



Report to the Minister of Justice and Solicitor General Public Fatality Inquiry

Fatality Inquiries Act

WHEREAS a Public Inquiry was held at the Law Courts
in the City of Edmonton, in the Province of Alberta,
(City, Town or Village) (Name of City, Town, Village)
on the 24, 25 and 26 day of June, 2015, (and by adjournment
year
on the _____ day of _____, _____),
year
before The Honourable Elizabeth A. Johnson, a Provincial Court Judge,
into the death of Shaunnie Rebecca Payne 31
(Name in Full) (Age)
of Alberta Hospital, Edmonton and the following findings were made:
(Residence)

Date and Time of Death: September 23, 2012, 9:30 a.m.

Place: Alberta Hospital, Edmonton

Medical Cause of Death:

("cause of death" means the medical cause of death according to the International Statistical Classification of Diseases, Injuries and Causes of Death as last revised by the International Conference assembled for that purpose and published by the World Health Organization – *The Fatality Inquiries Act*, Section 1(d)).

See attached discussion

Manner of Death:

("manner of death" means the mode or method of death whether natural, homicidal, suicidal, accidental, unclassifiable or undeterminable – *The Fatality Inquiries Act*, Section 1(h)).

Undetermined

Circumstances under which Death occurred:

I. THE INQUIRY AND ITS MANDATE

Shaunnie Rebecca Payne died at Alberta Hospital, Edmonton. She was found in the morning of September 23, 2012 in her bed, deceased. Her roommate had alerted staff to a problem.

At the time of her death, Ms. Payne was a formal patient at Alberta Hospital, a “facility” as defined in the *Mental Health Act*. Section 11(b) of the *Fatality Inquiries Act* (the “*Act*”) requires that the person in charge of such a facility notify the medical examiner of such a death.

Section 32 of the *Act* requires the Chief Medical Officer to notify the Fatality Review Board (the “Board”) of any death described under s. 11 which has been the subject of an investigation. The Board reviewed the Medical Examiner’s case file respecting Ms. Payne and recommended that a public fatality inquiry be held for the stated reason “prevention of similar deaths”.

The *Act* calls upon the judge conducting the Fatality Inquiry to make a report to the Minister containing findings as to: the identity of the deceased; the date, time and place of death; the circumstances under which the death occurred; the cause of death; the manner of death (s. 53(1)). The judge may make recommendations as to the prevention of similar deaths (s. 53(2)).

The findings of the judge may not include any findings of legal responsibility or any conclusion of law (s. 53(3)).

II. PRE-INQUIRY CONFERENCE AND INQUIRY PARTICIPANTS

A Pre-Inquiry Conference was held on March 5, 2015. Ms. Payne’s father, mother and sister (over the telephone) attended.

Counsel representing Alberta Health Services (“AHS”) made application on behalf of his client for interested person status pursuant to s. 49(2) (d), which application was granted.

At the outset of the Inquiry, a similar application was made on behalf of Dr. Vozar, Ms. Payne’s attending physician, and that application was granted.

AHS and Dr. Vozar appeared at the Inquiry by counsel.

The *Act* provides that Ms. Payne’s next of kin may appear at and participate in the Inquiry.

The family members - Mr. Thomas Payne (Ms. Payne’s father), Ms. Patterson Payne (Ms. Payne’s mother) and Ms. Payne Birch (Ms. Payne’s sister) – appeared at and participated in the Inquiry, questioning witnesses, making submissions and providing materials. Their participation was helpful and appreciated.

III. WITNESSES

The Inquiry heard from the following witnesses:

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| Dr. Michael Reider. | Dr. Reider was retained by AHS to provide an opinion as to the cause of death of Shaunnie Payne. He is a clinical pharmacologist. |
| Dr. Robert Ariano. | Dr. Ariano was retained by AHS to prepare an opinion report into the death of Shaunnie Payne. He is a clinical pharmacist. |

Dr. Bernard Bannach. Dr. Bannach is the Assistant Chief Medical Examiner for Alberta.

Dr. Craig Chatterton. Dr. Chatterton is the Deputy Chief Toxicologist employed by the office of the Chief Medical Examiner.

Mark Latham. Mr. Latham is a registered nurse working at Alberta Hospital. He was working in the unit on the day Ms. Payne was found deceased.

Dr. George Vozar. Dr. Vozar is a psychiatrist who works at Alberta Hospital. Ms. Payne was his patient.

Kathleen Hall. Ms. Hall is a psychiatric nurse who was employed at Alberta Hospital and was charge nurse during the night shift of September 22/23, 2012.

Benjamin Nartey. Mr. Nartey is a psychiatric aide who was employed at Alberta Hospital and on shift at the time Ms. Payne was discovered deceased.

Spencer Jean. Mr. Jean is a psychiatric aide employed at Alberta Hospital and on shift at the time Ms. Payne was discovered deceased.

Mark Snaterse. Mr. Snaterse is the Executive Director of Addictions and Mental Health for AHS.

IV. BACKGROUND

Ms. Payne was admitted to Alberta Hospital, Edmonton on July 1, 2012 with a clinical diagnosis of drug-induced psychosis.

Ms. Payne had a long psychiatric history and was well-known to Alberta Hospital. Since 2005 she had exhibited symptoms of schizoaffective disorder, a major psychotic disorder similar to schizophrenia with a strong component of mood disorder. She also suffered from substance-induced psychotic illness and used substances including alcohol, cocaine, crystal meth, and marihuana.

Ms. Payne's admission on July 1, 2012 was her sixth psychiatric admission to Alberta Hospital. She had been hospitalized in other facilities in Edmonton.

Before her July 2012 admission she had been living in Jasper. As a result of some bizarre behaviour on her part, the police were called. The police took her to the hospital in Jasper and she was transferred to Alberta Hospital where she was admitted as a certified (formal) patient pursuant to the *Mental Health Act*. That status continued until her death.

She was admitted to Unit 10-1, a psychiatric intensive care unit which takes the most ill patients from Alberta Hospital as well as other hospitals in the region.

Dr. Vozar became Ms. Payne's attending physician on July 7, 2012. He described her as floridly psychotic with delusional beliefs and auditory hallucinations. He testified that she posed a potential risk to herself and others. She was not able to care for herself. Dr. Vozar described her condition as intractable, difficult to manage and dangerous. She was very ill.

Dr. Vozar described her condition as treatment-resistant. During her prior hospitalizations a number of different treatments had been attempted. Those treatments had not been successful in managing Ms. Payne's condition.

Dr. Vozar said that 30% of patients do not respond to typical anti-psychotic medication. For treatment-resistant psychosis there are limited treatment options: the drug clozapine or electroconvulsive shock therapy.

Dr. Vozar said he discussed the options with Ms. Payne (although in her condition such a discussion was difficult) and with Ms. Payne's father (who held a power of attorney). Agreement was reached to pursue the clozapine option.

Ms. Payne began receiving clozapine on August 14, 2012, beginning with a "test" dose of 25 milligrams. Dr. Vozar said that a test dose is given to see whether the drug causes any idiosyncratic reaction. That dose was gradually increased – Dr. Vozar said by 25 milligrams every two days. The last daily dose she received before her death was 675 milligrams.

Ms. Payne was on a number of other scheduled medications, including: Alesse 28 (a birth control pill), Docusate sodium (stool softener), Sennosides (stool softener), nicotine patch (for smoking); Venlafaxine (anti-depressant), and Divalproex (mood stabilizer). As well, she was receiving acetaminophen, benztropine, haloperidol, lorazepam and nicotine gum on an "as needed" basis.

On August 30, 2012 records indicate that she had tachycardia (elevated pulse). Dr. Vozar said she denied chest pain, shortness of breath or other physical symptoms.

Ms. Payne had an ECG the following day (August 31). Dr. Vozar said the purpose of that test was to see whether there was anything abnormal with her heart and for a comparison with a prior ECG.

Dr. Vozar reviewed the result from the ECG and was not concerned – he said it was similar to her previous ECG; there was no indication of any acute changes. The QT interval from that test was 468; Dr. Vozar said he would not be concerned with that interval as long as it was under 500 milliseconds.¹

Dr. Vozar felt Ms. Payne was showing some improvement during the 48 hours before her death. His notes from September 21 indicate that she was more coherent, better organized and well oriented. Although her insight was still impaired, he thought she was improving.

Nurses' notes from the evening of September 21 indicate Ms. Payne was compliant with medications and cooperative with monitoring. She was reactive and engaged with the nurse. Nurses' notes from September 22 during the day indicate that she kept a low profile in her room or watching TV, was polite, pleasant and reactive and said her mood was "great". The evening notes from September 22 indicate she spent time in her room laying on the bed. She had an evening snack, came on her own for medications and was cooperative with the mouth check. She shared future plans. Kathleen Hall, the nurse on duty the night of September 22/23 confirmed that Ms. Payne seemed to be improving, that she was more future-oriented and engaged.

Ms. Payne was in a two-person room. Shortly after 9:15 the morning of September 23, Ms. Payne's roommate came out of the room to say that there was something wrong with Ms. Payne.

¹ The QT interval was described by Dr. Reider as follows:

when you see a heart monitor like on a TV show that there's a spike think running across it, that's ... one of those spike things is called the QT complex, so it's the QRS complex and the T wave afterwards. That's a sign that the heart is working, and it's a fairly short time because that's when the heart ventricle which is the main pumping part of the heart is actually ... activated. If that interval gets prolonged for some reason, it can put you at risk for certain problems with cardiac arrhythmias and clozapine is known to prolong the QT interval."

Mr. Jean was the first to arrive at the room and observed Ms. Payne lying motionless on her stomach on the bed. He said she was very stiff and described blood pooling in her stomach area. Mr. Jean and Mr. Latham began CPR. The Automatic External Defibrillator (“AED”) was brought to the scene. No shock was advised.

Ms. Payne could not be revived.

At the time of her death, Ms. Payne was on “Q15 observation” which meant that she was supposed to be observed every 15 minutes.

V. THE MEDICAL EXAMINER’S REPORT

Dr. Graeme Dowling, Chief Medical Officer performed an autopsy on Ms. Payne, reviewed her medical records and prepared an Autopsy Report, the Medical Examiner’s Medical Certificate of Death and the Certificate of Medical Examiner.

In the Medical Examiner’s Medical Certificate of Death under “Manner of Death and Details” Dr. Dowling said: “Died as a result of the toxic effects of clozapine administered for treatment of psychosis (schizoaffective disorder)”.

In the Certificate of Medical Examiner, Dr. Dowling identified the “immediate cause of death” as “clozapine toxicity” and the “manner of death” as “undetermined”.

In the Autopsy Report he said:

“...At Autopsy, no injuries and no obvious natural diseases were identified to account for death. In particular, there was no inflammation of the heart muscle (myocarditis) and no enlargement of the heart (cardiomyopathy) that can arise as a complication of clozapine therapy. Likewise, there were no microscopic abnormalities of the liver and kidneys to suggest that their ability to break down (metabolize) and remove clozapine from the bloodstream was impaired”.

Postmortem toxicology revealed the presence of a very high level of clozapine in the blood (3.78mg/l) as well as a high level of desmethylclozapine (a breakdown product of clozapine). Therapeutic levels of venlafaxine (an antidepressant medication) and valproic acid (a medication used to treat some psychiatric illnesses), both of which were administered during her hospitalization, were also detected.

The cause of death has been attributed to the toxic effects of clozapine (clozapine toxicity). It could not be determined whether the very high level of clozapine resulted from an accumulation of this drug over time as the dosage was increased, from a medication error or errors, or from the patient herself somehow gaining access to and ingesting the drug.”

Dr. Bernard Bannach, Assistant Chief Medical Examiner testified at the Inquiry in relation to the Medical Examiner’s findings. Dr. Bannach is a forensic pathologist, who has been with the Office of the Chief Medical Examiner in Edmonton for about 21 years.

Dr. Bannach found the Medical Examiner’s conclusion that the cause of death was clozapine toxicity to be a “reasonable conclusion”, however he did not agree with the third possibility (gaining access to and ingesting the drug) presented in the Autopsy Report to explain the high level of clozapine. He said that, having reviewed Ms. Payne’s chart and noting that she was receiving liquid clozapine and was subject to mouth checks, the possibility that she was keeping medication in her mouth was greatly reduced. He would not have included the suggestion that

the high level of clozapine may have been the result of the patient gaining access to clozapine and ingesting it.

Dr. Bannach indicated that he was not able to address the issue of accumulation of the drug in the blood versus the fatty tissues. He confirmed that Dr. Dowling's conclusion respecting the accumulation of the drug over time was a theory of Dr. Dowling's.

Dr. Bannach testified that another reasonable conclusion would be that Ms. Payne's death was not due to the clozapine alone, but that both clozapine and the anti-depressant medication Venlafaxine combined to produce a prolongation of the QT interval which then led to the mechanism of arrhythmia.

He also confirmed that seizures can be a complication of various drug therapies. He confirmed that, absent some indicia (such as a bitten tongue during the terminal seizure) there would be no sign in an autopsy that a seizure had taken place.

Dr. Bannach confirmed that it is scientifically impossible to pinpoint an exact time of death. However, from his review of the nursing notes and the condition of the body as observed in photographs taken post mortem, Dr. Bannock estimated that Ms. Payne had been dead for about 6 hours at the time she was found.

VI. THE TOXICOLOGY REPORT

Dr. Chatterton, Deputy Chief Toxicologist with the office of the Chief Medical Examiner described the role of the toxicologist as helping the Medical Examiner to assign a cause and manner of death largely by performing analyses on biological samples, bodily fluids and other forensic samples. Dr. Chatterton performed tests in relation to Ms. Payne and completed a Toxicology Report setting out his analysis of the substances found in Ms. Payne's bloodstream.

Dr. Chatterton said he tested samples of femoral blood and from the liver. He said good practice would examine blood from different sites, and femoral blood less subject to the phenomena of post mortem redistribution. Post mortem redistribution is the movement of a drug from one area of the body to another after death.

On the subject of post mortem redistribution, the Report said:

After death, drugs may move from one area of the body to another, a process known as post mortem redistribution. As a result of this redistribution, it is extremely difficult to interpret post-mortem drug concentrations and their possible significance as to behaviour and/or cause of death.

The Report showed the post mortem clozapine level as 3.78 mg/l (from a sample taken from femoral blood). Dr. Chatterton described the measured clozapine level as "high" based on his experience as a toxicologist and his review of scientific literature. Testing showed high levels in the liver as well. The Report said:

Clozapine is an anti-psychotic drug, which has been used for the treatment of schizophrenia. In one study in the literature, oral 100 mg doses of clozapine twice daily resulted in peak plasma concentrations averaging 1.32 mg/l (range 0.10 – 0.77 mg/l). In separate reports, blood concentrations of 3.2, 4.5 and 5.81 mg/l have been reported following over dosage.

Dr. Chatterton confirmed that the results to which these comments refer were post-mortem measures in persons whose deaths were attributed to clozapine. He was not able to say from

which portion of the body the blood in those cases was taken.

The Toxicology Report concluded: “The reported concentration of clozapine would be expected to pose a significant threat to life”. Dr. Chatterton confirmed that this comment referred to the concentration of clozapine in a living person. He confirmed that it is not possible to say (based on his testing) what the pre mortem level of clozapine in Ms. Payne’s blood would have been.

Although he said he would not expect to see a two to fourfold increase (from ante mortem to post mortem) in the clozapine level as a result of post mortem redistribution, he would not be surprised to see such an increase.

Dr. Chatterton said it was not possible to say that Ms. Payne’s post mortem clozapine level indicated an overdose, nor was it possible to say that it did not indicate an overdose. In discussing blood levels, toxicity and overdose he said:

“... you don’t need to have an excessive overdose concentration of a drug to induce toxicity. Different than an anaphylactic type of reaction to a, to a bee sting for example, but individuals can take drugs in very small, what would generally be considered therapeutic concentrations and suffer adverse or toxic reactions, yet the concentration present in their body at that time is comfortably within therapeutic or maybe even a sub-therapeutic range generally speaking. So I would just say for both reports [the Medical Examiner’s Report and the Toxicology Report] the words toxicity and overdose can sometimes be misinterpreted or confused. There is no doubt in this case that the post-mortem concentration is, in my opinion, high and is associated with an increased likelihood of toxicity. That doesn’t mean the concentration is consistent with overdose. It doesn’t mean the concentration isn’t consistent with high therapeutic use. Somebody who’s therapeutically taking Clozapine can still have adverse or toxic reaction of effects.”

When asked whether he was using the word “toxic” as equivalent to “adverse” he said:

“Similar, yeah. Adverse is something that would perhaps be less likely, less expected. Toxicity is a result of the adverse reaction”.

It was Dr. Chatterton’s opinion that it was extremely unlikely that Ms. Payne’s death was the result of a single large dose as he was aware that she had been on the medication for some period of time.

The Report identified venlafaxine as well as clozapine in Ms. Payne’s bloodstream. He said the concentration of venlafaxine was “largely insignificant” when considered in isolation. He said there is the potential for interaction between clozapine and the family of drugs to which venlafaxine belongs, that he discussed that potential with Dr. Dowling, and it would be Dr. Dowling’s decision whether to include any comment respecting venlafaxine in connection with the ultimate cause of death.

VII. POST MORTEM REDISTRIBUTION

As indicated, Dr. Chatterton spoke about the phenomenon of post mortem redistribution. Other witnesses also addressed post mortem redistribution. Dr. Reider described it this way:

When you die a bunch of things happen. One of the things that starts to happen is the drug that is stored in the fat starts to leave the fat. So it’s getting out, leaving the fat. It’s not even metabolized anymore because your liver is not working. So it gets into the blood and just accumulates because things can be ... in you or I, when we take a drug, our livers are working; so it gets rid of the drugs as it comes out in the fat. But when you’re

dead the drug comes out of the fat but it doesn't get rid of it. So it can ... so drugs with a large volume of distribution, once you die you can get a (Indiscernible) that is not reflective at all of what was happening before – before you died when you were alive.

Dr. Reider opined that the use of post mortem clozapine levels to ascertain whether clozapine is a mortem cause of death is unreliable because post mortem redistribution can result in post mortem concentrations of clozapine of up to five times compared to ante mortem concentrations.

Dr. Ariano, too said he would not trust post mortem concentrations of clozapine as indicative of ante-mortem blood concentrations.

Mr. Snaterse agreed that because of post mortem redistribution, post mortem clozapine levels are not reliable to establish cause of death.

VIII. ADMINISTRATION AND MONITORING OF CLOZAPINE

A. Generally

The Inquiry heard evidence about the drug clozapine from a number of the witnesses, including Dr. Vozar, Dr. Reider, Dr. Ariano, Mr. Snaterse as well as Dr. Bannach and Dr. Chatterton.

Clozapine is an atypical antipsychotic. Dr. Vozar said that 30% of patients do not respond to typical anti-psychotic medication. For patients with treatment-resistant psychosis there are limited treatment options: the drug clozapine or electroconvulsive shock therapy. Forty to fifty percent of patients who do not respond to typical antipsychotics will respond well to clozapine.

Clozapine is always administered orally. It is available in tablet form and can be made into a liquid.

It first became available in the Canadian market in 1990 and had been available in Europe before that.

Side effects of clozapine can include stomach upset, dry mouth, constipation, fainting spells as well as more serious side effects. One serious side effect is agranulocytosis, a hematologic problem in which the body stops making white blood cells. This condition occurs in fewer than 1% of patients receiving the drug.

When clozapine was allowed in the North American market it was in connection with what Mr. Snaterse characterized as a “robust blood monitoring system” to monitor the risk of agranulocytosis. The blood monitoring system is administered by a third party agency – Clozaril Support and Assistance Network (“CSAN”). A patient receiving clozapine must be registered with CSAN. Each patient is given a unique identifier so that the agency can track all patients in Canada who are receiving clozapine.

Other serious (and less common) side effects can include hepatitis, thyroid problems and cardiac problems – either myocarditis (inflammation) or cardiomyopathy (cardiac muscle problem).

Clozapine is one of a number of drugs that can prolong the QT interval. Dr. Reider indicated if that interval gets prolonged for some reason it can create a risk for cardiac arrhythmias. He said that monitoring of a patient receiving clozapine may include ECGs.

Dr. Vozar was aware that venlafaxine and clozapine were both associated with a prolonged QT interval but did not view that as a dangerous interaction, particularly with low doses of venlafaxine (such as Ms. Payne was on).

Clozapine is administered starting with a small or “test” dose of 12.5 or 25 milligrams. The patient is monitored for any side effects. The dose is increased slowly over time while monitoring the patient. The goal is to increase the dose until clinical improvement has been achieved. This varies from patient to patient. Clozapine is dosed individually, based on the patient and his or her reaction. Mr. Snaterse testified that there is no correlation between efficacy and concentration of clozapine – each patient is different. Dosing is not done according to serum levels but according to patient and how they respond. Some patients can tolerate much larger doses of clozapine than others.

B. Clozapine at Alberta Hospital

Alberta Hospital has been involved in administration of clozapine since it became available on the Canadian market. AHS policy respecting clozapine administration (which policy was exhibited at the Inquiry) embeds the requirements of Health Canada for blood monitoring and registration with CSAN. Mr. Snaterse estimated that some 600 to 700 patients had received clozapine at Alberta Hospital during his 12 years there.

Mr. Snaterse described the means by which clozapine is produced at Alberta Hospital. Clozapine comes from the pharmaceutical company in tablet form – 25 mg and 100 mg tablets. Alberta Hospital follows a formula published in the late 90’s for manufacturing liquid clozapine from tablets. The liquid clozapine is manufactured by pharmacy technicians in the pharmacy at Alberta Hospital. That formula together with instructions for manufacture and storage are set out in an AHS policy. A record is kept of each compound made in the pharmacy.

At Alberta Hospital, liquid clozapine is provided from the pharmacy to the unit or units requiring it in 200 ml bottles. As the supply of clozapine runs low the unit orders another bottle. Pharmacy records are kept showing the amount of clozapine sent from the pharmacy to each unit at Alberta Hospital and the date.

Medications are stored in a locked medication room on unit 10-1. Only the nurses have keys to the room.

After being prescribed clozapine, Ms. Payne was registered with CSAN and regular blood tests were done.

Pharmacy records show 200 ml of clozapine going to unit 10-1 on September 17, October 1 and October 15.

Ms. Hall administered medications to Ms. Payne on September 22, 2012. She testified that she gave Ms. Payne liquid clozapine in the prescribed dosage (33.75 ml) from the stock on the unit. She said she would have had someone else check her calculations but was not able to say who. She did not make a note of whether she did a mouth check (to make sure Ms. Payne swallowed the medication) but said it was generally something she would do.

Mr. Snaterse testified that after receiving the Medical Examiner’s Report, and reviewing the suggestions in that Report to account for the high level of clozapine in Ms. Payne’s blood, inquiries were made at Alberta Hospital about the clozapine available for Ms. Payne.

An examination of pharmacy records was undertaken in order to determine whether there was any missing clozapine. Pharmacy records and the amount of clozapine that had been sent to the unit were reviewed. The volumes of clozapine sent to the unit correlated with the volume that would have been administered to Ms. Payne. Ms. Payne was the only other patient on unit 10-1 receiving clozapine.

At the time of Ms. Payne's death there were 10 patients at Alberta Hospital receiving clozapine. Alberta Hospital checked on the other 9 patients receiving clozapine from the same batch as Ms. Payne and determined that none of those patients showed any signs of clozapine toxicity.

Alberta Hospital determined that Ms. Payne had never left the unit and her ability to obtain any non-allowed quantity of clozapine would have been minimal.

IX. OBSERVATION LEVELS AT ALBERTA HOSPITAL

At the time of Ms. Payne's death, AHS had policies and procedures for observation of patients in acute inpatient psychiatric units. Levels of observation (as determined by a physician or a nurse practitioner) are established and appropriate documentation is required.

Ms. Payne was on "Q 15" observation level which means that she must be observed every 15 minutes. The observation must be properly documented. Mr. Snaterse testified that the observation policy and related procedures were designed to ensure that patients were safe. The procedure did not specify a particular methodology for observation – staff was to do their observation so as to ensure the patient was safe.

Ms. Hall (charge nurse on the night shift of September 22/23) testified that observation rounds are to look for signs of suicide or distress and to ensure that the individual is present. She described the process at night – they use a flashlight and listen for sounds of breathing. They want to be able to check on people without disturbing their sleep. Sleep is especially important for mental health patients.

The written observation record for Ms. Payne for September 22 and 23 was in evidence at the Inquiry. Initials on the record indicate that Ms. Payne was observed every 15 minutes.

Ms. Hall participated in the observations reflected on the chart for 23:30 (September 22), and 6:45 (September 23) with one of the psych aides. She recalled Ms. Payne sleeping on her stomach in the bed furthest from the door, facing the wall away from the door.

Mr. Nartley did the observations from 7 until 8:30. He said he was trained to go into the patients' room quietly when they are sleeping so as not to disturb them. He said on the first observation of Ms. Payne (7 am) she was sleeping. He did not see any reason to wake her. Ms. Payne's roommate's bed was closer to the door from which Mr. Nartley made his observation. He was not able to see Ms. Payne's face as it was turned away facing the wall. He said he recalled hearing Ms. Payne breathing. The room was dark and he used a flashlight.

Spencer Jean did the observations for 8:45 and 9 am. He said he is trained to look for sudden changes in demeanour. He said when he does rounds for someone sleeping he would stand at the door and shine the flashlight on their torso looking for breaths.

Dr. Bannach's evidence suggested Ms. Payne may have been deceased for some hours before she was discovered, notwithstanding the fact that she was observed every 15 minutes.

Alberta Hospital did a review to determine how it might have been possible that Ms. Payne's death may have been missed by those responsible for doing observations. Mr. Snaterse testified about that review. He said they went into the large double room occupied by Ms. Payne and noted that there is a fan beside the bed occupied by Ms. Payne. Mr. Snaterse observed that the fan caused rustling of sheets and blankets.

He said the staff was insistent that they observed movement and he speculated that the rustling

may have contributed to that perception.

Mr. Snaterse introduced copies of a new draft policy and procedure which is currently being developed dealing with observation of patients, including changes initiated, in part, by the death of Ms. Payne. The significant change in the draft procedure under consideration is the addition of the following:

In the case of the patient who appears to be sleeping, monitoring of at least three (3) regular respirations (e.g., direct visualization of chest movement or clear sounds associated with sleep, such as snoring, deep breathing) shall be done at a frequency equivalent to the patient's observation level ...”

X. EXPERT OPINIONS RESPECTING MS. PAYNE'S DEATH

A. Dr. Michael Reider

Dr. Reider was retained by AHS to provide an opinion report as to the cause of death in the case of Shaunnie Payne.

Dr. Reider is a clinical pharmacologist with a special interest and expertise in the area of adverse outcomes related to therapy with a focus on adverse drug reactions. Among his many qualifications, he holds a medical degree (1980), completed a residency in pediatrics, training in emergency pediatrics and clinical pharmacology. He holds a PhD (1992) in clinical pharmacology in the area of adverse drug reactions. He holds research and teaching positions. He has served as Coroner for the West Region of Ontario and has determined the manner and cause of death in coroner's cases for 10 years.

In providing his opinion, he reviewed the following: Ms. Payne: hospital records, pharmacy records, Observation Unit Rounds Checklist, Medical Administration Record, Autopsy Record.

He provided the following opinion:

1. The most likely cause of death for Ms. Payne was Sudden Cardiac Death due to Cardiac Arrhythmia with Drug Therapy as a Contributing Factor.
2. Clozapine therapy may have been one of several factors leading to the death but Clozapine Toxicity cannot be reliably attributed as the Cause of Death.

Dr. Reider was of the opinion that the clinical circumstances surrounding Ms. Payne's death do not support or are not consistent with acute clozapine overdose. He noted that the nursing notes from September 22 indicate no evidence of symptoms consistent with overdose. While Ms. Payne spent time lying on her bed, she also conversed with staff about her plans and played a card game with staff before going to bed. This behaviour is not consistent with acute clozapine overdose. The fact that she was taking liquid clozapine and subject to regular mouth checks would lead to the conclusion that she was not able to secrete or stockpile clozapine.

He said that while clozapine may have played a part in the mechanism of death he did not believe that clozapine toxicity was the cause of death.

He noted that Ms. Payne was taking clozapine and venlafaxine, both of which can prolong the QT interval. Ms. Payne's ECG indicated that her QT interval was in the borderline. Being female is a risk factor for QT prolongation. Given these factors Dr. Reider opined that the most likely cause of death was sudden cardiac death due to arrhythmia which may have been related to drug interactions. He also noted that she had a history of crack cocaine use and sudden cardiac

death occurs at a higher rate for those users.

He provided the following explanation

“...there’s no question in my mind it’s a natural death in terms of that, you know, this is not ... because natural deaths include deaths as a consequence of therapy that they are being given. So as an example, if you have cancer and your oncologists give you medicine to treat ... chemo to treat your cancer but it drives your white counts down to nothing and you die of infection, the conflict is natural. It’s not that the oncologist meant to kill you with cancer drugs; they didn’t. It’s just that’s a complication, a known conflict of therapy.”

He viewed Ms. Payne’s sudden death as a complication of therapy.

Dr. Reider was asked about the difference among the terms “cause of death”, “manner of death” and “mechanism of death”.

He said that “manner of death” is a broad definition of the way you die and generally speaking there are five manners of death– natural, accident, suicide, homicide and undetermined.

He described “cause of death” as the disease that causes you to die, and the “mechanism” is what actually happened.

B. Dr. Robert Ariano

Dr. Ariano was retained by AHS to prepare an opinion report into the death of Shaunnie Payne.

Dr. Ariano is a clinical pharmacist. He holds a doctorate in pharmacy (1988), became a board certified pharmacotherapy specialist (1997) and has received recognitions for his teaching, research and clinical practice. He has worked at the St. Boniface General Hospital for 27 years and is currently working in critical care services. He is the author of multiple publications. Although he has not worked as a medical examiner or coroner, he has been involved in determining the cause and manner of death in a number of cases involving the administration of drugs and potential overdose.

In preparing his report, he reviewed the records from Alberta Hospital, pharmacy dispensing records, observation unit records, medical administration records the autopsy and toxicology reports and materials provided by Mr. Payne which were tabled at the Inquiry.

Dr. Ariano examined each recorded dose of clozapine and correlated those with Ms. Payne’s measured clozapine levels. Using pharmacokinetic computer modelling he was able to generate a profile of her complete clozapine exposure during the 40 days she received the drug (August 14 to September 23). This profile showed her concentrations of clozapine after each dose as well as the highest achievable concentration from the last dose before her death. That value had accumulated to a “final peak” of 1.29 mg/L on the evening of September 22. Dr. Ariano indicated that his value would not be considered to be within the toxic range for this drug.

Dr. Ariano then addressed the question whether the post mortem value of 3.78 mg/L (a level 2.9 times what would have been predicted given her recorded doses) would be the expected result of post mortem redistribution or whether an indicative of an overdose.

It was Dr. Ariano’s opinion that the post mortem clozapine level of 3.78 mg/L cannot be used to suggest overdose, but would rather be consistent with post mortem redistribution.

Dr. Ariano referred to the comment in the toxicology report “As a result of this [post mortem] redistribution it is extremely difficult to interpret post mortem drug concentrations and their possible significance as to behaviour and/or cause of death.” Dr. Ariano agreed that this is a correct statement of the scientific literature.

However, Dr. Ariano disagreed with the statement and conclusion that followed in that report: “If blood is collected from an isolated peripheral site, i.e. isolated femoral vein or artery, the likelihood of this redistribution is reduced”. Dr. Ariano indicated that that conclusion derives from the results of the single study suggesting that femoral sampling would result in a lower level of post mortem redistribution. Dr. Ariano said that study would not be helpful in interpreting the results in Ms. Payne’s case because that study dealt with subjects (pigs) that had been exposed to clozapine for a short period of time (1 week). Ms. Payne had been taking clozapine for 40 days. The longer the drug is taken the higher the muscle and fat stores of clozapine and the higher the level of post mortem redistribution.

Dr. Ariano reviewed the drugs Ms. Payne was taking and did not “see a cause for concern with her medical combinations”.

As to cause of death, Dr. Ariano suggested consideration be given to an arrhythmic event. He noted that Ms. Payne had a slightly prolonged QT interval. QT intervals can fluctuate day to day as a result of medications as well as nutritional status and heart rate. Ms. Payne’s risk factors for arrhythmia would be having a higher baseline QT interval, being female and taking a concurrent anti-psychotic medication.

XI. WHAT CAUSED MS. PAYNE’S DEATH?

One of the duties of the Medical Examiner under the *Act* is to record the cause of death in relation to those deaths which fall within his/her purview. The *Act* requires that the judge conducting a Fatality Inquiry make a report to the Minister which includes findings as to, *inter alia*, the cause of death.

In the Certificate Medical Examiner, Dr. Dowling identified the “cause of death” as “the toxic effects of clozapine or clozapine toxicity”. He indicated that it could not be determined whether the high levels of clozapine resulted from an accumulation of the drug over time, a medication error or errors, or the patient gaining access to clozapine.

Dr. Dowling’s theories as to how the clozapine toxicity arose all suggest an excess of clozapine.

A. Clozapine Toxicity

The evidence is clear that, because of post mortem redistribution, the post mortem level of clozapine in Ms. Payne’s bloodstream is not an accurate indication that there was a high level of clozapine in Ms. Payne’s bloodstream before she died. Dr. Ariano was of the opinion that the high post mortem level of clozapine detected in Ms. Payne was what would normally be expected for someone who had taken the drug for 40 days as Ms. Payne had.

Dr. Reider, Dr. Ariano, Dr. Vozar and Mr. Snaterse also spoke about clozapine toxicity – its meaning and manifestation. Each used the term in connection with an overdose.

Dr. Reider described clozapine toxicity as being associated with a single large overdose. In such circumstances he said one would expect to see central nervous system depression, resulting in coma, stupor, unresponsiveness, high heart rate and confusion.

Dr. Reider said the dose of clozapine Ms. Payne was receiving was within the usual therapy indication. The nurses' notes from the evening of September 22, indicate that Ms. Payne's behaviour was not consistent with acute clozapine toxicity or overdose.

Dr. Ariano said toxicity is only associated with concentrations of clozapine in bloodstream – not in fat stores where it accumulates. He said it is possible to have significant amounts of clozapine in the fat stores and it will have little pharmacological effect.

Dr. Ariano said the records he reviewed showed appropriate doses and no overdose.

Dr. Bannach was not able to comment on the accumulation of clozapine in the blood stream as opposed to the fatty tissues.

Dr. Vozar described clozapine toxicity as a clinical diagnosis. It is not necessarily related to the level of the drug taken but rather to the effect it has on the patient. Indications of overdose of toxicity would be sedation – a patient would become unconscious or comatose.

Mr. Snaterse also described clozapine toxicity as a clinical diagnosis. In someone developing clozapine toxicity one would expect to see sedation – dizziness when standing, confusion, blurred vision and urinary retention. He said Ms. Payne's clinical record from the evening prior to her death showed no indication that she was experiencing any of these signs.

The evidence of all of these witnesses indicate that Ms. Payne was not showing signs of clozapine overdose.

However, Dr. Chatterton indicated that "toxicity" may be used in a context similar to "adverse", suggesting that someone taking a therapeutic dose (as opposed to an overdose) of clozapine could have an adverse reaction.

B. Dosing and Accumulation of Clozapine

The evidence of Dr. Vozar, Dr. Ariano and Dr. Reider and Mr. Snaterse indicate that Ms. Payne was receiving doses of clozapine that fall within therapeutic levels.

Clozapine is closely monitored at Alberta Hospital. No clozapine was missing. Other patients receiving clozapine from the same batch as Ms. Payne did not show any symptoms consistent with an error in compounding the clozapine.

The evidence is not consistent with medication error.

C. Cause of Death

The Medical Examiner's Report indicates that the cause of death was clozapine toxicity.

Insofar as that conclusion suggests an overdose or medication error resulting in Ms. Payne receiving more clozapine than prescribed or accumulation in the bloodstream, it is not consistent with or supported by the evidence the Inquiry heard.

Dr. Reider concluded that in view of the fact that she was on two drugs (clozapine and venlafaxine) which can prolong the QT interval, and she had an elevated QT interval, the most likely cause of Ms. Payne's death was sudden cardiac event due to arrhythmia which may have been related to drug interactions.

Dr. Ariano felt that the mechanism of death for Ms. Payne was a QT prolongation which can give

rise to a fatal arrhythmia which would result quickly in death. He said that in a majority of patients he would not expect a potential for interaction and QT prolongation from venlafaxine inhibiting the metabolism of clozapine.

Dr. Bannach was asked about Dr. Ariano's opinion that the cause of death was most likely an arrhythmia. Dr. Bannach said that arrhythmia is not a "cause of death" but a "mechanism of death".

Cause of death" is defined in the *Act* as follows:

"1(d) "cause of death" means the medical cause of death according to the international Statistical Classification of diseases, Injuries and Causes of Death as last revised by the international Conference assembled for that purpose and published by the World Health Organization;

The World Health Organization documents to which this definition relates include arrhythmia under the rubric of "cause of death".

Dr. Bannach agreed that some of the things the World Health Organization would classify as "causes of death", his office would view as "mechanisms of death". He said a cardiac arrhythmia can be caused by a number of things and to list it as a cause of death does not tell you anything about the cause of death.

Dr. Bannach agreed that anyone taking clozapine can potentially have a prolonged QT interval which puts them at risk for an arrhythmia.

This Inquiry is required to make a Report as to cause of death and is bound by the definitions in the *Act*. Arrhythmia is included as a "cause of death" as that term appears in the *Act*.

The evidence does not support a finding of toxicity through accumulation of the drug over time, medication error or Ms. Payne having access to additional clozapine.

The evidence and opinion supports a conclusion that clozapine can prolong the QT interval, that venlafaxine can also prolong the QT interval and that prolongation of the QT interval can result in an arrhythmia.

Ms. Payne had other risk factors for prolongation of the QT interval (being female and taking drugs).

The evidence suggests that cardiac arrhythmia associated with drug therapy is the most likely reason for Ms. Payne's death, although another undetectable cause (such as a seizure) cannot be entirely ruled out.

Recommendations for the Prevention of Similar Deaths:

This Inquiry is empowered to make recommendations, where appropriate, directed at preventing similar deaths. In considering whether to make recommendations, there are several things that must be borne in mind.

Any recommendations from this Inquiry should be useful. To be useful they must go beyond the specific facts about this case and have a broad systemic application. They must be based on evidence. The Inquiry must consider the potential for future unforeseen adverse consequences which could arise from any recommendations.

This Inquiry involved highly trained professionals including physicians, nurses and pharmacists. Their activities and scope of practice are governed by statute, and by their professional organizations.

Although it is not clear that a different approach to the observation of Ms. Payne would have prevented her death, had it not been for the changes under consideration at Alberta Hospital relating to observation, I might have made a recommendation in this respect. However, the matter is currently under consideration and the organization knows best how to implement those changes.

There are no recommendations.

DATED July 20, 2016,

at Edmonton, Alberta.

Original signed by

The Honourable Elizabeth A. Johnson
A Judge of the Provincial Court of Alberta