which took place outside the UK, would be decided on a case-by-case basis. The Panel noted the supplementary information to Clause 8.2 included that UK companies had responsibilities under the Code when UK delegates were supported and/or UK speakers were contracted to go to events/meetings outside the UK.

Noting the involvement of the UK affiliate, the engagement of the UK speakers and the invited delegates, the Panel determined that the activity fell within the scope of the UK Code.

On-street banners

The complainant provided a photograph showing two banners relating to the From Now ON meeting hung on streetlights and stated that these were intended to direct the health professional attendees from the hotel to the meeting venue. The complainant alleged that, by placing these banners outside the meeting venue on a busy public street in an international business district, the prescription medicine Ontozry had been promoted to the public.

The Panel observed that the two banners in the photograph were identical except for their colours. The banners included the dates of the meeting at the top and two logos (Angelini Pharma's corporate logo and a 'Brain Health' logo) at the bottom. Between these, reading vertically, was the conference logo (From Now ON) and the phrase "Charting a different course in epilepsy care". The letter O of the word "ON" included a graphical element from the Ontozry logo. The Panel noted that it did not contain the Ontozry brand logo, as alleged by the complainant, but that only a graphical element of it was used from the second O of the Ontozry brand logo.

Clauses 3.2 and 26.1 of the Code required that prescription only medicines must not be advertised to the public.

The Panel noted that the banners did not include either the brand name, Ontozry, or the non-proprietary name, cenobamate. However, they did mention the therapy area, epilepsy, and included positive language, "Charting a different course in epilepsy care". It was a well-established principle that a medicine could be promoted without its name being mentioned.

The Panel noted that the banners were displayed on a street in Italy and queried how likely they were to be seen by members of the UK public. In any instance, in the Panel's view, a member of the public would be unlikely to equate Ontozry with the word "ON" with the graphical element

within the letter O, even when combined with the epilepsy strapline. The Panel considered that there was no additional imagery or wording on the banners to prompt recognition of the prescription only medicine by the public. The Panel did not consider that the complainant had established that the banners had advertised Ontozry to the UK public and therefore ruled **no breaches of Clauses 26.1 and 3.2** in relation to each banner.

The complainant alleged that promotion to the public was a breach of the EFPIA (European Federation of Pharmaceutical Industries and Associations) and Italian Farmaindustria Codes and cited Clause 3.4 of the ABPI Code. Clause 3.4 required that companies must comply with all applicable codes, laws and regulations to which they are subject. The Panel acknowledged the complainant's concern about banners for a promotional meeting being displayed on a public street. However, noting its rationale and ruling above, the Panel considered it had not been established that Ontozry had been promoted to members of the public from the information on the banners, nor that Angelini had failed to comply with the local codes, laws or regulations. The Panel therefore ruled **no breaches of Clause 3.4** in relation to each banner.

The complainant further alleged that the two banners had not been certified for use and cited Clause 8.1 which detailed the requirements for certification of promotional material.

Angelini submitted that, since the complainant's allegation related to promotion to the public, certification was not appropriate under Clause 8.1. Angelini rejected allegations relating to Clause 8.1 but did not state that the banners had been certified or provide copies of any certificates.

In the Panel's view, while the banners did not promote Ontozry to the public, they could nonetheless be promotional to health professionals. The Panel considered that the intended audience of the banners was health professionals attending the promotional meeting and that these health professionals would likely be epilepsy specialists familiar with Ontozry.

The Panel took into account the wider context:

- the event was a "Ontozry-focused" promotional meeting;
- the email invitation, registration website and agenda each featured the From Now ON brand logo and strapline "Charting a different course in epilepsy care";
- both the invitation and agenda displayed the prominent Ontozry brand logo towards the top of each material with the distinct graphical element in the second O;
- upon registering for the event, the confirmation email included the From Now ON brand logo and mention of Ontozry: "The first international Ontozry-focused event from Angelini Pharma".

The Panel considered, in this context, the banners were promotional material aimed at health professionals. On the evidence before it, the Panel considered that the two banners had not been appropriately certified. The Panel therefore ruled **two breaches of Clause 8.1**: one for each banner.

The Panel considered that the failure to certify the banners meant that Angelini had shown a lack of oversight regarding the arrangements for the promotional meeting. The Panel noted the importance of certification and its role in underpinning the self-regulatory compliance system. The Panel considered that Angelini had failed to maintain high standards in this regard and, therefore, ruled a **breach of Clause 5.1**.

Presentation in the afternoon of day one relating to access to medicines

The complainant made allegations about the presentation titled "Failure to use new breakthrough treatments for epilepsy: potential additional European drawbacks". This presentation immediately followed a presentation from a US health professional titled "Failure of adoption of new treatments for refractory epilepsy".

The complainant alleged that:

- The speaker advocated for the use of cenobamate as a monotherapy.
- The speaker disparaged the European Medicines Agency (EMA) and questioned the competence of the organisation when it came to granting the appropriate marketing authorisation for a medicine.
- Reference to the EMA, as the licensing authority, was a breach of the Code.
- For a pharmaceutical company to disparage and undermine the competence of a licensing authority in a promotional meeting to a group of UK health professionals brought discredit upon, and reduced confidence in, the pharmaceutical industry.
- Inadequate briefing of speakers meant that high standards had not been maintained.
- No action was taken to correct the statements made by the speaker, which also meant that high standards had not been maintained.

The complainant cited two sets of breaches of Clauses 11.2, 15.2 and 2: in relation to the in-person meeting and the recording of the presentation made available online.

The Panel observed that the speaker's presentation consisted of six slides, with three slides taken up by the title, disclosures and thank you slide. The third slide was titled "Typical development program of antiseizure drugs" and showed a flow diagram with the first box reading "Multicenter placebo-controlled add-on studies in treatment-resistant adults with focal onset seizures" with a negative arrow leading to an 'X', and a positive arrow leading to another box reading "**European Medicine Agency:** Labeling for add-on therapy only, no monotherapy licence". The fourth slide presented a table of interactions of antiseizure drugs. The fifth slide, titled "Drawbacks of combination therapy", consisted of four bullet point statements.

The Panel considered that the full content of the speaker's short presentation was relevant to the allegations and so included a full transcript within its ruling:

> "I was asked to add just some ideas about additional Europe-specific drawbacks. There's basically one. You mentioned – all the topics you mentioned are the same in Europe, and additional drawbacks. And it's a catastrophe, I think, that two very, very powerful anti-seizure medications are not used as they should be used both in the US and in Europe. But there's one additional comment I want to make very briefly. There are some institutions I like – in Europe and in Germany – there's certainly one institution I do not like and that is the European Medicine Agency – and I will tell you why.
>
> Here [referring to slide on screen] we have the typical development programme of anti-seizure drugs. We were speaking about that. Usually you start with multi-centre placebo-controlled add-on studies in treatment-resistant adults with focal onset seizures. You saw the pivotal trial results for cenobamate during this session of today. And, if these studies are negative, that's it, it's usually the end of the programme. We have now some examples of substances we all know, or knew 20 years ago and are coming back in a way in some drug questions – but usually that's the death of a substance. However, if a

substance is successful and better than placebo, like cenobamate was, then we get a labelling and the European Medicine Agency is stupid enough just to allow the labelling for add-on therapy only – no monotherapy licence because they say we get the licence only for what the studies showed. Meaning that, for example, looking at the monotherapy licence, that pregabalin, which apparently is not one of our favourite anti-seizure medications but still was working in placebo-controlled trials, lost against lamotrigine and therefore got no monotherapy licence. Whereas zonisamide almost lost against carbamazepine and made it. And that is indeed a major drawback that if we get a new substance which is apparently very, very effective, the first-line approach to epilepsy treatment which is monotherapy is prevented by the European Medicine Agency – and that is a very European-specific drawback.

So if you look at the potential interactions of anti-seizure drugs, I think it was Phil Patsalos who once calculated that if you combine only two, you have more than 400 possibilities. That is beyond rational anti-seizure medication strategies, apparently. However, in many many instances with all the recently launched and labelled anti-seizure medications we are pressed to do that.

So the drawbacks of combination therapy are apparent. We cannot change it with cenobamate due to the labelling in Europe. However, we have almost no evidence for super-additive effects – with the exception of valproate-lamotrigine, as you all know. With long-term efficacy and tolerability impaired. We are speaking about that the whole day when anti-seizure medications with interacting profiles or properties are used. Anti-seizure medications with interaction profiles are predestined for monotherapies. Well, a drug with a profile of cenobamate, in my eyes, is the perfect monotherapy drug, but in Europe we are not allowed to apply that. And the willingness to risk treatment for such a drug is reduced in case of a pure adjunct label, especially if physicians or neurologists are not so experienced in treating epilepsy patients – and that is definitely a major drawback, at least in my country, and I'm sure in all European countries where this label is effective."

Clause 11.2 required that the promotion of a medicine must be in accordance with the terms of its marketing authorisation and must not be inconsistent with the particulars listed in its summary of product characteristics. Ontozry was indicated for the adjunctive treatment of focal-onset seizures with or without secondary generalisation in adult patients with epilepsy who have not been adequately controlled despite treatment with at least two anti-epileptic medicinal products.

Regarding the allegation that the speaker had advocated the use of cenobamate as a monotherapy, the Panel took into account that slide 5 of the presentation included the following statements:

- "Antiseizure medications with interaction profile are predestined for monotherapies…"
- "Willingness to risk a treatment for such a drug is reduced in case of a pure adjunct label".

The Panel further noted the speaker's comments in relation to monotherapy including:

- "The European Medicine Agency is stupid enough just to allow the labelling for add-on therapy only – no monotherapy licence"
- "We cannot change it with cenobamate due to the labelling in Europe. However, we have almost no evidence for super-additive effects"

- “Anti-seizure medications with interaction profiles are predestined for monotherapies. Well, a drug with a profile of cenobamate, in my eyes, is the perfect monotherapy drug, but in Europe we are not allowed to apply that”
- “And the willingness to risk treatment for such a drug is reduced in case of a pure adjunct label”

The Panel was concerned with the negative impression relating to cenobamate as an adjunctive therapy. Slide 5 listed drawbacks of combination therapy with messaging such as “almost no evidence for super-additive effects”, “long-term efficacy and tolerability are impaired when antiseizure medications with interacting properties are used” and “the willingness to risk treatment for such a drug is reduced in case of a pure adjunct label”. In the Panel’s view, the speaker’s comments, taken together with the slides, conveyed the message that the current adjunct-only license for cenobamate was inappropriate and potentially detrimental to patients.

While the Panel considered it was made clear that monotherapy use was “not allowed in Europe” and such use would be outside the terms of the license, the Panel considered this did not negate the overall impression that “a drug with a profile of cenobamate … is the perfect monotherapy drug”. In the Panel’s view, the speaker advocated and endorsed the use of cenobamate as monotherapy and had promoted it in a manner inconsistent with the particulars in the summary of product characteristics. The Panel therefore ruled a **breach of Clause 11.2** in relation to the in-person presentation.

Clause 15.2 required that promotional material must not include any reference to the Commission on Human Medicines, the Medicines and Healthcare products Regulatory Agency (MHRA) or the licensing authority, unless this is specifically required by the licensing authority.

Taking into account the reference to the EMA on slide 3 of the presentation and the multiple verbal references to the EMA made by the speaker, the Panel ruled a **breach of Clause 15.2** in relation to the in-person presentation, as acknowledged by Angelini.

Regarding the allegation that by disparaging and undermining the competence of a licensing authority in a promotional meeting to health professionals, Angelini had brought discredit upon, and reduced confidence in, the pharmaceutical industry, the Panel noted Angelini’s comments about phraseology and that the speaker was not a native English speaker. The Panel considered, however, that the complainant’s allegation was not restricted to the use of the word “stupid” – it was a broader allegation about the message and tone of the presentation.

In the Panel’s view, the message from the presentation as a whole was a dismissal of the EMA and a criticism of its decisions and methodology. This was a short presentation that opened with the speaker stating that “there’s certainly one institution I do not like and that is the European Medicine Agency” and was focused entirely on their opinion of the EMA’s decision to license medications such as cenobamate for adjunctive use only.

It was a well-established principle that a company was responsible for the acts and omissions of its consultants, agents and third parties. The Panel considered that such a presentation, which focused on criticising the EMA’s licensing decisions, by a contracted speaker at a company-organised promotional meeting, had brought discredit upon, and reduced confidence in, the pharmaceutical industry and ruled a **breach of Clause 2** in relation to the in-person presentation.

In its original response to this complaint, Angelini submitted that the comments about the EMA were edited out of the version of the video that was uploaded into the portal that UK health professionals could access after the event. Angelini later amended this statement and acknowledged that the comments had not been edited out. The Panel reviewed the recording of the meeting submitted by Angelini and labelled as "Portal Videos edited" and confirmed that this was the case. The Panel therefore ruled corresponding **breaches of Clauses 11.2, 15.2 and 2** in relation to the online version of the meeting.

The complainant alleged that Angelini had failed to maintain high standards by not taking action at the meeting to correct the statements made by the speaker. The Panel acknowledged that, while it was not always possible for pharmaceutical companies to prevent contracted speakers from making statements that were not in line with the requirements of the Code, companies were responsible for consultants acting on their behalf. In this case, the contracted speaker's repeated advocacy of monotherapy use along with their criticism of the EMA and licensing was not an isolated comment but a consistent message throughout their presentation. In the Panel's view, Angelini employees present should have intervened to make clear that the use of cenobamate as monotherapy was off-label, inconsistent with the terms of its marketing authorisation and would give rise to reporting obligations. The Panel considered that by not doing so, and allowing the speaker's presentation to go unchallenged, Angelini had allowed repeated inappropriate messaging to remain uncorrected. The Panel considered Angelini had failed to maintain high standards and ruled a **breach of Clause 5.1**.

The complainant also alleged Angelini had failed to maintain high standards because health professional speakers had been inadequately briefed. Angelini submitted that the speakers had been specifically briefed and contracted to act professionally and specifically briefed not to be disparaging and not to refer to the regulatory bodies at all.

The Panel took particular account of the following points from the "Guidance for speakers" slide:

- "Please ensure that the content of the presentation is **accurate, balanced, fair, objective, capable of substantiation, fully references and based on up-to-date evidence**"
- "Make the **licensed indication clear and prominent** ahead of any corresponding data"
- "**All data and case studies presented must be 'on label'**, i.e. consistent with the licensed indication for the product and with the information provided in the SPC for the product, including dosage"
- No reference to the Medicines Commission, the Commission on Human Medicines, Medicines Health and Regulatory Authority (MHRA), European Medicines Agency (EMA) or licensing authority, the Committee on Safety of Medicines (CSM), unless this is specifically required by the licencing authority
- No products, healthcare bodies or other pharmaceutical companies should be disparaged
- "Please note that discussions and answers during any Q&A sessions must remain 'on-label'"

The Panel noted that the "guidance for speakers" provided by Angelini as part of its response to this complaint was a single slide that appeared to be generic guidance relevant to any presentations, rather than a specific briefing outlining what the speaker should cover in their presentation. Angelini submitted that it believed a briefing was provided verbally to the speakers.

It was not clear to the Panel whether the speaker had received any additional briefing, written or verbal, in relation to their presentation. The presentation delivered did not follow the guidance provided in the single slide. The speaker placed emphasis on the EMA's approach, including disparaging remarks, and highlighted the drawbacks of adjunctive therapy while advocating for the use of cenobamate as monotherapy.

The Panel noted the slide "Drawbacks of combination therapy" which contained the statement "antiseizure medications interaction profile are predestined for monotherapies". In the Panel's view, it could have been reasonably anticipated from this slide and the title of the presentation, "Failure to use new breakthrough treatments for epilepsy: potential additional European drawbacks", that the speaker would have discouraged adjunctive therapy and encouraged use of cenobamate as monotherapy. The Panel considered it was insufficient to provide a single generic briefing slide and queried whether the briefing should have covered topics that the company could have reasonably foreseen to encourage off-label use. In this regard, the Panel considered Angelini had not adequately briefed the speaker in this regard. The Panel therefore ruled a **breach of Clause 5.1**.

"Social sharing session" on day two

The complainant made allegations about a "social sharing session" on the second day of the meeting. According to the complainant, health professional speakers shared their experience with cenobamate in an informal group session, with speakers rotating between five groups of attendees. While the Panel noted that the complainant had alleged five breaches of most of the clauses cited, the Panel considered that the allegations arose from the same activity, albeit across different groups. In the absence of specific information relating to each group, a single ruling of each clause would sufficiently address the matters at issue.

The complainant alleged that:

- The speakers were briefed verbally and were told that, while their slides should be consistent with the marketing authorisation for cenobamate, they would not be stopped from speaking about their experience with cenobamate that was inconsistent with the marketing authorisation
- When attendees asked questions relating to use of cenobamate outside of its marketing authorisation, Angelini employees gave verbal approval for the speakers to respond. The speakers told the five groups of attendees about their use of cenobamate in ways that were inconsistent with the marketing authorisation, specifically:
    - in paediatric patients
    - as a monotherapy treatment
    - in pregnant patients
- Important safety information from section 4.6 of the summary of product characteristics ("Fertility, Pregnancy and Lactation") was not provided to attendees while discussing the use of cenobamate in these patient groups. This resulted in an unbalanced presentation of the data and didn't reflect the clinical evidence documented in the summary of product characteristics. It also prejudiced patient safety in a particularly vulnerable patient group. This promotion was inconsistent with the marketing authorisation for the product.
- There were no attempts to collect adverse event reports from either the health professionals in attendance or speakers discussing such use. This was not in line with company SOPs or the ABPI principles, and prejudiced patient safety.

Angelini submitted that this session of the meeting was not recorded.

The Panel noted that the parties' accounts differed; it was difficult in such cases to know exactly what had transpired. A judgement had to be made on the available evidence, bearing in mind the extreme dissatisfaction usually necessary on the part of an individual before they were moved to actually submit a complaint.

The Panel noted Angelini's submission that all presented slides were within the licensed indication for Ontozry and all speakers were briefed to remain within the licensed indication and took into account the following points from Angelini's "Guidance for speakers" slide:

- "Please ensure that the content of the presentation is **accurate, balanced, fair, objective, capable of substantiation, fully references and based on up-to-date evidence**"
- "Make the **licensed indication clear and prominent** ahead of any corresponding data"
- "**All data and case studies presented must be 'on label'**, i.e. consistent with the licensed indication for the product and with the information provided in the SPC for the product, including dosage"
- "Please note that discussions and answers during any Q&A sessions must remain 'on-label'"

The Panel decided it was not possible to determine what had been said verbally during the speaker briefing or the "social sharing session" itself and considered that it had not been established that cenobamate had been promoted outside of its marketing authorisation. The Panel therefore ruled **no breach of Clause 11.2**.

Regarding the complainant's allegation about important safety information not being provided to attendees, the Panel acknowledged Angelini's submission that epilepsy specialists would be very familiar with the risks associated with epilepsy treatments in specialist populations. Noting that the complainant's allegation was specific to the discussions in the "social sharing session", the Panel decided it was not possible to determine what had been said verbally. The Panel considered that it had not been established that data had been presented in an unbalanced manner or that patient safety had been prejudiced. The Panel therefore ruled **no breach of Clauses 6.1, 5.1 and 2**.

The Panel noted that the complainant had cited five further breaches of Clause 11.2 in relation to their allegation about fertility, pregnancy and lactation safety information but considered that these concerns had already been addressed in the overall allegation about off-licence promotion above, which included the sentence "Additionally, experience of the use of cenobamate in pregnant patients was discussed". The Panel considered that the complainant had made no additional allegation and therefore made no further rulings on this matter.

The complainant's final allegation regarding the "social sharing session" was that there were no attempts to collect adverse event reports from the health professionals or speakers during the discussions in this session.

Angelini submitted that:

- it was not aware of any adverse event reports made at any point during the meeting and there was no evidence that any reportable adverse events were discussed during the "social sharing session"
- questions pertaining to use in specialist populations are typically not reportable adverse event declarations

- the speaker contracts included a very clear reference to adverse event reporting
- all UK staff that attended the meeting had been appropriately trained.

The Panel considered that the complainant had not established, on the balance of probabilities, that Angelini had failed to collect or report adverse events as alleged. The Panel therefore ruled **no breach of Clause 2**.

The Panel noted that while the case preparation manager had raised Clause 9.2, there did not appear to be an allegation that Angelini personnel were not fully conversant with pharmacovigilance requirements relevant to their work; the complaint was limited to reporting adverse events. The Panel therefore made no ruling in relation to Clause 9.2.

'From Now ON' online platform

Angelini submitted that all attendees at the From Now ON meeting were given access to a portal from which they could watch two video recordings, one for each day of the meeting, and view/download copies of the slides for the 18 presentations at the meeting.

The complainant alleged that:
- The videos and slide sets had not been certified in line with the requirements of Clause 8.1.
- They did not have an adverse event reporting statement.
- The slides did not have UK prescribing information.

The Panel observed that the portal included, among others, the following sections:
- "Discover the agenda" – clicking on this section opened a promotional one-page pdf of the agenda
- "For UK & Ireland attendees: agenda, prescribing information and adverse event reporting." – clicking on this section opened a two-page pdf. The first page included an agenda, with an adverse event reporting statement towards the bottom making clear Ontozry was a black triangle product subject to additional monitoring. The second page included the Ontozry prescribing information (GB, NI, ROI) and a boxed adverse event reporting statement
- "Day 1: watch the replay" – clicking on this section opened the video of day 1
- "Day 1: presentations" – clicking on this section brought up a list of 15 presentations, each with a link to "download file"; clicking each "download file" opened a pdf of the slides for that presentation
- "Day 2: watch the replay" – clicking on this section opened the video of day 2
- "Day 2: presentations" – clicking on this section brought up a list of 3 presentations, each with a link to "download file"; clicking each "download file" opened a pdf of the slides for that presentation.

Regarding certification, Angelini acknowledged a single breach of Clause 8.1. Angelini submitted that it regarded the portal itself as the item of promotional material that required certification and that this was not certified by a UK signatory.

Angelini submitted that it was not possible to download the two videos from the portal. The Panel considered that, as promotional material, the videos should have been certified – either individually or as part of the certification of the portal itself. The Panel had no evidence before it

that the two videos of the meeting had been certified for use. As the two videos were not downloadable and so did not necessarily require separate certification to the rest of the portal, the Panel determined that a single **breach of Clause 8.1**, as acknowledged by Angelini, was sufficient in relation to the videos.

While stating that "The videos and slides only as elements within that portal as records of the overall meeting video and slide format; they were neither considered nor approved as standalone items for use in any other way", Angelini submitted that "the entire set of slides was certified prior to use, for presentation and upload". Angelini submitted that the filename "All slides for upload" clearly implied the slide deck was to be approved for upload into the portal.

Following the Panel's request for clarification on a number of points, Angelini submitted that "each individual speaker slide deck was certified prior to the meeting". However, the Panel had no evidence before it to indicate that the 18 sets of slides had been individually certified for use in the portal, only that they had been certified as a single large PowerPoint file.

The Panel queried whether it was clear in the approval system that the slides had been intended for both presentation at the in-person meeting and for use in the portal. It appeared to the Panel that the notes on the approval system referred specifically to the in-person meeting ("Speaker presentation decks for From Now ON Meeting in Milan 28th-29th November 2023.") and the only suggestion that the slides might be used after the event was in the filename of the PowerPoint file uploaded to the system for approval ("All slides FNO for upload"). In the Panel's view, "for upload" could as easily refer to uploading to the approval system as to uploading to the portal for on-demand access.

Regardless of whether the certification of the presentations had included use on the portal or not, the Panel considered that certification of the single PowerPoint file containing all 18 presentations did not fulfil the requirements of Clause 8.1 for material to be certified in its final form. As the slides were available to view and download from the portal as 18 separate files, these files would need to be certified as standalone items to ensure that they each met the requirements of the Code.

Angelini submitted that six of the slide decks made no reference to cenobamate and, as such, were not promotional; a seventh slide deck made "only passing reference to cenobamate" and Angelini did not regard it as promotional in isolation. The Panel noted that three of these did not appear to be present on the online portal. The Panel considered the content of only those slide decks that it understood had been made available on the portal, noted that the presentation titles on the portal did not exactly match the title slides within the PowerPoint file, and made the following determinations:

Presentation title in the portal	**Assumed presentation title and position in the certified "All slides FNO for upload" file**	**Promotional or non-promotional as a standalone file without audio?**
Angelini's commitment to brain health	Not apparently present in the "All slides FNO for upload" file – the Panel made its determination based on the slides shown in the video recording	Promotional

Brain Health	The importance of brain health and the burden of neurological disorders (Slides 2–26)	**Not promotional**
Burden of epilepsy	Physical, emotional and social burden of uncontrolled epilepsy (Slides 27–56)	Promotional – e.g. slides 39–41
Burden of epilepsy	Emotional and social burden of uncontrolled epilepsy (Slides 57–79)	**Not promotional**
Epilepsy treatment: news and trends	Impact of delayed treatment or medication switch in Epilepsy (Slides 97–112)	**Not promotional**
Epilepsy treatment: news and trends	Antiseizure medicines sequencing and chances of success (Slides 80–96)	Promotional – e.g. slide 88
Epilepsy treatment: news and trends	Here and now: overview of the current guidelines and literature update (Slides 113–137)	Promotional – e.g. slide 129
Cenobamate in treatment gaps	The distinctive pharmacological and clinical profile of cenobamate: how does it address the current treatment gaps? (Slides 138–157)	Promotional
Efficacy & safety	Long-term efficacy and safety data (Slides 158–168)	Promotional
Efficacy & safety	Longer-term use of cenobamate (Slides 169–183)	Promotional
From clinical trials to clinical practice	Cenobamate: from clinical trials to early access, the Irish experience (Slides 184–197)	Promotional
From clinical trials to clinical practice	From RCTs to EAP to RWE: what have we learnt so far? (Slides 198–218)	Promotional
Is earlier better?	Use of cenobamate: is sooner better? The place of cenobamate in antiseizure medicine sequencing (Slides 219–247)	Promotional Adverse events reporting statement included on slide 220 (the second slide of this presentation)
New approaches into practice	Failure of adoption of new treatments for refractory epilepsy (Slides 248–266)	Promotional
New approaches into practice	Failure to use new breakthrough treatments for epilepsy: potential additional European drawbacks (Slides 267–272)	**Not promotional** (slide content in isolation)
Clinical Case	Personalized Medicine (Slides 357–372)	Promotional – e.g. slides 366–372
Clinical Case	Cenobamate in a severely pharmacoresistant patient with	Promotional e.g. slides 383–386

	progredient Rasmussen encephalitis (Slides 373–386)	
Clinical Case	Clinical case (post-traumatic epilepsy) (Slides 387–406)	Promotional – e.g. slide 398 The final slide presents the prescribing information for Ontozry (cenobamate) and the adverse events reporting statement

The Panel determined that the content of 14 slide decks was promotional for cenobamate and therefore required certification in accordance with Clause 8.1. These slide decks had not been certified as required and the Panel ruled **14 breaches of Clause 8.1** in relation to the use of these slides in the portal.

The Panel determined that the content of four slide decks (see above) was not promotional in isolation. Noting that the allegation was specific to the requirements of Clause 8.1 in relation to the certification of promotional material, the Panel ruled **no breaches (x4) of Clause 8.1** in relation to the above sets of slides in use in the portal.

The complainant made no allegations about certification of the rest of the portal and so the Panel made no rulings in this regard.

The Panel noted that, although the complainant's phrasing of the allegation about the adverse events reporting statement appeared to imply that this allegation was relevant to both the videos and the slide sets, the complainant had only alleged 18 breaches of Clause 12.9, which indicated that the allegation was relevant only to the slide sets. The allegation about prescribing information was limited to the slide sets. The Panel therefore limited its rulings on these two matters to the 18 slide sets available in the portal.

While Angelini submitted that "a clear and obvious link" to UK prescribing information and adverse event reporting was provided within the portal, the Panel had some concerns about whether it was sufficiently clear to the user that the prescribing information could be found on the second page of the agenda document. In any event, this was not sufficient in relation to the downloadable slides. The Panel considered that, as the 18 slide sets were available to download from the portal individually, each would need to be capable of standing alone in relation to the requirements of the Code.

The Panel referred to its determination, above, that four of the slide sets were not promotional. The Panel therefore ruled **no breaches (x4) of Clause 12.1** and **no breaches (x4) of Clause 12.9** in relation to these sets of slides in use in the portal.

The Panel considered that the 14 promotional slide sets (see above) that could be downloaded from the portal needed to stand alone with regard to the requirements of Clauses 12.1 and 12.9 of the 2021 Code and thus required prescribing information and the adverse event reporting statement. The Panel found Angelini's statement that prescribing information was not required for these slide decks "as they are provided within the portal as a reference for delegates who may wish to consolidate their learning after the event; not as promotional content, *per se*" concerning. In the Panel's view, there was no doubt that these slide sets met the definition of promotion under the Code.

On the evidence available, the Panel determined that prescribing information and the adverse events reporting statement were present in one of the slide sets available to download from the portal (see above). The Panel therefore ruled **no breach of Clause 12.1** and **no breach of Clause 12.9** in relation to this set of slides in use in the portal.

On the evidence available, the Panel determined that neither prescribing information nor the adverse events reporting statement were present in the remaining 13 slide sets available to download from the portal. The Panel therefore ruled **13 breaches of Clause 12.1** and **13 breaches of Clause 12.9** in relation to these sets of slides in use in the portal.

The Panel noted that, in their letter to the company, the case preparation manager had suggested that Angelini's response address the requirements of Clause 5.1 and Clause 2 in relation to these matters. The Panel considered that in not certifying the elements of the online portal and in failing to include obligatory information, Angelini had failed to maintain high standards. The Panel noted the importance of certification and its role in underpinning the self-regulatory compliance system and the importance of prescribing information and the adverse events reporting process for patient safety, particularly for a black triangle medicine subject to additional monitoring. The Panel considered that Angelini had failed to maintain high standards in this regard and, therefore, ruled a **breach of Clause 5.1**.

Clause 2 was a sign of particular censure and reserved for such use. The Panel took into account that the slides had been certified before their use at the in-person meeting, the users of the portal were attendees who had seen the presentations in person, that prescribing information and the adverse events reporting statement were included within the portal itself, and that the Panel had already ruled on the content of the meeting above, particularly the breach of the Clause 2 for the comments about the EMA present in one of the videos on the portal. The Panel considered, on balance, that its concerns had been sufficiently addressed by the rulings above and therefore ruled **no breach of Clause 2**.

Internal reporting of non-compliance

The complainant alleged that they had raised their concerns "with senior members of the Angelini Pharma UK-I leadership team at the event, who expressed no concern". There was no evidence before the Panel of the concerns having been raised in this manner.

The complainant alleged that they had raised their concerns again with a senior medical employee following the event. Angelini acknowledged that this discussion had taken place but the Panel had no additional evidence before it of the concerns having been raised in this manner.

The complainant alleged that, following advice from the senior medical employee, they had raised their concerns with a global senior compliance employee. The complainant provided a copy of their email to the senior compliance employee and the response received. The complainant alleged that the response indicated that "after investigating internally, it was found that there was no non-compliance at the event" and that "the senior leadership team of the UK organisation considered the activity at the 'From Now ON' meeting to be acceptable". The complainant alleged that "Whilst there is a policy in place at Angelini Pharma with regards to whistleblowing and speaking up, in practice when this policy is exercised, concerns are denied and corrective and preventative actions cannot be considered."

Angelini submitted that while it welcomed comments and concerns from staff, it was "under no obligation to agree with their concerns". Angelini submitted that the complainant's concerns were investigated by the Global team but nothing was found to be non-compliant from a Global perspective. Angelini provided a timeline of the steps taken in investigating and responding to the concerns. In Angelini's view, given the role of the complainant, it considered this a professional interaction in the context of feedback following the event, rather than a 'whistleblowing' concern expressed through the 'Speak Up' channels, and was responded to in that manner.

The Panel took into account:

- the style/tone of the email from the complainant to the global senior compliance employee
- the specific concerns raised by the complainant in that email
- the response received from the global senior compliance employee
- Angelini's whistleblowing policy.

In the Panel's view, while the complainant's email cited "concerns", it was presented more as feedback on the event than as a whistleblowing concern. The email included phrases such as:

> "Following the From Now On event, I wanted to raise some concerns with you with regards to the compliance of the event."
>
> "In the interest of trying to learn from this experience, I have tried to highlight the situations and concerns below and hope to discuss them and potential CAPAs soon."
>
> "I hope that you receive this feedback in the spirit it is intended, and we can have a constructive approach to ensure such occurrences can be prevented in future so we can continue to contribute to UK HCPs to such events."

The Panel observed that the complainant had raised four concerns in the email, some (but not all) of which were subsequently raised in the complaint to the PMCPA. Of the concerns that were also the subject of this complaint, the Panel noted that it had ruled no breaches in relation to promotion to the public and no breaches in relation to the 'social sharing' breakout session.

In the Panel's view, the response from the senior compliance employee was reasonably short, but not dismissive of the complainant's concerns. The response explained that the complainant's points had been shared with "relevant internal stakeholders" and acknowledged that there was "room for improvement" regarding late submission of presentations. The response ended with a suggestion for future improvement: "For the future, we could organize with the relevant colleagues, alignment calls aimed at better addressing this kind of topics."

The Panel noted with concern that the first sentence of the email paragraph "With reference to the discussions among HCPs, my understanding is that when peers share their professional experiences, the content of the slides may be not strictly followed by the presenter. However, I have got confirmation that all slides/presentations were in line with applicable requirements" might imply endorsement of speakers discussing off-label topics.

Overall, the Panel considered that, while the email in this case did not appear to be an example of whistleblowing, Angelini had a whistleblowing policy in place. While the Panel was concerned

that Angelini had failed to recognise issues with the From Now ON event as ruled in breach above, the complainant had been able to raise their concerns, which appeared to have been investigated by Angelini and responded to. The Panel considered that the complainant had not established that Angelini had failed to maintain high standards in this regard and, on balance, ruled **no breach of Clause 5.1**.

Clause 2 was a sign of particular censure and reserved for such use. The Panel ruled **no breach of Clause 2**.

Complaint received **31 May 2024**

Case completed **23 September 2025**