Author's response to the Decision to Retract

In the proposed retraction notice, two main reasons are given for the decision to retract:

1. **Lack of reproducibility due to use of individualised homeopathy and insufficient reporting of changes in dosing or potency** of the individualised prescriptions.

2. **Failure to disclose a conflict of interest**, based on the fact that "…the same homeopathic medicinal products were being marketed and prescribed by the first author's clinic while the clinical trial was ongoing".

I will address each of these points below.

1. Reproducibility of Individualised Homeopathic Treatment

When considering whether sufficient detail has been provided for a trial to be replicated, there are two related issues to consider – whether **the technique itself is inherently replicable and the level of reporting detail**.

Firstly, it is essential to clarify that **individualizing both the homeopathic medicinal substance and potency to suit each patient is a fundamental requirement for individualized homeopathic treatment (IHT) to be efficacious**. The homeopathic regimen was therefore delivered correctly for a trial which aimed to assess the efficacy of IHT.

To clarify what this involves in practice, the homeopathic pharmacopoeia details the precise set of symptoms each homeopathic medicine can potentially treat. The prescription process involves the physician establishing the set of symptoms being experienced by the patient (including mental-emotional and physical symptoms across multiple body systems) and identifying the homeopathic medicine which matches that 'symptom picture' as closely as possible. The closer the match, the better the results observed in clinical practice.

Thus, as IHT is a truly personalised medicine, during a standard DB-RCT design, what is being assessed is the technique itself, not efficacy of the individual medicines: **this has already been demonstrated by multiple independent research teams**.

A systematic review on this topic demonstrates that IHT has been assessed under placebo-controlled RCT conditions in 32 studies by 26 independent research teams, from 12 countries (Mathie et al. 2014). Given that our study has replicated an existing prescribing technique, the argument that it could not be replicated again simply does not hold.

It is important to note that, although none of the previous trials assessing IHT captured within the Mathie et al. 2014 systematic review involved non-small cell lung carcinoma, this data still pertains directly to the point of concern because 'individualized homeopathic

treatment' is the same intervention, regardless of the medical condition it is being used to treat. Furthermore, Mathie et al. 2014 found that homeopathic medicines prescribed in this manner are up to twice as likely to provide clinical benefit as placebo (OR = 1.98, 95% CI 1.16 to 3.38) and that this result fully withstands sensitivity analysis.

Omission of details regarding changes in dosing or potency

In terms of reporting details, the issue is whether a **suitably qualified person** could replicate the study – not whether another medical professional, with no prior training or experience in prescribing the intervention could do it. It is true that individuals without any training in homeopathy would not understand 'potencies of homeopathic remedies were selected on the basis of homeopathic principles', but that is not relevant; the information provided was sufficient for **a practitioner trained in 'individualized homeopathic treatment' (IHT)** to repeat the study because this is a specific, well-defined and characterised technique used worldwide.

The retraction notice correctly states that the selected homeopathic medicines were presented transparently in the published Tables 6 and 7, but **fails to acknowledge that the dosing strategy for the Q potency preparations was transparently reported in the paper** i.e. how to take the medicine daily (see Table 5 lower panel) and details of the standard method for use of Q potencies – escalating the potency every 3 weeks: Q1, to Q2, to Q3 etc. – was in the text (see p.6 of the PDF).

The retraction notice also fails to consider that the main prescribed homeopathic medicine was changed in only 25% of patients, equally in both homeopathy and placebo groups, as detailed in Table 6. This means that **75% – the majority – of included patients were kept on the same selected homeopathic medicine and followed the Q potency dosing strategy as outlined fully in the paper, throughout the trial.**

Considering the additional LM, D and C potencies prescribed as **'rescue' treatment for acute side effects**, these are described in Table 7. As expected, the vast majority of patients required one of the two most commonly prescribed homeopathic medicines for chemotherapy side effects – *Nux vomica* LM and *Cadmium sulfuricum* C – whilst others needed more bespoke prescriptions depending on their symptoms. I acknowledge that not all precise potencies were stated for all 'rescue' medications, these can be provided on request. I was never asked specifically to provide individual patient data at that level of detail.

2. Undeclared Conflict of Interest

I must confess that this argument was unexpected and is deeply confusing. I can only surmise that it represents a genuine, yet fundamental misunderstanding of the nature of homeopathic medical practice, and risks misrepresenting both myself, as the lead author, and the homeopathic profession at large.

The proposed retraction notice claims that "*homeopathic medicinal products were being marketed and prescribed*" while the clinical trial was ongoing and suggests that this provision of medicines (as part of normal homeopathic medical practice) is a conflict of interest: I fail to see how.

The intervention assessed in this study (IHT) is the same technique, involving the same range of unpatentable medicines, as that used by homoeopathically-trained physicians worldwide.

If the concern is that I was using this modality in my private practice during the study, this same situation frequently applies to doctors who work in both conventional clinical practice and research.

Prescribing an individualised HMP, in Austria, has the same medical and legal standing as prescribing a conventional pharmaceutical medicine. There is no more conflict of interest in prescribing a HMP for patients to obtain from a pharmacy of their choice, than there is for a conventional medical doctor, for example, prescribing antibiotics or over-the-counter pain relief. In our study, all HMPs were paid for by the trial funds and provided by one central, independent, homeopathic pharmacy so there could be no conflict of interest: there was no financial contract between the pharmacy and any of the authors.

As for categorization of the medicines themselves, there is no pathway available for me to benefit personally or financially by prescribing them, in such a way as to create bias in the trial outcome. These are unpatentable medicines which have been widely available from homeopathic pharmacies for decades, that are regulated accordingly in each country; any homeopath, anywhere in the world, can prescribe them. Thus, no marketing of medicines occurred and there was no conflict of interest of any kind.