

INDEPENDENT REVIEW INTO THE INCORRECT DOSING OF CYTARABINE TO TEN PATIENTS WITH ACUTE MYELOID LEUKAEMIA AT ROYAL ADELAIDE HOSPITAL AND FLINDERS MEDICAL CENTRE

REVIEW PANEL

PROFESSOR VILLIS MARSHALL AC
A/PROFESSOR ROBERT LINDEMAN
MS ELIZABETH NEWMAN
DR CHRISTINE CARRINGTON
MS ELLEN KERRINS
MS JULIE MARKER

November 2015

Executive Summary

1. Over a period of six months [end July 2014– end January 2015], during the consolidation phase of treatment for Acute Myeloid Leukemia, five patients at the Royal Adelaide Hospital and five patients at Flinders Medical Centre received a daily dose of Cytarabine instead of a dose twice a day. This was the result of the Royal Adelaide Hospital’s Acute Myeloid Leukemia protocol containing the incorrect dose.
2. On 5 August 2015 the South Australian Minister for Health and Ageing and the Chief Executive of SA Health requested that an independent review be conducted.
3. The Terms of Reference of the review were to:
 - review the events and decisions that led to the incorrect dosing protocol being used
 - review the system of reporting incidents at the Royal Adelaide Hospital and Flinders Medical Centre, the process of investigation and open disclosure to ensure all were in compliance with SA Health policy directives
 - review the systems of governance and confirm that appropriate actions were taken throughout the process of investigation
 - review the appropriateness of recommendations made by Central Adelaide Local Health Network and SA Pathology in relation to said local investigation, including progress in actioning these recommendations
 - make recommendations on review findings to the Chief Executive to assist in mitigating the risk of reoccurrence and respond to breaches of compliance.

Major Findings

4. The review panel found that under dosing of Cytarabine was caused by a series of significant clinical governance failures at the Royal Adelaide Hospital Haematology unit, including:
 - failure to follow routine clinical processes and procedures for the development, review and publishing of patient chemotherapy protocols
 - failure to advise patients that the chemotherapy protocol was a non-standard protocol that required approval from the relevant committee and informed patient consent
 - failure to provide adequate clinical supervision to nursing staff administering Cytarabine
5. Additionally, the review panel found that certain clinical staff did not comply with SA Health incident management and open disclosure policies by failing to:
 - report and lodge the incidents in the SA Health incident management system
 - conduct timely and appropriate open disclosure with patients
 - provide an immediate clinical response to patients who had been under dosed.
6. The review panel formed the view that the clinical conduct of certain clinicians demonstrated a lack of adequate knowledge, skill, care and judgment.

Recommendations

7. The review panel makes the following recommendations:

Recommendation 1: That in view of the serious clinical governance failings identified by this review:

- failure to follow accepted practice whilst implementing a new non-standard clinical protocol;
 - failure to seek and to be granted the approval of the relevant committee in relation to the introduction of a non-standard protocol;
 - failure to report and lodge the incidents in the SA Health incident management system;
 - failure to conduct timely and appropriate open disclosure with patients; and
 - failure to provide an immediate clinical response to patients who had been under dosed,
- the Chief Executive Officer of the Central Adelaide Local Health Network gives consideration to referring relevant clinicians to the Australian Health Practitioner Regulation Agency for review.

Recommendation 2: That the Chief Executive Officer Central Adelaide Local Health Network ensures staff fully understand their responsibility to act in accordance with SA Health policies, particularly incident management and open disclosure policies. That effort is made to ensure that the requirement to report all incidents into the Safety Learning System is clear and that open disclosure and incident management training is made available to all staff, including all medical staff.

Recommendation 3: That the Chief Executive Officer Central Adelaide Local Health Network implement a rectification plan to ensure that the appropriate governance frameworks are in place within SA Pathology and, in particular, the Haematology service provided to the Royal Adelaide Hospital. That this plan takes into consideration the recommendations made in the report “Governance of Clinical Services Conducted by SA Pathology Clinical Staff: A Review” Peter Brennan, Jeff Szer, June 2012 and the National Safety and Quality Health Service Standards related to Governance, Partnering with Consumers and the provision of patient centered care.

Recommendation 4: That the Chief Executive Officer Central Adelaide Local Health Network ensures appropriate processes and procedures for the development, review and publication and, where indicated, revision of chemotherapy protocols are developed and implemented that are consistent with the current evidence base. And that the resulting policies, procedures and protocols are understood and acknowledged by all relevant staff, are consistent with SA Health policies and procedures and are appropriately filed and stored.

Table of Contents

- Executive Summary..... 2
- Major Findings..... 2
- Recommendations..... 3
- Background and Context..... 6
- Terms of Reference..... 6
- Approach..... 6
- Documentation Review..... 7
- Patient Meetings..... 7
- Staff Meetings..... 7
- The Patient and Family Experience..... 7
- Understanding the Disease and Treatment..... 9
- Acute Myeloid Leukamia (AML) Consolidation Treatment..... 9
- Overview of the event..... 10
- Flinders Medical Centre adopts the RAH protocol (14175)..... 11
- The error is identified and corrective action commenced..... 11
- A family member lodges a formal complaint and incidents are lodged in South Australian safety and learning (SLS) incident management system..... 13
- Additional information for consideration..... 14
- Key Findings..... 15
- Events and decisions that led to the incorrect dosing protocol being used..... 15
- Was the system of reporting the incidents at the Royal Adelaide Hospital and Flinders Medical Centre, process of investigation and open disclosure in compliance with SA Health Policy Directives?..... 16
- Incident reporting..... 16
- Incident investigation..... 16
- Open disclosure..... 16

Systems of governance and appropriateness of actions taken throughout the process of investigation..... 18

Appropriateness of recommendations made by CALHN and SA Pathology in relation to said local investigation, including progress in actioning these recommendations.....19

Protocols be reviewed for accuracy.....19

Recommendations for additional chemotherapy to be provided by clinical leads..20

Haematology protocol database be reviewed.....20

Formal training on incident reporting and open disclosure.....20

Recommendations on findings to assist in mitigating the risk of reoccurrence and respond to breaches of compliance.....21

Background and Context

8. Over a period of six months [end July 2014 to end January 2015], during the consolidation phase of treatment for Acute Myeloid Leukemia, five patients at the Royal Adelaide Hospital and five patients at Flinders Medical Centre received a daily dose of Cytarabine instead of a dose twice a day. This was the result of the Royal Adelaide Hospital's Acute Myeloid Leukemia protocol containing the incorrect dose.

Terms of Reference

9. On 5 August 2015, the South Australia Minister for Health and Chief Executive of SA Health requested that an independent review be conducted.
10. The Terms of Reference of the review were to:
 - review the events and decisions that led to the incorrect dosing protocol being used
 - review the system of reporting incidents at the Royal Adelaide Hospital and Flinders Medical Centre, the process of investigation and open disclosure to ensure all were in compliance with SA Health policy directives
 - review the systems of governance and confirm that appropriate actions were taken throughout the process of investigation
 - review the appropriateness of recommendations made by Central Adelaide Local Health Network and SA Pathology in relation to said local investigation, including progress in actioning these recommendations
 - make recommendations on review findings to the Chief Executive to assist in mitigating the risk of reoccurrence and respond to breaches of compliance.

Approach

Members of the Independent Review Panel

11. Professor Willis Marshall AC, Chair of the board of the Australian Commission on Safety and Quality in Health Care was asked to lead the review. To ensure the independence of the review, relevant clinical expertise was sought from outside South Australia to assist Professor Marshall with the review process. In addition, to ensure the review incorporated a patient centered approach, a representative from Health Consumers Alliance and Cancer Voices SA were included as part of the review team. The following people were appointed to the review panel:
 - A/Professor Robert Lindeman, Consultant Haematologist, Prince of Wales Hospital, New South Wales
 - Ms Elizabeth Newman, Senior Practitioner Haematology, Concord Repatriation General Hospital, New South Wales
 - Dr Christine Carrington, Assistant Director of Pharmacy- Cancer Services, Senior Consultant Pharmacist- Cancer Services, Princess Alexandra Hospital, Queensland
 - Ms Ellen Kerrins, Health Consumers Alliance
 - Ms Julie Marker, Cancer Voices SA.

Documentation Review

12. The Royal Adelaide Hospital (RAH) and Flinders Medical Centre (FMC) were asked to provide all documentation related to the incident, including the medical records of the ten patients affected.

Patient Meetings

13. Patients and families were invited to attend individual meetings with Professor Marshall and Ms Kerrins to share their experience and provide advice on what could have been done differently. Seven of the nine surviving patients agreed to meet.

Staff Meetings

14. The Chief Executive Officers at CALHN and Southern Adelaide Local Health Network (SALHN) were asked to facilitate meetings with relevant staff at the RAH and FMC respectively.
15. Separate meetings were held for governance, medical, pharmacy and nursing staff. If a staff member had a role in governance and clinical care they attended two meetings.
16. The review panel met with staff on 9 and 10 September 2015, and 6 October 2015. Staff were invited to give their perspective about what happened, outline actions taken and make suggestions as to what could be done to prevent a similar event occurring in the future or, if it did occur, how it could best be handled.

The Patient and Family Experience

17. The patients and families appreciated being given the opportunity to share their experiences and give their opinion about how the incident was handled and provide advice on how it could be handled better in the future.
18. It should be noted that all patients were consistently complimentary about the routine care they had received from medical and nursing staff.
19. The patients advised that they were informed of the incident in February or March 2015 and could not recall any further advice until a media announcement in August 2015. They suggested that it may have been helpful if, after they had been informed of the incident, they had been asked how to best handle the interaction with them in the months that followed.
20. Some patients felt that the way they received the initial information regarding the under dosing could have been improved. In some cases it was:
 - unplanned
 - tacked onto an existing appointment
 - abrupt
 - not always delivered by a consultant
 - delivered when they were unwell
 - delivered without written advice or planned follow up
 - not supported by counselling (psychological) or care (social) or a dedicated service to continue to discuss options.
21. Patients were concerned that when they were informed of the under dosing they did not always experience a sense of empathy, care or apology but one of defensive explanation and lack of individual focus. Some patients also thought that the discussion about their options for further treatment may not have been handled as well as it could have been.

22. They considered the media coverage, which occurred months after they had been made aware of the under dosing, to be a distressing event.
 - It focused on reporting that, due to their diagnosis, they were not going to do well even if they had received a twice daily dose of Cytarabine.
 - It occurred without warning and no attempt was made to contact them even after the event to see if they needed support as a result of the media coverage.
 - Some patients had not confided in family and friends about the issue and had to respond to concerned family and friends when approached by them as a result of the unexpected media coverage.
 - In addition they were distressed that there was no attempt by anyone to contact them to see if they needed support after the media coverage.
23. It was suggested that if possible, patients should be notified in advance that media announcements were to take place and that there should be some mechanism to assist the patients to deal with the information provided.
24. FMC sent patients a letter of apology in May 2015. This letter caused some patients distress as it arrived so many months after the initial disclosure and they felt it to be lacking in warmth and empathy.
25. The patients provided this information in good faith and hoped that the advice would assist in guiding how a similar incident is handled in the future.
26. It is acknowledged by the reviewers that time has elapsed since the patients became aware of the error and not surprisingly some patients have relapsed. This is, sadly, a disease which is difficult to cure and the treatments are invariably associated with severe side effects. Although all patients were aware of the risk and the hoped for benefits associated with their treatment, those who have relapsed have unfortunately had to cope with the knowledge that they accidentally received a reduced dose. While patients were informed of the error and varying levels of open disclosure were undertaken, in hindsight it did not seem that the level of patient and family distress was always fully appreciated. Given the distress that the patients experienced it would be important to seek 'informed consumers' and expert opinion regarding the most effective manner to support and counsel the patients and their families.
27. The effect that this event has had on families cannot be underestimated and in some cases may be somewhat more significant than to the patient.
28. One patient stated that:

"To call the transcription error a "typo" is to trivialise it. In addition, in my particular case, the knowledge that my treatment could and should have been corrected for that second consolidation cycle will haunt my family for ever should I not survive".

Understanding the Disease and Treatment

29. Acute myeloid leukaemia (AML) is a type of cancer that affects the blood and bone marrow. AML is characterised by an overproduction of immature white blood cells, called myeloblasts or leukaemic blasts. These cells crowd the bone marrow, preventing it from making normal blood cells. They can also spill out into the blood stream and circulate around the body. Due to their immaturity, they are unable to function properly to prevent or fight infection. Inadequate numbers of red cells and platelets being made by the marrow cause anaemia, and easy bleeding and/or bruising.

Acute Myeloid Leukemia (AML) Consolidation Treatment

30. The mainstay of treatment of AML is a combination of Cytarabine (also known as Cytosine Arabinoside AVA-C) and an Anthracycline (Idarubicin or Daunorubicin). Either one or, if necessary, two induction cycles are administered to achieve a complete remission, followed by consolidation cycles of treatment.
31. Clinical trials have focused on the optimum dosing and sequencing of these regimens, but there is no consensus on the appropriate Cytarabine dose. High doses of Cytarabine in induction cycles have been associated with moderate improvements in remission rates, but expose patients to higher rates of morbidity and mortality. There is consensus that modest doses of induction therapy (Cytarabine 100 mg/m²/day for seven days) are safe and produce an acceptable remission rate, but that this induction treatment should be followed by intensified consolidation therapy.
32. Intensive consolidation exposes older patients to unacceptable toxicity and morbidity and mortality rates.
33. Some subsets of AML are best treated with high dose Cytarabine consolidation, but for non-core binding factor AML, a combination of lower dose Cytarabine and Anthracyclines is likely to provide similar long-term survival rates with more acceptable short-term toxicity.
34. The ALLG (Australasian Leukaemia and Lymphoma Group) is a consortium of haematologists who agree on clinical trial protocols, and includes working parties of experts in specific treatment areas. The investigational protocols offer the opportunity to enroll large numbers of patients from multiple treatment centres in uniform studies investigating novel drugs or drug combinations. The development of these protocols occurs by consensus among experts, and respects the requirement that procedures should be consistent with the current accepted "standard of care" to encourage participation of the maximum number of treatment centres.
35. The SA Pathology Clinical Director of Haematology is a participant in the AML working party of the ALLG. The ALLG M15 protocol was developed to investigate whether maintenance Lenalidomide (i.e. the addition of this drug at the end of standard treatment) would improve the outcome of "standard treatment" which would ordinarily not involve maintenance therapy after consolidation treatment had been completed. The backbone of AML M15 protocol was a consolidation regimen that exposed patients to a dose of Cytarabine that was appropriate to their age and fitness. The designated dose for patients aged 56-65 was 1 g/m² twice daily on days 1, 3 and 5, together with Idarubicin 12 mg/m² on days 1 and 2, and two consolidation cycles were mandated by the study. This would generally be regarded as reasonable treatment, although as already indicated, the optimum consolidation regimen remains unknown. The selection of this "backbone" was not referenced in the study, but was arrived at by consensus among the trial investigators based on experience in a study published in 2005. Cytarabine is

conventionally either given as a standard 24 hour a day continuous infusion or as twice daily 3-4 hour infusions on alternate days (as in this AML M15 protocol), although other regimens involving daily infusions are also sometimes used (for example with Fludarabine and G-CSF).

Overview of the event

36. The RAH Haematology Unit decided to implement the AML M15 study at their centre in mid-2014, and therefore made a decision to adopt the study protocol backbone as their standard of care. The decision to implement the AML M15 was discussed with the haematologists as a group.
37. The SA Pathology Clinical Director of Haematology made a decision to update the RAH in-house AML protocol on the 12 July 2014, to reflect the study protocol backbone. This was following discussions with the ALLG at a scientific meeting.
38. Updating the RAH-in-house AML protocol to reflect the study protocol backbone in essence made it a trial protocol as it contained non-standard care and the level of evidence used to support the use of this backbone was Grade IIB (i.e. consensus view of experts based on experience rather than randomized trials). As such, ethics approval should have been sought. It appears that ethics approval was not obtained and there is no evidence that the patients were made aware that the treatment they were undergoing was non-standard.
39. The SA Pathology Clinical Director of Haematology provided a project officer with a marked up copy of the original RAH AML protocol and asked that the protocol be amended to incorporate the changes.
40. On 15 July 2014, the project officer sent a copy of the amended protocol to the SA Pathology Clinical Director of Haematology for his review. Additional changes were requested and on 16 July 2014, the second draft was presented to the SA Pathology Clinical Director of Haematology, in hard copy, at the end of a 'busy clinic' for approval. The project officer was 'anxious' to get the revised policy approved prior to commencing leave the next day.
41. The SA Pathology Clinical Director of Haematology approved its release, but did not notice that the Cytarabine dose was incorrect at 1 g/m² once daily on days 1, 3, 5 instead of 1 g/m² twice daily.
42. The protocol containing the incorrect dose was circulated widely by group email across the Royal Adelaide Hospital, Flinders Medical Centre, Women's and Children's Hospital and the Queen Elizabeth Hospital. It replaced the previous protocol that involved the administration of high dose Cytarabine twice daily on days 1, 3, 5. The email was for information and recipients were not asked to review or comment on the protocol.
43. On Saturday 19 July 2014, the SA Pathology Clinical Director of Haematology sent a group email to the same distribution list used by the project officer, thanking the project officer and outlining four salient changes. The email did indicate that Cytarabine 1g/ m² would be administered twice daily on days 1, 3 and 5. However no comment was made that the uploaded protocol differed from what was intended. There is no evidence of a reply or acknowledgement by anyone on the group email.

44. The revised protocol was implemented at the RAH, with handwritten charting of drugs. Patients were treated as inpatients during induction therapy, but consolidation therapy was administered to patients as outpatients. Haematology outpatients were treated in a combined haematology and oncology setting.
45. A move to outpatient treatment had been implemented about three or four years previously. The nurses working in the outpatient area were a cohort who had not historically been involved in treating haematology inpatients, and who were therefore not familiar with the intensive treatment protocols for AML.
46. The move to outpatient consolidation treatment at the RAH had not been accompanied by the appropriate change management procedures, and the nursing staff had not been offered appropriate education and training. A Clinical Nurse Educator was not employed until recently [2015], and there was no program of in-service education.
47. The intention of the move to outpatient consolidation treatment was that Cytarabine infusion would be commenced in the outpatient setting by a registered nurse and completed by a district nurse at home (when the Outpatient Unit was closed). Thus there was no direct supervision by a haematologist, and the fact that Cytarabine was being administered once daily was not noticed by anyone with the seniority and knowledge to be alerted to this anomaly.
48. It was known that the intention of the revised protocol was to reduce the dose of Cytarabine to these older patients, and even those with sufficient clinical experience to question the regimen might reasonably have thought that the drop to once daily dosing might have been intentional if they were not familiar with the treatment of AML.

Flinders Medical Centre adopts the RAH protocol (14175)

49. It appears that the arrangement to utilise the protocol at FMC was relatively informal. A doctor who was initially employed as a fellow at the RAH and then a consultant at FMC requested the RAH protocol be used at FMC for the treatment of patients with AML. The aim, to achieve a uniform approach to the treatment of AML across the two hospitals in an attempt to facilitate the entry of FMC patients into the RAH for allogeneic transplantation if indicated or their enrolment into the AML M15 trial which was not open at FMC, was commendable.
50. The Head of Unit at FMC approved the implementation of Protocol 14175 but the RAH was not formally notified of its implementation (although a consultant at FMC indicated that informal communication had occurred). As a result the RAH did not immediately notify FMC when it became aware of the error in the protocol. This delay resulted in a patient, at FMC, receiving the incorrect dose after the error in the protocol had been recognised at the RAH.
51. FMC's protocol, dated 21 July 2014, was first used to treat a patient in July 2014. Because the protocol was based on the RAH protocol it was not subjected to the usual FMC procedures for the introduction of a new therapeutic protocol.

The error is identified and corrective action commenced

52. On the 19 January 2015, the Deputy Director, Clinical Haematology and Bone Marrow Transplant at the RAH, prescribed a consolidation cycle of treatment for one patient, wrote the order directly from knowledge of the AML M15 protocol, and included twice daily Cytarabine.

The discrepancy from what had previously been prescribed to other patients (and indeed another patient to be treated the same day) was noted by the Inpatient Dispensing/Haematology Pharmacist and reported to the Deputy Director, Clinical Haematology and Bone Marrow Transplant.

53. The Deputy Director, Clinical Haematology and Bone Marrow Transplant notified the project officer, who had uploaded the protocol, via an email the same day alerting them to the protocol error. The SA Pathology Clinical Director of Haematology who had approved the uploaded protocol was on leave until 27 January 2015.
54. The project officer, with direction from the Deputy Director, Clinical Haematology and Bone Marrow Transplant, corrected the protocol and issued the modified protocol (designated version 14175.1) on 20 January 2015. This was communicated via a group email titled 'updated AML (excluding APML) protocol uploaded'.
55. The body of the email read:

“please note that a revised AML protocol (1.1), with one correct, has been uploaded to the intranet. This version remains as version dated 15th July 2014 with (1) added to the end to mark the update, as the rest of the information is unchanged. Dr X would like to bring to your attention that: under section 3.6 HiDAC 2-ida consolidation: Cytarabine IV 1 g/m² is to be given twice daily.”
56. The email did not highlight that the reason for the one correction related to the identification of the Cytarabine dosage error contained in the previous version, not a routine change to dosing.
57. The same day, the Inpatient Dispensing/Haematology Pharmacist sent the Deputy Director Clinical Haematology and Bone Marrow Transplant an email listing the RAH patients who had been treated on the incorrect protocol and indicated how many cycles had been administered. He also informed the Deputy Director, Clinical Pharmacy and Medicines of the error. Concerns were raised that a pharmacist had been told not to lodge an incident into the Safety Learning System (SLS), as it was being dealt with. The review panel was unable to clarify who had requested that pharmacist to not lodge an incident.
58. Between July 2014, and the identification of the protocol error on 19 January 2015, 13 consolidation cycles were administered to ten patients, five at the RAH and five at FMC. A further consolidation cycle was administered to a patient at FMC on 22 January 2015, as FMC were still unaware of the error.
59. Patient records document that the patients became appropriately cytopenic, and a number of treatment cycles were associated with febrile neutropenia, as would be expected in this clinical setting using that dose of Cytarabine.
60. FMC did not become aware of the error until 30 January 2015, when the RAH Inpatient Dispensing/Haematology Pharmacist mentioned the incorrect dosing to a consultant working at FMC. The consultant immediately started the process of identifying the patients who received the incorrect dosing at FMC.
61. One of the patients at FMC was informed of the error while an inpatient at FMC on 5 February 2015. The consultant understood that patients at RAH were being informed by their clinicians, and thought that was the correct process to use at FMC. As the consultant was relatively new to

the position, the consultant was unaware that there was an affect beyond the individual patient and that the incident needed to be lodged into the SLS and escalated to senior management.

62. However the consultant did inform the Head of Haematology Services of the error during a ward round upon returning from leave on 11 February 2015. The pharmacist who had previously queried whether the dose should be twice daily was also made aware at that time. The pharmacist immediately informed the Director of the Pharmacy, and the Head of Haematology Services notified the Director of Medical Services at SALHN.

A family member lodges a formal complaint and incidents are lodged in South Australian safety and learning (SLS) incident management system

63. A formal complaint was lodged by the wife of the patient informed of the error on 5 February 2015, by letter dated 8 February 2015. The letter was received by the SALHN Consumer Advisory Service on 13 February 2015. This was reported into both the consumer feedback and incident management sections of the SLS the same day.
64. Incidents were lodged in SLS for the other four patients affected at FMC by the Nursing Director for Cancer Services on 16 February 2015. Open disclosure meetings were held with each patient during February 2015. A letter of apology was drafted by the Head of Haematology Services in April 2015, however the letter was not sent from the Chief Executive Officer of SALHN until 27 May 2015, after being amended in line with recommendations from SAICORP, the government insurer.
65. Since these events, there has been ongoing contact between the haematologists and the FMC patients, one of whom has been an inpatient. A procedure for the implementation and ratification of protocols has been further developed, including version and document control, and debriefing of staff undertaken.
66. On the 12 February 2015, the ward pharmacist sent an email to the Head of Pharmacy at RAH with the updated protocol. The Head of Pharmacy was concerned and approached the Director of Cancer Services CALHN. An incident was lodged into the SLS by the Deputy Director, Clinical Pharmacy and Medicines, regarding one patient on 12 February 2015. Incident reports were lodged in the SLS for the remaining four patients on 17 February 2015.
67. Following receipt of an email from the project officer outlining the sequence of events and discussing the error discovery and correction, on 16 February 2015 the Head of Clinical Haematology RAH prepared a draft brief for the Chief Executive Officer CALHN. The same day further correspondence was received from the project officer with an attachment "Reviewing and Publishing Haematology Unit Protocol" outlining the development of a new procedure for implementing protocols.
68. On 18 February 2015, the SA Pathology Clinical Director Haematology, prepared some brief recommendations for the management of the affected patients. The recommendations included a bone marrow biopsy in patients who were treated more than three months earlier, and consideration be given to a third consolidation cycle in patients treated more recently.
69. A detailed brief signed by the Executive Director, SA Pathology and the CEO's of CALHN and SALHN was submitted to the Chief Executive of SA Health on 20 February 2015.

70. The new procedure was presented at the RAH Protocol meeting on the 23 February 2015 and the SA Pathology Clinical Director of Haematology prepared a guideline for the management of affected patients.
71. While open disclosure for one of the affected patients at the RAH occurred on 23 February 2015, open disclosure for the remaining four did not occur until March 2015.

Additional information for consideration

72. During the review, the RAH staff indicated a need for an electronic prescribing system. While it would not avoid a transcription error at point of protocol development, it would stop transcription errors when prescribing. It was often junior medical staff who wrote prescriptions.
73. In addition, the reviewers were told that patients at the RAH were frequently kept waiting because clinicians hadn't written and signed pharmacy orders for patients chemotherapy, despite numerous requests, requiring nurses and pharmacists to chase up clinicians.
74. It was acknowledged that an electronic system had the potential to improve the situation but it was not likely that SA Health's new Enterprise Patient Administration System (EPAS) would be able to accommodate the complexity of the leukaemia protocols in the foreseeable future. FMC has adopted a template which appears to have eradicated hand written prescriptions and facilitated the timely delivery of the scripts.

Key Findings

Events and decisions that led to the incorrect dosing protocol being used

75. The review panel found the underlying cause that led to the incorrect protocol being used was a failure of the RAH Haematology Unit to have appropriate governance systems in place and the lack of adequate processes and procedures for the development, review and publication of their chemotherapy protocols.
76. At the RAH a two person process was used for updating then publishing the incorrect protocol, there was neither pharmacy involvement nor a third person check. The review panel found that this fell significantly short of the rigor required for the revision of a chemotherapy protocol.
77. The source document that was used to derive the amendments to the RAH protocol was not referenced in the protocol. This made it extremely difficult for pharmacists to undertake an appropriate assessment of the protocol when scripts were presented to them.
78. It was also apparent to the review panel that no consideration was given to the need of obtaining ethics approval for a protocol that contained non-standard treatment.
79. The review panel found that while FMC had stringent processes in place for the development, review and publication of their own chemotherapy protocols, an equivalent process was not used to vet the RAH protocol prior to its adoption by FMC. The RAH AML protocol should have been scrutinized with the same rigor FMC uses for its own protocols.
80. The FMC protocol referenced the RAH's AML May 2012 "age based Cytarabine consolidation" but because the original source document was not referenced in the RAH protocol, the original source could not be verified. At the time of its implementation, the FMC Haematology Pharmacist queried the Cytarabine dose by email, as did a senior member of the nursing staff (verbally), but was reassured by a consultant that the protocol was correct and that the dose of Cytarabine was intended to be 1 g/m² daily on days 1, 3 and 5. It was understood that this was in the context of an intended dose reduction of Cytarabine in consolidation for patients in this age group.
81. The review panel established that it was routine practice for the RAH to issue new and updated protocols by the use of a group email. These emails are sent to the same email group irrespective of the nature of the protocol.
82. To alert staff, in this way, that a protocol had been updated because of an error in the previous version was an inappropriate means of communication.
83. The poor construct of the email, which failed to indicate that the Cytarabine dose in the previous version of the protocol was incorrect nor convey any sense of urgency, most likely led the recipients to regard it as routine in nature. This, coupled with the fact there was no follow up contact with the recipients to ensure that they were aware of its significance, significantly delayed the recognition that immediate action was required which resulted in the continued use of the incorrect protocol at FMC.

Was the system of reporting the incidents at the Royal Adelaide Hospital and Flinders Medical Centre, process of investigation and open disclosure in compliance with SA Health Policy Directives?

Incident reporting

84. The SA Health Incident Management Policy requires that incidents of this type be reported in the SLS and managed in a timely manner.
85. This policy was not followed by the RAH staff who became aware of the incidents on 19 January 2015, but did not finish reporting the incidents into the SLS until 17 February 2015.
86. The review panel formed the opinion that this was not a one off occurrence of non-compliance as the panel was informed that medical staff at the RAH did not frequently lodge incidents in the SLS and were slow to respond, if at all, when asked to review an incident that had been lodged by someone else.
87. It appeared to the panel that the RAH only started to respond actively to the incidents after they became aware, on 12 February 2015, that the protocol had been used at FMC. Prior to that date no incidents had been lodged in SLS by RAH staff, no open disclosure had occurred and recommendations for the management of the affected patients were not made until 18 February 2015, even though they had been aware of the incident since 19 January 2015.

Incident investigation

88. It appears to the review panel that when the error was discovered, the RAH considered the underlying cause to be that of a transcription error which required no stringent investigation. They did not undertake the level of investigation required by the SA Health Incident Management Policy and did not conduct a root cause analysis investigation as requested by the South Australian Department for Health and Ageing.
89. The review panel is of the opinion that had an appropriate investigation been undertaken by RAH staff, the investigation would have identified the failures in governance that led to the incident and informed appropriate action including in a more rapid and thorough review of protocols.

Open disclosure

90. Documentation of open disclosure varied greatly in how much detail the content of the open disclosure was described; in some cases it appeared non-existent. Hence it was difficult for the review panel to ascertain how sensitively or thoroughly this process was done.
91. However based on the available information, including information gained when the review panel met with staff, it is apparent that the approach to open disclosure differed significantly between RAH and FMC.
92. It was evident that the RAH did not follow the SA Health mandated policy for open disclosure and fell well short of the National Safety and Quality Standards relative to this area.
 - There seemed no sense of urgency or coordinated approach to open disclosure once the error was identified.

- It seems little thought was focused on the patients or how best to communicate this error sensitively and appropriately with those affected.
 - There appeared to be no agreed structure or process in place to inform the patients and their families.
 - In one case, a registrar alone was asked to conduct the open disclosure and had to leave the patient and a family member waiting for twenty five minutes while they followed up for further information.
 - There appeared to be a lack of understanding of the short term and likely longer term emotional impact of this incident on the patients and their family.
 - No support for the staff involved seems to have been arranged. Staff mentioned having no training on open disclosure, indicating it was disorganised, ad hoc, individual choice rather than organised, systematic training.
 - The RAH Consumer Advisor was not informed or invited to be engaged.
 - While offers of support were made, they did not seem to be followed through effectively and appropriately trained or experienced counsellors were not provided to patients, their family or the staff involved.
93. These findings of non-compliance are reinforced by the fact that nine RAH patients were potentially affected by a similar protocol transcription error identified on 10 September 2015. A review of these cases and whether or not a transcription error occurred was underway at the time of this Review.
94. While FMC was not fully compliant, its open disclosure process was better aligned with the SA Health Policy:
- Open disclosure was conducted in a more timely fashion, in a consistent and planned manner.
 - Meetings with the patient and their family were attended by a number of senior staff so that the gravity of concern was conveyed clearly by this prompt and structured response.
 - It appeared that staff understood the emotional impact this incident had on the patients and their family and were acutely aware of how 'gut wrenchingly hard' it was for patients invited to go back for 'one more round' of 'catch-up' of this most grueling chemotherapy, after they thought they'd finished with it.
 - Staff peer support was provided to ensure staff were best equipped to support each other and their patients.
95. However the review panel is of the opinion that the letter of apology sent in May 2015 by FMC, was not empathetic, offered no comfort or additional information, and may have been better not sent rather than arriving so long after the initial disclosure and re-kindling the upset to patients and their family.
96. The fact that legal input resulted in significant changes to the content of the letter and a delay in its delivery, highlights the tension that exists between the open disclosure process and risk management.

Systems of governance and appropriateness of actions taken throughout the process of investigation

97. Good clinical governance requires:
 - integrated governance systems
 - strong strategic and cultural leadership
 - clarity of responsibility
 - reliable processes for ensuring systems for the delivery of clinical care are designed and performing well and clinicians are fully engaged in the design, monitoring and development of service delivery systems
 - well-designed systems for identifying and managing risk.

98. It was evident to the review panel that there was an abject failure of governance at the RAH on all levels. These failures resulted in:
 - the transcription error in the protocol going undetected prior to publishing
 - the error not being detected in a more timely manner once published, and
 - the incident not being appropriately escalated once discovered.

99. While SA pathology had a governance process in place for laboratory procedures this did not extend to clinical protocols. There was no clear policy in place at the RAH, to guide the development, review and publication of clinical protocols in the haematology department.

100. The review panel also noted issues with the retention and storage of outdated protocols. Initially the reviewers were informed that the previous protocol had been removed from the server and a copy was not available. However a copy was eventually provided by the RAH project officer on return from leave. Apparently superseded protocols are stored separately, but this did not appear to be common knowledge. This appeared to be unacceptable practice as if patients treated by a particular protocol developed complications at a later date it would be important that the original document could be readily identified. At the very least there should be clear documentation identifying where superseded protocols are located so they can be easily found.

101. The review panel was unable to determine lines of reporting and accountability from the organisational chart for SA Pathology and RAH Cancer Services.

102. The Director Cancer Services CALHN provided the following information in an attempt to assist the panel understand the reporting lines of the Head of Clinical Haematology RAH and the SA Pathology Clinical Director of Haematology.
 - The Head of Clinical Haematology RAH is employed through SA Pathology and reports to the SA Pathology Clinical Director of Haematology.
 - The formal reporting to the CALHN Cancer Services Director has always been ambiguous.
 - The SA Pathology Clinical Director of Haematology has a clinical role in the CALHN cancer directorate that reports to the Head of Clinical Haematology RAH.

103. It is therefore perhaps not surprising that when interviewed by the panel, the SA Pathology Clinical Director of Haematology said he did not know what to do when informed of the incident, the Head of Clinical Haematology at RAH said he was not made aware of the incident, and the Director Cancer Services CAHLN indicated he was not involved.

104. While dual reporting lines are also present at the FMC with the Head of Haematology being part of both the SA Pathology and the SALHN governance system, the reviewers were informed that there is a clear understanding of which governance system specific issues needed to be escalated through. Anything to do with the safety and quality of patient care is escalated through SALHN Governance, which is why the Head of Haematology immediately notified the Director of Medical Services at SALHN when they became aware of the error.
105. The reviewers were made aware that a review on the "Governance of Clinical Services conducted by SA Pathology Clinical Staff" was undertaken by Brennan and Szer in 2012.
106. The report stated that ambiguities have arisen about clinical services delivered by trained pathologists practicing in the public hospital system. They recommended that SA Pathology should continue to be the employer and the Local Health Networks (LHNs) should purchase clinical capacity from SA Pathology through service level agreements. They further recommended a new approach to the appointment of these specialists to LHNs based on a rigorous framework of accountability supported by agreed key performance indicators and annual performance reviews. As far as the review panel could establish, these recommendations have not been progressed.
107. The review panel observed that there were stark differences between the two hospitals in terms of governance systems and procedures for providing routine patient-centred care and also for managing this incident.
108. The RAH seemed to have disorganised, ad hoc and in some cases – dysfunctional patterns of operation which were quickly made obvious during the review panel meetings. It was acknowledged by staff that the situation at the RAH was not right, and had been that way for a long time, yet still perpetuated without change.
109. By contrast, FMC seemingly had very good systems, processes, a coordinated team and a patient-centred care approach which was articulated by all levels of staff and clearly linked to the National Safety and Quality Health Service Standards for Governance and Partnering with Consumers.

Appropriateness of recommendations made by CALHN and SA Pathology in relation to said local investigation, including progress in actioning these recommendations

Protocols be reviewed for accuracy

110. It was recommended that all current haematology protocols be reviewed for accuracy by a designated second clinician and pharmacist not involved in authoring them.
111. While this was an appropriate recommendation, the serendipitous discovery of a similar dosing error in an RAH protocol in September 2015 clearly shows this has not been completed appropriately.
112. It is of great concern that the protocol had not been reviewed since its development in 2005. Of greater concern is that the fact the protocol had been supposedly reviewed in July 2015, however was awaiting formal presentation at a protocol meeting and ratification prior to being uploaded on the Haematology intranet protocol database. If a transcription error was identified in a protocol it should have been immediately escalated for action.

113. The review panel considers this a source for considerable concern about the governance of the unit and its commitment to safe high quality care.

Recommendations for additional chemotherapy to be provided by clinical leads

114. It was recommended that formal evidence based (where possible) recommendations concerning the proposed additional chemotherapy to be administered to involved patients be provided by the clinical leads in AML therapy in South Australia with the potential to receive such advice from third party expert (whether national or international).
115. The review panel was informed that discussions had occurred amongst South Australia's principle adult AML clinicians about how to manage the ongoing treatment of the affected patients, and recommendations had been made.
116. However the panel has no documentation to support that these were formal evidence based recommendations or that any advice had been requested from a third party expert.
117. It is of concern to the panel that there was a delay of three to four weeks before the additional treatment options were offered. This appears to fall short of a reasonable standard of care.

Haematology protocol database be reviewed

118. It was recommended that the governance of the Haematology protocol database be reviewed with a view to establishing policies and procedures that minimise the risk of an "incorrect protocol" being published.
119. The review panel was not provided any documentation that confirms this recommendation has been actioned.
120. While the project officer developed a document entitled "Reviewing and Publishing Haematology Unit Protocol" this could not be taken as proof that an actual review of governance had taken place.
121. When asked to provide minutes of protocol meeting held to discuss and approve the use of a protocol none could be supplied.
122. The review panel is also of the opinion that the review of governance needs to be a lot wider than just that of the database.

Formal training on incident reporting and open disclosure

123. It was recommended that all Haematology and Oncology Medical Officers undergo formal training concerning the importance of incident reporting and open disclosure.
124. While an appropriate recommendation it is apparent it has not occurred. The Panel was advised that when a special session was organized to provide training in incident management and the use of SLS, only three staff participated.

125. While the review panel has no evidence that formal recommendations were made by FMC, the panel were advised that as soon as FMC became aware there was an error in the protocol they undertook to recheck all their protocols.
126. In addition, FMC has extended its process for the development, review and publication of its own protocols to encompass protocols developed by other LHNs thereby ensuring the accuracy of the protocol is not just assumed in future. A copy of the comprehensive document was supplied to the panel.

Recommendations on findings to assist in mitigating the risk of reoccurrence and respond to breaches of compliance

Recommendation 1:

That in view of the serious clinical governance failing identified by this review:

- failure to follow accepted practice whilst implementing a new non-standard clinical protocol;
- failure to seek and to be granted the approval of the relevant committee in relation to the introduction of a non-standard protocol;
- failure to report and lodge the incidents in the SA Health incident management system;
- failure to conduct timely and appropriate open disclosure with patients; and
- failure to provide an immediate clinical response to patients who had been under dosed, the Chief Executive Officer of the Central Adelaide Local Health Network gives consideration to referring relevant clinicians to the Australian Health Practitioner Regulation Agency for review.

Recommendation 2: That the Chief Executive Officer Central Adelaide Local Health Network ensures staff fully understand their responsibility to act in accordance with SA Health policies, particularly the incident management and open disclosure policies. That effort is made to ensure that the requirement to report all incidents into the Safety Learning System is clear and that open disclosure and incident management training is made available to all staff, including all medical staff.

Recommendation 3: That the Chief Executive Officer Central Adelaide Local Health Network implement a rectification plan to ensure that the appropriate governance frameworks are in place within SA Pathology and, in particular, the haematology service provided to the Royal Adelaide Hospital. That this plan takes into consideration the recommendations made in the report "Governance of Clinical Services Conducted by SA Pathology Clinical Staff: A Review" Peter Brennan, Jeff Szer, June 2012 and the National Safety and Quality Health Service Standards related to Governance, Partnering with Consumers and the provision of patient centred care.

Recommendation 4: That the Chief Executive Officer Central Adelaide Local Health Network ensures appropriate processes and procedures for the development, review and publication and, where indicated, revision of chemotherapy protocols are developed and implemented consistent with the current evidence base. And that the resulting policies, procedures and protocols are understood and acknowledged by all relevant staff, are consistent with SA Health policies and procedures and are appropriately filed and stored.