Philip Spinney His Majesty's Senior Coroner
for the County of Devon
Plymouth, Torbay and South Devon Coroner Service

	REGULATION 28 REPORT TO PREVENT FUTURE DEATHS **THIS REPORT IS BEING SENT TO:** The Faculty of Intensive Care Medicine Churchill House 35 Red Lion Square London WC1R 4SG
1	**CORONER** I am Louise Wiltshire, Assistant Coroner for Plymouth Torbay and South Devon
2	**CORONER'S LEGAL POWERS** I make this report under paragraph 7, Schedule 5, of the Coroners and Justice Act 2009 and regulations 28 and 29 of the Coroners (Investigations) Regulations 2013. http://www.legislation.gov.uk/ukpga/2009/25/schedule/5/paragraph/7 http://www.legislation.gov.uk/uksi/2013/1629/part/7/made
3	**INVESTIGATION and INQUEST** On 11 June 2021 an inquest was opened touching the death of Katie Anne WILLIAMS (aged 45) who died at Derriford Hospital in Plymouth on 24 May 2021. She died having taken intentional overdose of [redacted] on 15 May 2021, and as a result of subsequent hospital care and treatment provided to her for that overdose and associated complications. The inquest concluded on 23 November 2023 with the following narrative conclusion: *"Katie Anne Williams died on 24 May 2021 from serotonin toxicity caused by an overdose of [redacted] and hospital administered [redacted]."* In Box 3 of the record of inquest: *"Katie Anne Williams died on 24 May 2021 at Derriford Hospital. On 16 May 2021, she took an overdose of [redacted]. She was admitted to hospital where she was treated for this overdose and associated complications, including an aspiration pneumonia and paralytic ileus. [redacted] was initially withheld given the risk of serotonin toxicity, but re-introduced on day four of her ICU stay, as the period of risk for serotonin toxicity was felt to have passed. Sadly, as a result of the paralytic ileus Katie had developed, the absorption of modified release [redacted] was delayed. This, in combination with [redacted] administered in the ICU caused a re-precipitation of serotonin toxicity which was ultimately fatal."*

	The medical cause of death was recorded at the inquest as: 1a) Circulatory failure 1b) Serotonin toxicity 1c) Drug overdose As part of the inquest it was found as a matter of fact that the [redacted] administered by the ICU team in the hospital (as part of their standard procedure for sedating intubated patients) had caused a reprecipitation of the serotonin toxicity which was previously thought to have resolved. This was thought to have occurred because the patient had developed a paralytic ileus which had delayed the absorption of the modified release [redacted] she had taken prior to her admission. This caused or contributed to Katie's death. Following this case the University Hospitals Plymouth NHS Trust (the "Trust") has amended its sedation policy such that lower risk opiates (such as morphine) are recommended for sedating patients who are admitted following overdose of medications like venlafaxine, to reduce the risk of reprecipitating serotonin toxicity.
4	**CIRCUMSTANCES OF THE DEATH** On 15 May 2021 Katie Anne WILLIAMS took an overdose of her prescribed [redacted]. She had taken [redacted] modified release tablets. Equivalent to 56 days' worth of this prescribed medication. She was taken to Derriford Hospital by ambulance in the early hours of 16 May 2021 where she was reviewed in the emergency department and then shortly afterwards admitted to ICU. On arrival at the emergency department, Katie was recognised to be extremely unwell. She was unconscious with a GCS of 3 as a result of her overdose. She had also had a number of seizures on her way to the hospital, and prior to the ambulance arrival. She required intubation and ventilation to protect her airway and stabilise her condition. A chest x-ray was undertaken which demonstrated evidence of an aspiration. Katie also had a temperature of 40°c on admission to the emergency department; this, and the evidence of early muscle injury, led the treating ICU team to conclude that Kate was likely to be suffering with serotonin toxicity. Given the ongoing risk of serotonin toxicity, and following Toxbase advice, no infusion of the opiate drug [redacted] was administered to Katie during days 1, 2 or 3 of her ICU admission. At this stage, the venlafaxine was felt to still to be her system, and the plan was to support Katie whilst this cleared, and to treat her evolving aspiration pneumonia with antibiotics. Where additional sedation was required remifentanil was used. On day 4 of Katie‘s ICU admission (19 May 2021) a decision was made to switch the remifentanil infusion to a [redacted] infusion as per usual ICU practice. In the following days Katie‘s kidney function continue to normalise. There was no recurrence of a hyperpyrexia, or any other clinical features to suggest a recurrence of the serotonin syndrome.

The rationale for moving to [redacted] was that from day three onwards it was felt that the majority of the venlafaxine would have been metabolised by the body and therefore the risk of interaction with any other drugs such as fentanyl would not have been a significant concern.

[redacted] was infused on an hourly basis in accordance with usual practice and tolerance of the drug was monitored based on clinical effect, including considering a patient's tolerance of the ET tube and interrupting the infusion on a regular basis to check for drug accumulation.

Sadly, over the next few days, Katie's condition deteriorated. A CT scan confirmed the appearances of severe aspiration pneumonia and a paralytic ileus.

The concern at day five was the evolving severe aspiration pneumonia. Katie was now severely ill. As a result of this she required ventilating in the prone position. Prone ventilation required heavy sedation and as such the [redacted] infusion was increased to 5ml/hr. At this stage, it was felt that the [redacted] poisoning had passed.

Over the coming days Katie's condition improved, and she was able to be managed once again in the standard supine position. The [redacted] infusion was reduced from 5 ml/hour to 3 ml/hour. She was having regular sedation breaks from which she was rousing quickly which meant that the infusion could not be further reduced. Again at this stage, the risk of an ongoing serotonin toxicity was not considered to be an issue.

Katie had also developed a paralytic ileus. In Katie's case the paralytic ileus (it appears) delayed the absorption of the modified release [redacted]. This meant that the ICU team treating her at the time felt that the [redacted] had cleared from her system, and that it was therefore safe to introduce [redacted]. With the benefit of hindsight, and having seen the toxicology report, it appears that that was not the case; Katie still had a significant amount of [redacted] in her system. I am told there is no way of monitoring these levels in life.

In the morning of 24 May 2021 Katie appeared to be improving. She was reviewed on the ward round at 11am. She was haemodynamically stable, requiring no drugs to support her blood pressure. He abdomen remained distended, but there was no particular clinical concern for this at the time the plan was to continue with supportive care in the expectation she would continue to improve in the days ahead.

Very sadly however, and suddenly, Katie's condition began to deteriorate at around 1pm that day. Her blood pressure began to drop and a noradrenaline infusion was commenced. Over the course of the afternoon her blood chemistry steadily deteriorated, reflecting her increasingly shocked state. Her oxygen requirement increased and she developed a severe refractory, circulatory failure and associated pulmonary oedema. Initially the team thought that Katy had become septic and that there might be an acute pathology such as a bowel ischemia or perforation. It was therefore decided to take Katie for a CT scan. However, sadly, whilst preparing Katy for transfer to the CT scanner she went into cardiac arrest. Attempts were made to resuscitate her over the following 40 minutes, but there was no reversible cause for the cardiac arrest that could be identified. Katy did not respond and resuscitation efforts ceased at 19:10 hours.

	Retrospectively, treating clinicians have considered the cause for Katie's collapse on 24 May 2021. Having reviewed the toxicology report they are of the view that the paralytic ileus delayed the absorption of the modified release [redacted]. This, combined with the [redacted] (that was used as a sedative drug in accordance with standard practice in the ICU setting) had reprecipitated a serotonin toxicity, which caused Katie to collapse on the 24 May 2021. It is their view that Katie's death was caused by a very unusual and rare presentation of a serotonin toxicity that occurred as a result of the delayed absorption of the [redacted], because of the paralytic ileus, and an idiosyncratic reaction between the [redacted] and the [redacted] Following Katie's death, the ITU team has amended its sedation policy such that [redacted] would now be replaced with morphine in cases such as Katie's, where patients presenting with a [redacted] (or similar) where there is an ongoing risk of serotonin toxicity.
5	**CORONER'S CONCERNS** During the course of the inquest the evidence revealed matters giving rise to concern. In my opinion there is a risk that future deaths will occur unless action is taken. In the circumstances it is my statutory duty to report to you. The **MATTERS OF CONCERN** are as follows. – The administration of [redacted] from day four of Katie's hospital admission reprecipitated her serotonin syndrome and directly contributed to her death. The Trust has recognised this and amended its sedation policy to recommend "lower risk" opiates (such as morphine) are used in patients who have taken overdoses of medications where there is a risk of serotonin syndrome / toxicity. It is accepted that the way the [redacted] interacted in this case was unexpected, and appears to have occurred due to the particular circumstances of Katie's case; in particular an aspiration pneumonia requiring treatment in the prone position, and the development of a paralytic ileus. However, these complications are not unusual in patients who have taken overdoses of these types of medications and as such I consider there is a risk a future death may occur in similar circumstances. I am concerned that other NHS organisations may not fully appreciate the risks associated with the use of [redacted] in patients such as Katie and that this information should be shared with those organisations on a national level.

6	**ACTION SHOULD BE TAKEN** In my opinion action should be taken to prevent future deaths and I believe your organisation has the power to take such action.
	YOUR RESPONSE You are under a duty to respond to this report within 56 days of the date of this report, namely by 5 January 2024. I, the coroner, may extend the period. Your response must contain details of action taken or proposed to be taken, setting out the timetable for action. Otherwise you must explain why no action is proposed.
8	**COPIES and PUBLICATION** I have sent a copy of my report to the Chief Coroner and to the following Interested Persons: **University Hospitals Plymouth NHS Trust** **Family members of Katie Anne Williams** I am also under a duty to send the Chief Coroner a copy of your response and all Interested Persons who in my opinion should receive it. The Chief Coroner may publish either or both in a complete or redacted or summary form. He may send a copy of this report to any person who he believes may find it useful or of interest. You may make representations to me, the coroner, at the time of your response, about the release or the publication of your response by the Chief Coroner.
9	Dated: 24 November 2023 Louise WILTSHIRE, Assistant Coroner for Plymouth, Torbay and South Devon Signature