23 June 2025

By email: ListingsComplianceMelbourne@asx.com.au
ASX Limited
Rialto Towers
Level 50, 525 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

INOVIQ Limited ACN 009 070 384 (ASX Code: IIQ or Company) – 'New treatment kills 88% of Breast and Lung Cancer Cells' announcement – Response to ASX queries

In response to your letter dated 19 June 2025, we answer each of your questions in the order asked and using the same defined terms.

1. **Does IIQ consider the header of the Announcement conveyed a fair and balanced impression of the contents of the announcement, given the early stage of the research? If so, please explain the basis for that view.**

   In our view, 'INOVIQ's New Cancer Treatment Kills 88% Of Breast And Lung Cancer Cells In Lab Tests' conveys a fair and balanced representation of the contents of the Announcement. Moreover, the header is consistent with the ASX Market Announcements Platform (**MAP**) announcement header functionality limitations that limits headings to circa 60 characters. Importantly, the header included the words 'Cells in Lab Tests', the highlights included 'In lab studies', and the first paragraph included 'in recent *in vitro* studies', which together is clear that the **research was an *in vitro* study conducted in cancer cell lines in a laboratory environment.** Therefore, the header of the Announcement was both fair and balanced in the context used.

   The header also informs the market that IIQ has improved the previously reported efficacy of its CAR-NK-EVs to kill cancer cells in the laboratory. The *in vitro* study was **a treatment: control study design performed in the laboratory**. In an ***in vitro* lab study**, a treatment: **control** design involves exposing cultured cells, tissues or biomolecules to an experimental intervention (treatment group) while maintaining identical conditions for an untreated baseline group (control group). The treatment: control study design is recognized as standard best practice but is often mandated by regulatory authorities and scientific guidelines for generating credible, reliable, and interpretable results in both laboratory and clinical research settings.

2. **Does IIQ consider that it had a reasonable basis to make the Forward-Looking Statements? If so, please explain the basis for that view.**

   The potential advantages of CAR-exosomes over autologous CAR-T therapies in solid tumours are generally well known and accepted in the scientific literature based on previous researchers in vitro and in vivo studies. There is a reasonable basis to make the Forward-Looking Statements below:

a. *'Going forward this could lead to an 'off the shelf' therapy made in advance and used on many patients.* IIQ's exosome platform produces its extracellular vesicles (EVs, or Exosomes) from an immortalised NK92 cell line that enables continuous production of NK92 cells and exosomes. This means that its CAR-NK-EVs are being developed as an allogeneic or 'off-the-shelf' therapy that, if approved, could be used to treat multiple patients. This contrasts to existing CAR-T therapies that are engineered from an individual patient's own T cells to treat that individual patient. [1-22].

b. *'It could be:'*– these words indicate that each of the following points are forward-looking.
   i. *'Faster to produce;'* – IIQ's proprietary exosome platform includes the continuous production and isolation of CAR-NK-EVs from immortalised NK92 cells that are faster to produce as a potential off-the-shelf treatment than current autologous CAR-T production methods that are an individualised patient treatment.
   ii. *'Safer to use; and'* - exosomes are a natural extracellular vesicle and that it is generally well known and accepted in scientific literature that they offer potential safety advantages such as reduced risk of immune rejection and cytokine release syndrome.
   iii. '*More effective than traditional cell therapies like CAR-T.'* - it is generally well known and accepted in scientific literature that exosomes are small EVs of 30 – 150 nm in size that can cross biological barriers such as the Tumour Microenvironment and the Blood Brain Barrier providing potential efficacy advantages compared to autologous CAR-T therapies for treatment of solid tumours.

3. Noting the early stage of the research, how does IIQ justify the use of the term 'Treatment'?

The term "Treatment" is justified as the *in vitro* study was a Treatment: Control design. The cytotoxic effect of a treatment (i.e. IIQ's CAR-NK-EVs) on cells maintained in culture was compared to untreated cell controls. In an *in vitro* lab study, a treatment: control design involves exposing cultured cells, tissues or biomolecules to an experimental intervention (treatment group) while maintaining identical conditions for an untreated baseline group (control group). The treatment: control design is non-negotiable in *in vitro* laboratory studies for regulatory acceptance and scientific rigour. Regulatory bodies (FDA, OECD) and guidelines (GLP, GCCP 2.0) universally mandate it to ensure results are attributable to the intervention, not confounding variables. [23,24] Therefore, the use of the term 'treatment' is not misleading in the context that it has been used.

4. Please provide the following information:

4.1 confirmation that the studies were undertaken by Peter Mac on the same terms disclosed to the market on 31 March 2025;

The *in vitro* studies were conducted by INOVIQ at its laboratories at 23 Normanby Rd, Notting Hill Victoria, following further optimisation and validation of its CAR-NK-EV

production process and analytical testing procedures using the real-time xCELLigence assay to assess the cytotoxic effect of CAR-NK-EVs on cancer cells *in vitro*.

The data in the Announcement were generated in-house and are in addition to those disclosed to the market on 31 March 2025 which are currently being undertaken by the Peter MacCallum Cancer Institute. The IIQ in house *in vitro* study to assess the killing activity of CAR-EVs was completed ahead of the Peter Mac study. As the data are market sensitive, IIQ released its results on the ASX platform prior to Peter MacCallum's future results.

4.2 the *in vitro* study design;

The study reported in the Announcement was an *in vitro* Treatment: Control study design to evaluate the *in vitro* anti-tumour efficacy of EGFR-targeted CAR-NK exosome (CAR-NK-EVs) treatment against TNBC (Hs578T) and NSCLC (Calu-3) cell lines compared to negative controls HEK-293-derived EVs (TNBC only), untreated cells and PBS, and a positive control Lapatinib.

This *in vitro* study design is evidenced in Figures 1 and 2. "The real-time xCELLigence assay demonstrated that the CAR-NK-EV treatment exerted a significant cytotoxic effect on TNBC cells (Hs578T) compared to **controls**. Data **from three independent experiments** (each with three technical replicates) showed that treatment with 2.5 million CAR-NK-EVs/cell (green line) resulted in 87.8% cell death in Hs578T cells within 96 hours. In contrast, EVs derived from HEK-293 cell (blue line) conditioned medium did not induce cell death, confirming the specific cytolytic and anti-tumour activity of CAR-NK-EVs."

The FDA's guidance for industry on cell substrates and vaccine production emphasizes the use of control cell cultures processed in parallel with **treated cultures**, under identical conditions, to detect adventitious agents and validate assay results. The guidance also highlights the need for scientifically valid assays, which require appropriate controls for assay validation, accuracy, and reliability.

There were three (3) independent biological replicates per cancer type, each with three (3) technical replicates (n=9 per group). Data was analysed using one-way ANOVA with Tukey post-hoc correction; $p < 0.05$ considered significant.

4.3 the statistical significance of the values attached to the data in the Study Results;

Statistically significant effects of the treatment (CAR-NK-EVs) on the measure of cell viability were assessed by ANOVA with the variance partitioned between groups and time. Difference between group means were assessed using post hoc Tukey's test. Treatment of both breast and lung cancer cells significantly reduced cell viability as indicated by impedance measurement using the xCELLigence instrument (see Figures 1 and 2 below). Figures 1 and 2 also note statistical significance.

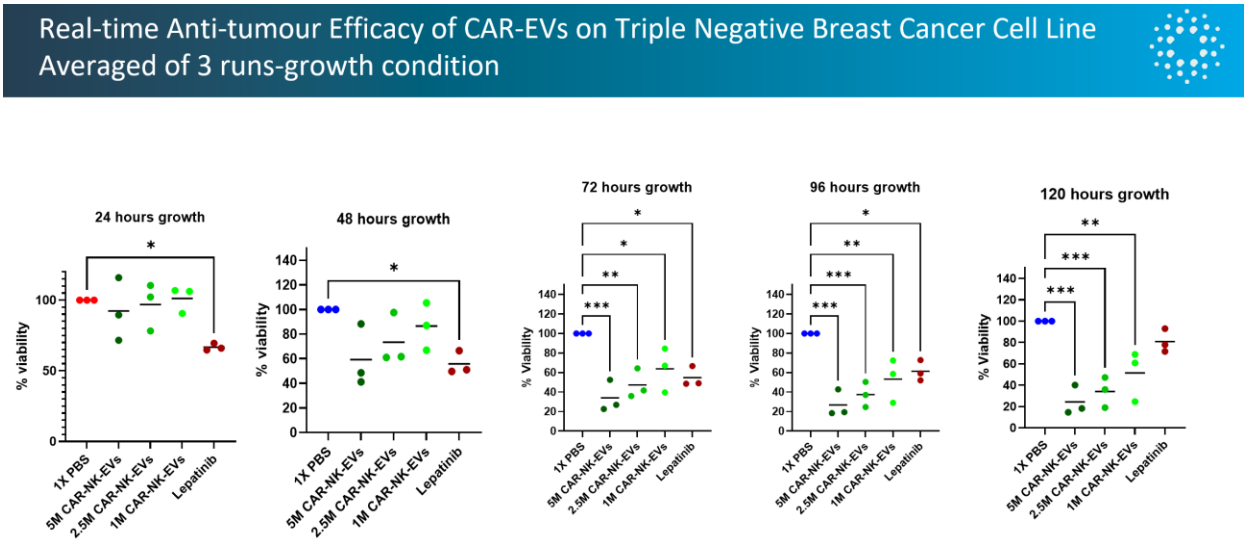

Figure 1: Effect of CAR-NK-EVs on the viability of Hs 578T (TNBC) cells *in vitro* measured at 48, 72 and 96h post treatment. The data are represented as scatter plots with the mean value of **three independent experiments** (each with **three technical replicates**) indicated by the horizontal bar. Statistical significance was assessed by one-way ANOVA and post hoc Tukey's test with *= p <0.05.**= p<0.01, ***= p<0.001.

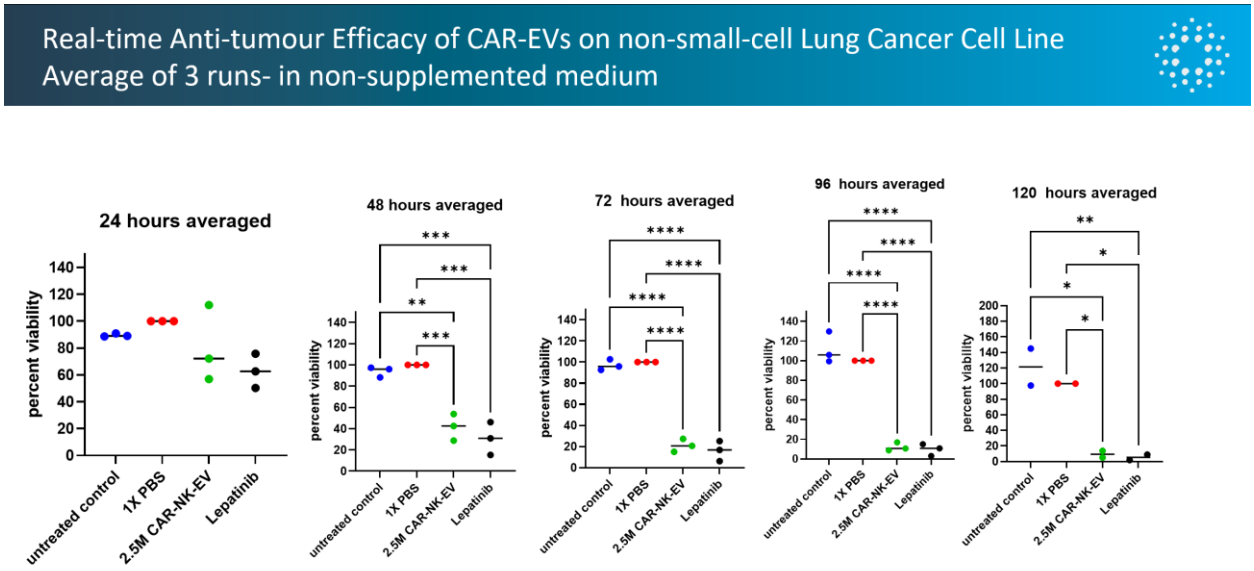

Figure 2: Effect of CAR-NK-EVs on the viability of lung cancer cells (Calu-3) *in vitro* measured at 48, 72 and 96h post treatment. The data are represented as scatter plots with the mean value of **three independent experiments** (each with **three technical replicates**) indicated by the horizontal bar. Statistical significance was assessed by one-way ANOVA and post hoc Tukey's tests with *= p <0.05.**= p<0.01, *** = p<0.001.

The data released in the Announcement are shown below with Standard Deviation envelops for all groups to also provide an indicator of the statistically significant difference between treatment and control groups (Figure 3 and 4 below). Effect of CAR-NK-EVs on the cell viability (Hs 578Tand Calu-3) *in vitro* was monitored continuously for up to 120 h post treatment. The data represent the mean of **three independent experiments** (each with **three technical replicates**).

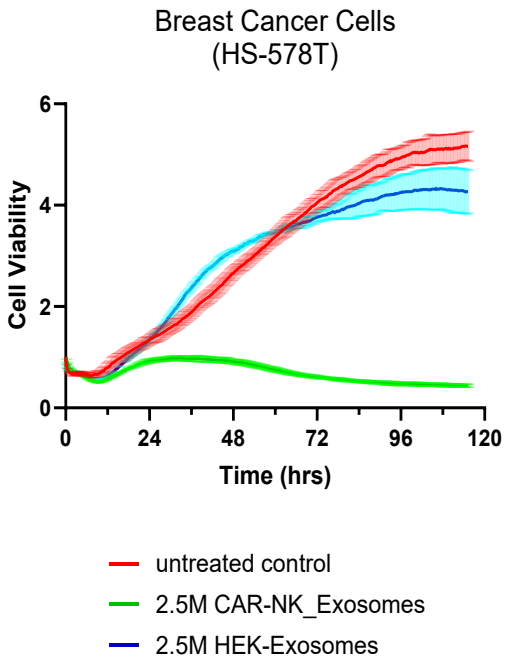

Figure 3: Effect of CAR-NK-EVs on the viability of Hs 578T (TNBC) cells *in vitro. Data represent the mean of three independent experiments.*

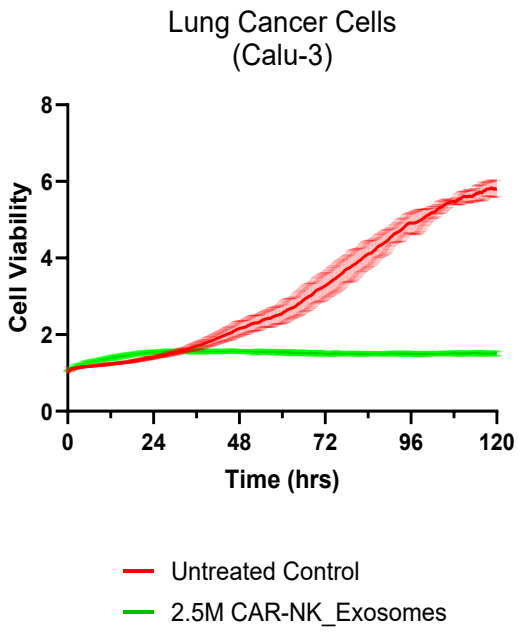

Figure 4: Effect of CAR-NK-EVs on the viability of lung cancer cells (Calu-3) *in vitro. Data represent the mean of three independent experiments.*

CONCLUSIONS. The data obtained indicated that the treatment groups (for the Breast Cancer experiment - Untreated Control, 2.5M CAR-NK_Exosomes, and 2.5M HEK-Exosomes and for the Lung Cancer experiment - Untreated Control, 2.5M CAR-NK_Exosomes) differ in their effects on cell response, growth and death over time. Statistical modeling and pairwise comparisons reveal that CAR-NK_Exosomes induce a significantly greater reduction in cell viability and growth rate compared to both untreated control and HEK-Exosome treatments. This is reflected in lower mean values, reduced exponential growth rates and larger percent differences at later time points for the CAR-NK_Exosome group. These findings indicate that CAR-NK_Exosomes exert both cytostatic (growth-inhibitory) and cytotoxic (cell-killing) effects, leading to pronounced suppression of cell proliferation and increased cell death relative to the other groups. These results are consistent with recent literature, which emphasizes that drug-induced changes in cell populations often reflect a combination of growth inhibition and cell death and that quantifying both is necessary for a complete understanding of treatment efficacy. [25-27]. Overall, this study demonstrates that CAR-NK_Exosomes have superior anti-proliferative and pro-death effects in this cell system, supporting their potential as a more potent therapeutic strategy.

4.4 the comparative information on control treatments for the non-small-cell lung cancer cells in Figure 2 of the Announcement, which ASX notes was provided for the TNBC cells in Figure 1;

For the TNBC cells in Figure 1, the negative controls included HEK-293 EVs, untreated cells and PBS. The positive control was Lapatinib.

For the NSCLC cells in Figure 2, the negative controls included untreated cells and PBS. The positive control was Lapatinib.

HEK-293 EVs were only included in the TNBC experiment to demonstrate that EVs from non-NK cells were not effective in killing cells. Once established there is no regulatory requirement to include it in subsequent experiments.

4.5 the number of tumours which were tested as part of the *in vitro* studies;

The study was a Treatment: Control *in vitro* study using breast and lung cancer cell lines. The data were obtained from three independent experiments, with three technical replicates in each experiment.

4.6 whether the tests resulted in the death of any cells other than TNBC and lung cancer cells; and

The two studies were conducted in breast cancer (Hs578T) cell lines and lung cancer (Calu-3) cell lines *in vitro*, meaning these cells were the only cell types present in the laboratory study and therefore, the only cells killed by the CAR-NK-EV treatment arm. This was not an *in vivo* study in an animal model.

4.7 confirmation that IIQ has disclosed all relevant information concerning the Study Results, and that the announcement is not misleading by omission.

IIQ confirms it has disclosed all relevant information concerning the Study Results, and that the Announcement is not misleading by omission.

5. Does IIQ consider the information provided as a response to question 4, or any part thereof, to be information necessary to enable a reasonable person to form a fair understanding of the Study Results? If so, please explain why IIQ did not initially disclose that information.

IIQ does not believe that the additional information provided in its response to question 4 is information necessary to enable a reasonable person to form a fair understanding of the Study Results.

The Announcement disclosed details of the *in vitro* study results being 88% cell death induced in TNBC and lung cancer cell lines within 96 hours, that the cytotoxic effect was statistically significant, and that the study design included CAR-NK-EVs as the treatment and untreated controls, as explained in Figure 1 and Figure 2.

IIQ does not believe that a more detailed study abstract would further enhance a reasonable person's understanding of the scientific merit and statistical significance of the results disclosed in this Announcement.

6. **Please confirm that IIQ is in compliance with the Listing Rules and, in particular, Listing Rule 3.1.**

   IIQ confirms its view, that it is in compliance with the ASX Listing Rules including Listing Rule 3.1. The Announcement, along with IIQ's announcement on 2 June 2025 were both considered market sensitive and marked as such within the ASX MAP.

7. **Please confirm that IIQ's responses to the questions above have been authorised and approved in accordance with its published continuous disclosure policy or otherwise by its board or an officer of IIQ with delegated authority from the board to respond to ASX on disclosure matters.**

   The response has been reviewed by the IIQ Board of Directors and approved for release.

Yours faithfully

Mark Edwards
Company Secretary
INOVIQ Limited
M: 0405 494 567

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19 June 2025

Reference: 110308

Mr Mark Edwards
Company Secretary
INOVIQ Limited
23 Normanby Road
Notting Hill Vic AU 3168

By email: medwards@inoviq.com

Dear Mr Edwards

INOVIQ Limited('IIQ'): 'New treatment kills 88% of Breast and Lung Cancer cells' Letter

ASX refers to the following:

A. IIQ's announcement titled "New treatment kills 88% of Breast and Lung Cancer cells" (the '**Announcement**') released on the ASX Market Announcements Platform at 8:47 AM on 18 June 2025 which stated:

> *major milestone in its exosome therapeutic program. In recent in vitro studies, INOVIQ's CAR-exosomes demonstrated exceptional efficacy, killing 88% of TNBC and lung cancer cells within 96 hours.*
>
> *This marks a major success for INOVIQ's new platform, showing it works well against two solid tumours.*
>
> *The treatment:*
>
> - *Uses engineered immune cell particles called CAR-NK-EVs;*
> - *These particles are designed to target and kill cancer cells more precisely; and*
> - *INOVIQ uses a special method called EXO-ACE™ to produce and purify these particles for quality and shelf life.*
>
> (the '**Study Results**')
>
> …
>
> *Going forward this could lead to an 'off the shelf' therapy made in advance and used on many patients – unlike other treatments that must be customised.*
>
> *It could be:*
>
> - *Faster to produce;*
> - *Safer to use; and*
> - *More effective than traditional cell therapies like CAR-T.*
>
> (the '**Forward Looking Statements**')

B. The change in the price of IIQ's securities from $0.3875 immediately prior to the release of the Announcement to a high of $0.47 following the release of the Announcement.

C. Listing Rule 3.1, which requires a listed entity to immediately give ASX any information concerning it that a reasonable person would expect to have a material effect on the price or value of the entity's securities.

D. Section 14 of Guidance Note 14 – *ASX Market Announcements Platform,* which states:

MAP should only be used to publish information that is appropriately given to ASX under the Listing Rules or the Corporations Act for publication to the market. It should not be used as a guise to publish material that is really promotional, political or tendentious in nature.

E. Section 4.14 of Guidance Note 8 – '*CONTINUOUS DISCLOSURE: LISTING RULES 3.1 – 3.1B*' ('**Guidance Note 8**') which states (relevantly):

The header for an announcement should also convey a fair and balanced impression of what the announcement is about so as not to mislead readers as to its contents or significance. For example, the header to an announcement that contains essentially negative information should not attempt to disguise that fact by picking out a small piece of positive information in the announcement and just mentioning that (sometimes referred to as "putting spin" on the announcement). Likewise, the header to an announcement that contains forward-looking information (such as earnings guidance or an exploration or production target) that is speculative or highly qualified should be careful not to overstate or sensationalise the true character of the information it contains.

F. Section 4.15 of Guidance Note 8 which states:

Finally, an announcement must be couched in language that is appropriate for release to the market. It should be factual, relevant and expressed in a clear and objective manner. Emotive, intemperate or defamatory language should not be used, nor should vague or imprecise terms such as "single digit" or "double digit", which do not allow investors to assess the value of the information for the purpose of making an investment decision.

ASX Observations

ASX observes that:

i. the Announcement appears to not provide the level of detail concerning the Study Results that ASX ordinarily expects from a market-sensitive study;

ii. the Announcement's header does not indicate that the studies were *in vitro*; and

iii. the Forward-Looking Statements appear to be highly aspirational without a present reasonable basis.

Request for information

Having regard to the above, ASX asks IIQ to respond separately to each of the following questions:

1. Does IIQ consider the header of the Announcement conveyed a fair and balanced impression of the contents of the announcement, given the early stage of the research? If so, please explain the basis for that view.
2. Does IIQ consider that it had a reasonable basis to make the Forward-Looking Statements? If so, please explain the basis for that view.
3. Noting the early stage of the research, how does IIQ justify the use of the term 'Treatment'?
4. Please provide the following information:

4.1 confirmation that the studies were undertaken by Peter Mac on the same terms disclosed to the market on 31 March 2025;

4.2 the *in vitro* study design;

4.3 the statistical significance of the values attached to the data in the Study Results;

4.4 the comparative information on control treatments for the non-small-cell lung cancer cells in Figure 2 of the Announcement, which ASX notes was provided for the TNBC cells in Figure 1;

4.5 the number of tumours which were tested as part of the *in vitro* studies;

4.6 whether the tests resulted in the death of any cells other than TNBC and lung cancer cells; and

4.7 confirmation that IIQ has disclosed all relevant information concerning the Study Results, and that the announcement is not misleading by omission.

5. Does IIQ consider the information provided as a response to question 4, or any part thereof, to be information necessary to enable a reasonable person to form a fair understanding of the Study Results? If so, please explain why IIQ did not initially disclose that information.

6. Please confirm that IIQ is in compliance with the Listing Rules and, in particular, Listing Rule 3.1.

7. Please confirm that IIQ's responses to the questions above have been authorised and approved in accordance with its published continuous disclosure policy or otherwise by its board or an officer of IIQ with delegated authority from the board to respond to ASX on disclosure matters.

When and where to send your response

This request is made under Listing Rule 18.7. Your response is required as soon as reasonably possible and, in any event, by no later than **4:30 PM AEST Tuesday, 24 June 2025**.

You should note that if the information requested by this letter is information required to be given to ASX under Listing Rule 3.1 and it does not fall within the exceptions mentioned in Listing Rule 3.1A, IIQ's obligation is to disclose the information 'immediately'. This may require the information to be disclosed before the deadline set out above and may require IIQ to request a trading halt immediately if trading in IIQ's securities is not already halted or suspended.

Your response should be sent by e-mail to **ListingsComplianceMelbourne@asx.com.au**. It should not be sent directly to the ASX Market Announcements Office. This is to allow us to review your response to confirm that it is in a form appropriate for release to the market, before it is published on the ASX Market Announcements Platform.

Suspension

If you are unable to respond to this letter by the time specified above, ASX will likely suspend trading in IIQ's securities under Listing Rule 17.3.

Listing Rules 3.1 and 3.1A

In responding to this letter, you should have regard to IIQ's obligations under Listing Rules 3.1 and 3.1A and also to Guidance Note 8 *Continuous Disclosure: Listing Rules 3.1 – 3.1B*. It should be noted that IIQ's obligation to disclose information under Listing Rule 3.1 is not confined to, nor is it necessarily satisfied by, answering the questions set out in this letter.

Release of correspondence between ASX and entity

We reserve the right to release all or any part of this letter, your reply and any other related correspondence between us to the market under listing rule 18.7A. The usual course is for the correspondence to be released to the market.

Yours sincerely

ASX Compliance