

# **Review of serious failures in reported test results for prostate- specific antigen (PSA) testing of patients by SA Pathology**

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## **Review Panel**

Associate Professor Ken Sikaris, Chemical Pathologist, Melbourne Pathology

Mr Kieran Pehm, former Health Care Complaints Commissioner NSW

Mr Michael Wallace, Chief Operating Officer

Australian Commission on Safety and Quality in Health Care

Adjunct Professor Debora Picone AM, Chief Executive Officer

Australian Commission on Safety and Quality in Health Care

Professor Mark Frydenberg AM, President

Urological Society of Australia and New Zealand

# Executive Summary

## *Defective PSA results*

1. From March 2015, SA Pathology began reporting levels of prostate-specific antigen (PSA) in patients at low levels following requests from urologists who found the results useful in monitoring their patients who had their prostates removed – men without a prostate gland should have no detectable PSA. The presence of PSA, even at low levels, may indicate the need for further treatment.
2. From 7 November 2015 the assay lots used by SA Pathology to detect PSA were inaccurate between the ranges of 0.03 – 0.08 micrograms per litre (ug/L) with a positive bias of 0.03 ug/L. Consequently, the PSA results for patients reported from this date, within this range, showed detectable PSA levels where PSA was undetectable, and higher levels of PSA where there were low detectable levels. From 17 March 2016 SA Pathology reported tests on two different methods simultaneously.
3. SA Pathology failed to act on the inaccurate PSA results despite technical warnings generated by their laboratory systems. One potential warning was inadvertently switched off and another was noted without its potential to detect the error being realised.
4. SA Pathology did not become aware of the inaccurate results it was producing until a complaint from a urologist at the end of January 2016. The complaint was wrongly classified with a low level of severity and, although SA Pathology did take the appropriate action to determine the cause of the inaccurate readings, that action was slow and not consistent with the urgency of the situation.
5. Complaints continued to be made to SA Pathology about PSA results through February and March 2016. SA Pathology determined to discontinue the defective test from six months after dual reporting was introduced. Until then SA Pathology continued to report the inaccurate results to clinicians. On 18 March 2016 SA Pathology wrote to all urologists explaining the problem with the test and the move to a new test, and placed a notice on the SA Pathology website. The public notice was framed as a routine notice without sufficient explanation to be considered as adequate notification to the public.
6. SA Pathology's complaint handling, open disclosure, governance and accountability systems during this period were totally inadequate.
7. Following media exposure of the issue in early April 2016, significant and appropriate action was taken by SA Pathology. A "lookback" process was commenced to identify the number of patients affected by the inaccurate tests. The scope of the lookback was expanded following advice from the Commission. The review team is satisfied with the process to determine the number of affected patients. Although action has been taken to contact the treating clinicians of the patients, the review recommends that

SA Pathology make a public apology to the affected patients.

#### *Management of SA Pathology*

8. The review found the management structure of SA Pathology did not provide for sufficient clinical supervision of, and accountability for, laboratory process. The review was briefed regarding a separate management review of SA Pathology which considered SA Pathology's structure dysfunctional and different from contemporary management structures in place in pathology laboratories throughout Australia.

#### *The PSA tests*

9. The review's expert chemical pathologist analysed data from SA Pathology and determined that the test kits in question were inaccurate at levels of 0.03 – 0.08 ug/L. As these kits were distributed to a number of laboratories in Australia, the review has provided its expert advice to the manufacturer and the Therapeutic Goods Administration.

## **Major findings**

10. SA Pathology's internal quality assurance processes were inadequate. SA Pathology failed to act on technical warnings from the laboratory system that the tests were inaccurate in low level PSA test results from assay kits in use from 7 November 2015. No action was taken until a complaint from a urologist in late January 2016.
11. The complaint was not given the appropriate level of attention and SA Pathology's investigations were slow. When SA Pathology did finally determine that the problem resulted from the test kits it was using, its action to notify affected users was totally inadequate and failed to appreciate the anxiety and distress of the inaccurate results on those patients who received the results.
12. When the issue received public attention, appropriate action was, and has since been taken, to identify the patients affected and notify their treating clinicians.
13. Management, governance and accountability so SA Pathology was seriously deficient and the review agrees with the findings and proposals of a separate management review recommending a restructure to bring SA Pathology in line with management practices in place at comparable Australian providers.

## Recommendations

14. The terms of reference for this review ask it to “advise on improvements required relating to clinical governance systems and processes, incident management, professional standards and accountability within SA Pathology”. This incident reflects a number of significant clinical governance failings by the then senior management of SA Pathology.

### **Recommendation 1:** Formal apology and implementation of lessons learnt

That SA Pathology issue a public apology for distress and anxiety experienced by the patients because of the inaccurate PSA testing, and provide regular updates to the community on the implementation of lessons learnt from the incident and the new measures introduced to assure the quality control of clinical testing in SA Pathology laboratories.

### **Recommendation 2:** New management structure for SA Pathology

The Programme Director of South Australia Statewide Clinical Support Services engage an appropriately qualified and experienced person to implement an organisation structure for SA Pathology that: aligns appropriately skilled staff placement with the operational needs of the service; provides adequate clinical expertise to monitor and inform the production of results; clearly defines the responsibilities and accountabilities of staff; and ensures the requirements of referring clinicians are reflected in the work rules of the service.

**Recommendation 3:** Immediately ensure appropriate pre-analytical, analytical and post-analytical quality control procedures are operational within SA Pathology which meet national standards and are reinforced and regularly audited

It is the role and responsibility of the senior management of a pathology service to see that policies, procedures and practices are in place that ensure staff understand the quality control system in use, and that staff understand their role in relation to quality control including reporting requirements. This review recommends that an immediate review is undertaken to ensure appropriate quality control procedures are operational within SA Pathology and staff are regularly assessed to ensure their understanding and compliance with quality control procedures.

### **Recommendation 4:** National Accreditation

To confirm that SA Pathology meets national laboratory standards, the service, as soon as practical, seeks independent assurance of technical competence through accreditation by the National Association of Testing Authorities.

**Recommendation 5:** SA Pathology ensures that the Safety Learning System is fully implemented and that all incidents are logged in the Safety Learning System. Clinical staff are trained in open disclosure.

SA Pathology should cease using Q-Pulse as its exclusive incident reporting system and fully implement the state wide Safety Learning System (SLS) together with a program that ensures that staff understand how the system operates and the mandatory reporting requirements when clinical incidents are identified. SA Pathology should also review its open disclosure policy and how it will operate in the event of incidents involving patient results. SA Pathology should ensure that its systems allow for all relevant information to be provided to treating clinicians who will conduct the appropriate discussion with the patient.

## Scope and Method of the Review

15. The Chief Executive Officer of the Central Adelaide Local Health Network (CALHN) appointed the Australian Commission on Safety and Quality in Health Care (the Commission) to undertake an independent review of serious failures in reported test results for prostate-specific antigen (PSA) testing of patients by the South Australian Pathology Service (SA Pathology). The review inquired into the reasons for falsely elevated PSA screening test results and the effectiveness of subsequent investigations, mitigation responses, reporting and disclosure of the error to patients, clinicians and relevant authorities.
16. The review was also asked to investigate a further incident where patients were issued with reports containing accurate PSA test results but with inaccurate accompanying comments as to the further action advised.
17. The full Terms of Reference of review are appended at Attachment A.
18. The review was conducted as follows:
  - A Relevant documents including emails** were sourced from CALHN related to the Terms of Reference for the Inquiry. The review relied on the provision of these documents, rather than conducting its own search for all documents and communications related to the incident.
  - B** The review undertook significant work to coherently assemble these documents and forensically assess their value including analysis of automated chemical pathology results spanning the period in question by Australia's leading PSA expert chemical pathologist and advice from the review's expert urologist.
  - C Written questions** were compiled and provided to relevant current and former staff of SA Pathology.
  - D Interviews** were conducted with key current and former staff as well as a urologist affected by the error and a representative of the Health Consumer's Alliance of SA.
  - E Further analysis of PSA results** was undertaken by the review's expert chemical pathologist on a more extensive set of test data resulting in further advice to SA Health, and inquiries with both the manufacturer of the PSA tests used by SA Pathology and the Therapeutic Goods Administration.
19. A draft report was compiled and provided to relevant persons for comment to ensure the accuracy of the facts relied upon.

## Major Findings

### SA Pathology provides low level PSA testing

20. From around 2012 the Clinical Director of Chemical Pathology received requests from urologists for the testing and reporting of low levels of PSA in post radical prostatectomy patients. In such patients, assuming complete removal of the prostate gland, PSA levels should be undetectable and the presence of PSA, even at very low levels (which would not concern any man with a prostate gland), is useful in detecting residual prostatic tissue and early recurrence of tumor. Therefore, serial PSA levels can help determine the success of a prostatectomy, and the need for further treatment and monitoring of the effectiveness of therapy.
21. The Urological Society of Australia and New Zealand follows the European guidelines for patients in this situation. These guidelines say that further treatment may be indicated where a patient, after a radical prostatectomy, has a test showing a PSA level of 0.2 micrograms per litre (ug/L) or greater with a repeat test recommended. The review's expert urologist noted, however, that the issue of further treatment at PSA levels less than 0.2 ug/L was controversial. Nevertheless, detectable PSA levels below 0.2 ug/L after a radical prostatectomy reflect a poorer prognosis than undetectable levels and consequently may cause anxiety to the patient. Given the requests of urologists for more accurate testing of PSA at low levels, SA Pathology conducted functional sensitivities of the PSA assay which it was using at the time. Having previously reported PSA levels down to 0.05 ug/L, and on the understanding that the manufacturer validated its assay down to 0.01 ug/L, SA Pathology began reporting PSA levels down to 0.03 ug/L from March 2015.

### Failure to respond to warning signs regarding accuracy of the PSA assay

22. As set out in more detail below, SA Pathology determined that particular PSA kits provided by the manufacturer and in use from November 2015, were associated with a high bias when reporting low levels of PSA. There were a number of quality control warnings during November and December 2015 that should have led to an earlier analysis of assay performance by SA Pathology, and the removal of this assay batch lot from use for this purpose. Due to significant failures of management, poor internal controls and failure of basic laboratory clinical governance procedures this did not occur.
23. The first warning sign was pre-analytical. The specific kits were the subject of a notice by the manufacturer and the Therapeutic Goods Administration on 6 January 2016 (communicated to 14 laboratories in South Australia, New South Wales, Queensland, Victoria, Western Australia and Tasmania). The notice concerned the over-

responsiveness of the PSA assay at a high PSA level (over 90 ug/L). Users were advised to continue using the kits with this understanding in mind. With the benefit of hindsight, it was an incorrect reassurance that the kit(s) had no other major issues. The manufacturers reassurance was based on their release criteria that results were within the +/-15% of expected target values, however their lowest check point was 0.76 ug/L and not near their stated lower analytical reporting limit of 0.01 ug/L.

24. The second warning sign was analytical. An analytical quality control sample with an expected result is routinely run in all laboratories, for every assay, a few times a day. Various rules are applied to such quality control samples including alarms to cease testing (e.g. if the result is outside three standard deviations of the expected result). There are also warnings rules such as when 10 results in succession are below the central target value (10x rule) or when four results in succession are more than one standard deviation away from the target value (41s rule). With regard to the lowest PSA quality control material (with a level of 0.76 ug/L), the 10x and 41s rules were functional in July 2015 and led to the rejection of unreliable analyses. From October 2015 onwards, the 10x rule was no longer functioning (due to an error in programming) and, while the 41s rule was functioning, its reports were accepted despite the repeated warnings. The SA Pathology laboratory was therefore operating outside its stated quality policy regarding Westgard rules which was not brought to the attention of the supervising pathologist.
25. The third warning sign was post-analytical. After accepting the results of analysis, abnormal results in particular are typically 'clinically validated' to ensure that they are clinically reasonable and not pre-analytical or analytical errors. Undetectable PSA levels (<0.03 ug/L) were seen about 30 times a week before 6 November 2015 and only about 3 times a week after 6 November 2015. Furthermore, the number of patients experiencing a shift from undetectable (<0.03 ug/L) to detectable (>=0.03 ug/L) went from 42% of patients with previously undetectable levels repeated before 6 November 2015 to 90% of patients with previously undetectable PSA levels repeated after 6 November 2015. This significant shift in reporting was not detected during clinical validation and there was no routine pathologist validation process in place for this test.

## **The first complaint concerning a patient and the response**

26. On 27 January 2016 SA Pathology received a call from a urologist about a PSA test for his patient that occurred on 27 November 2015. Concerned by the result from SA Pathology, the urologist had recommended a further PSA test from a private provider and that second test had detected no PSA in the patient. The urologist was concerned that, on the basis of the first SA Pathology test, the patient thought his cancer had relapsed and had become very upset.

27. The urologist told the review that when he called SA Pathology he spoke to a scientist who appeared to have no understanding of the clinical implications of the inaccurate low level tests. About three to four weeks later he had another patient with an unexpected test showing a low PSA level. This time the urologist called the Clinical Director of Chemical Pathology who informed him that SA Pathology was aware of the problem and was taking some action. The urologist remained unconvinced that the clinical implications of the inaccurate tests were appreciated by SA Pathology and discussed the issue with other urologists.
28. The urologist's telephone complaint of 27 January 2016 was logged by a scientist at SA Pathology. The Clinical Director of Chemical Pathology told the review that she wasn't sure that the problem was any wider than the single test but carried out functional sensitivity tests on the assay in use for January 2016, conceding that in hindsight, they should have gone further back. SA Pathology also sent some samples to a private laboratory as a cross check but given the laboratory also used the same PSA kit, its results were the same as SA Pathology's. On 5 February 2016, SA Pathology looked further back into its results and established that a new lot of the assay had commenced in November 2015. SA Pathology notified the PSA test manufacturer as well as conducting further testing and analysis itself. By 17 February 2016, SA Pathology had determined that the cause of the inaccurate results at low PSA levels were two assay lots: the first of which had commenced on 7 November 2015.
29. From the end of January through February 2016, SA Pathology received phone calls from concerned urologists and patients who had received the inaccurate tests. None of these calls were separately documented and therefore cannot be quantified, or the level of concern expressed by clinicians and the impact on patients assessed. The initial telephone complaint from the urologist that was received on 27 January 2016 was recorded on SA Pathology's Q-Pulse system as an Opportunity for Improvement (OFI) and given a Severity Assessment Code (SAC) of 4: Low. This is the lowest available severity rating and which the relevant policy says should be managed "using routine procedures". No incident report was made in the SA Health state wide Safety Learning System as required by the procedure. Even if such a report was made, however, the low SAC rating which was assigned would not have prompted any more senior or external review. SA Pathology had been using Q-Pulse for two years before the introduction of SA Health's Safety Learning System and preferred Q-Pulse's functionality. When interviewed, the Clinical Director recognised that she should have escalated the SAC level as complaints accumulated and the cause of the inaccurate results was determined.

30. Towards the end of February 2016, having satisfied herself that the assays demonstrated a high bias at low levels of PSA testing, the Clinical Director of Chemical Pathology decided to move to dual testing and reporting of samples using both the original manufacturer and an alternative manufacturer of the PSA tests. This required the approval of the Pathology Operations Group (POG), which was chaired by the Chief Scientist of SA Pathology.
31. There was some urgency to the issue by this time and although the POG was not due to meet until April 2016, it was convened “out of session” at the end of February. It considered a completed standard form titled “Application for Changes to Test Services” dated 24 February 2016 which identified the “problem with low end sensitivity [of the existing test]. Consequently, there is a high risk of patient misdiagnosis”. An attachment to the application noted that the application was “as a result of customer complaint”. The POG approved the application to move to dual testing on both platforms on 1 March 2016.
32. Although the POG met out of session the Chair, SA Pathology’s Chief Scientist, said the application did not raise any wider concerns at the time and was relatively routine.

## **The second formal patient complaint**

33. On 3 March 2016, a patient contacted the Executive Director, SA Pathology and senior management via an email titled “Being on ‘Death Row’ for 30 days” which explained his anxiety on receiving an inaccurate SA Pathology test, that his cancer may have returned, until a subsequent test with a private provider showed a negligible PSA level. He said that his urologist told him that he had raised the problem with SA Pathology and thought the test they were using was unreliable.
34. The former Executive Director of SA Pathology stated that he became aware of this issue on 3 March 2016. Although one staff member told the review during interview that he had advised the Executive Director at an earlier time, it was advice which, if given, appears not to have registered with the former Executive Director as a significant matter. The former Executive Director sought advice about the “Death Row” email the day he received it and was emailed by the Clinical Director of Chemical Pathology advising of the problems with the PSA tests at low levels and the move to dual testing which had just commenced. He was also advised that the Clinical Director of Chemical Pathology had telephoned the complainant and advised him of the action that was being taken.
35. The Executive Director also asked why the issue hadn’t been brought up through clinical governance procedures. He was advised that an OFI had been opened (on the original telephone complaint from the urologist) and that it had been closed on 1 March 2016 as all appropriate action had been taken.

## **Failure by SA Pathology to notify the community of the problem**

36. Following the POG's approval of dual testing of PSA on both the new and original platforms on 1 March 2016, a meeting was convened to discuss the "communication strategy" on 3 March 2016. The action that resulted was a letter to all South Australian urologists notifying them of the inaccuracy of previous PSA tests at low levels and a notice was placed on the SA Pathology website. The letter, which was finally sent on 18 March 2016, explained the situation reasonably well. The website notice, titled "Pathology Brief", posted in March 2016, innocuously frames the dual testing as part of the "continuous quality improvement program" of SA Pathology with no mention of the incidents that gave rise to the discovery of the error and next to no emphasis on the inaccurate tests previously received by clinicians and patients, the anxiety that was caused or any apology.
37. The letter that SA Pathology sent to urologists on 18 March 2016 had a predictable outcome. The urologists concerned discussed it with their patients and at least one patient approached the Adelaide Advertiser. From 24 March 2016, SA Pathology and SA Health began receiving calls from the newspaper. The newspaper went public with the story on 4 April 2016.

## **Failure of governance – internal quality control, investigation and mitigation results in patients being provided with falsely elevated PSA test results**

38. The failure of SA Pathology to properly monitor and respond to the alerts from its automated testing, which repeatedly reported clinically significant inaccuracies at low levels of PSA, resulted in falsely elevated results being provided to patients and their clinicians. The assay batches should have been removed from use for this purpose. The urologist who made the first complaint at the end of January 2016, believed that the person taking the complaint did not appreciate the clinical significance of inaccurate low level PSA. Within SA Pathology, action to investigate the problem did occur, although there appears to have been little sense of urgency or appreciation of the impact on patients of receiving the inaccurate test results.
39. Testing of the assays used continued through February 2016, while concern was mounting among urologists and their patients who were calling SA Pathology to express that concern. These calls were not formally treated as complaints, as they should have been, and consequently there were no entries in Q-Pulse and the Safety Learning System.
40. The classification of the first complaint with a severity assessment code of 4 was inconsistent with the serious nature of the issue and the potential number of patients affected. The low classification also had the result that more senior staff in both SA Pathology and SA Health were not notified and did not have the opportunity to

consider how it should be managed.

41. When the proposed solution for the problem was put to the Pathology Operations Group at the end of February, it was not put in a manner that properly conveyed the widespread nature of the issue being the number of patients potentially affected or the impact upon them. Nevertheless, the brief to the POG did note that there was a “high risk of patient misdiagnosis” but this did not prompt any inquiry from POG members, some of the most senior clinicians and staff in SA Pathology, as to the extent of the potential impact on patients.
42. The former Executive Director claims he became aware of the issue after an email complaint directly to him. After receiving briefings on what had been done to address the issue, he was satisfied with the advice he was given that no further action was required. This was a totally inadequate response to a very serious problem affecting hundreds of patients.
43. The letter advising urologists of the issue was sent on 18 March 2016, a month after SA Pathology became convinced that the PSA test it was using was inaccurate at low levels. The notice put on its website conveyed no impression that patients might have been adversely affected and was presented as a routine quality improvement.
44. It appears that there was little understanding within SA Pathology of the clinical use to which the low level tests could be put and little appreciation of potential harm to patients. There is no record of any urological advice being sought by SA Pathology at this stage.
45. Following public exposure of the issue a more systematic attempt was made to establish the patients potentially affected and to notify their treating clinicians. This should have occurred at a much earlier stage. As well as conducting a thorough “lookback” to identify affected patients, more immediate action should have been considered, such as specific advice that the result was not reliable being provided to clinicians with test results from the time the low level inaccuracy of PSA results was suspected.
46. Despite being satisfied that two lots of assay used by SA Pathology for PSA testing from 7 November 2015 to 3 March 2016 had clinically significant inaccuracies at low levels, SA Pathology did not notify the Therapeutic Goods Administration or the National Association of Testing Authorities until after the media became interested.
47. The above course of events demonstrates serious deficiencies in the governance of SA Pathology by the former Executive Director. The clinical significance of the inaccurate low level PSA readings was not appreciated and action to investigate the cause was not pursued with any sense of urgency. As more complaints came in through February and March, the appropriate action was taken to move to a more accurate testing platform although the pace was slow. The response in terms of clinical

governance, however, was dismal. The severity of the problem was underrated resulting in no senior level notification and investigation as required by policies. There was no attempt to identify affected patients and no attempt to develop a comprehensive plan to notify them despite the knowledge that the inaccurate tests result could lead to misdiagnoses and unnecessary treatment.

48. During the review it became apparent that the structure of the organisation did not provide sufficient clinical input and management accountability at appropriate levels, and quality assurance procedures were not sufficient to identify emerging issues and problems and ensure the appropriate management. The review will return to these broader issues later in the report.

### **The patients and medical clinicians are notified through a “lookback” process**

49. Following the media report of 4 April 2016, the matter received wider attention. SA Pathology was contacted by the Therapeutic Goods Administration and the National Association of Testing Authorities, and SA Health advised receiving numerous calls from concerned patients. Urgent meetings were held to develop a response and to ensure a thorough internal review was undertaken. The issue was reported in the Safety Learning System with a SAC 1 rating on 7 April 2016.
50. Throughout April 2016, SA Pathology searched its databases to identify patients affected, fielded calls from concerned patients and clinicians, directly contacted urologists, contacted radiation oncologists, radiation providers and other clinicians who had referred patients for PSA tests during the period 7 November 2015 to 31 March 2016.
51. A Steering Committee was established to conduct a lookback and determine how many patients had received the inaccurate test results and, as a consequence, were at risk of further treatment. The group included a senior urologist and a consumer representative. The review team spoke with the consumer representative who articulated the concerns of post-prostatectomy patients.
52. A comprehensive lookback was undertaken to identify patients who had two PSA tests results greater than 0.03 ug/L in biased period and one undetectable test in the 12 months prior to 31 March 2016. In addition, treating clinicians of patients were contacted by telephone which identified one affected patient not captured by the search parameters. This process produced a group of 52 patients each of whose clinical history was ascertained to determine what role, if any the biased PSA results may have played in their treatment.

53. Of these patients, there was one who underwent further radiation treatment following consideration of two biased PSA test results which was not clinically justified. The treatment was ceased as soon as the patient's urologist was notified of the biased results. The patient has been offered support by the CALHN.
54. The Chair of the Steering Committee reported that six patients had further management, although their urologists confirmed that there were other clinical indications for that management and the Committee concluded that the management was justified on clinical grounds independently of the PSA test results. The rest of the identified group had further tests undertaken which did not detect PSA and consequently no further treatment.
55. To ensure completeness of the lookback the Steering Committee resolved to expand the parameters of its search.
56. The review team is satisfied that the lookback was thorough and comprehensive using an iterative approach to ensure sufficient review of affected and potentially affected patients.
57. SA Health is able to provide the full details of the lookback process.

## **Open disclosure**

58. Open disclosure requires disclosure of an error to a person affected, an explanation of why the error occurred, an apology for the error and the provision of assistance in dealing with its consequences. The issue of whether SA Pathology should contact patients directly about their inaccurate PSA tests arose once the error was discovered.
59. SA Pathology had no direct relationship with the patients submitting for PSA tests. The relationship was with the patient's treating clinicians, who had referred the patient for the tests. Direct patient contact from SA Pathology in these circumstances would have more likely heightened anxiety and aggravation for patients than assuaged it. Advice about the error would be much more effectively communicated by the patients' treating clinicians who, unlike SA Pathology, would be aware of the patients' overall clinical condition and be in a position to competently advise them of the impact of the inaccurate test(s) in that context.
60. Having considered all the circumstances, the approach to communicate the error in the test(s) to treating clinicians, rather than directly to patients was the correct approach and complied with the principles of open disclosure. As SA Pathology had no direct contact with patients, however, it has not had the opportunity to offer an apology to them for the error. Although somewhat belated, the review recommends that an apology should now be offered.

## **PSA results communicated with incorrect comments**

61. A further issue made part of the terms of reference of the review concerned the communication by SA Pathology of incorrect comments with reports of correct PSA results.
62. This problem arose as part of SA Pathology's dual reporting of PSA results. Once the dual reporting became the standard for SA Pathology, the computer generated reports of results had to be amended, which meant that the computer programs underlying the reports had to be re-written.
63. SA Pathology's ICT Manager explained that the applicable computer systems at SA Pathology dated from the 1980s and required extensive manual reprogramming. In anticipation of the new reporting system, a program was developed in a test environment to generate the new reports. Before the system went into use, however, the quality assurance processes failed to pick up that the standard comments, for example "test again in 12 months" or "test again in 6 months", depending on the PSA result, were generated with the right result. Consequently, 68 reports were generated and sent to referring clinicians before the error was identified. Fortunately, the reports were being sent to experienced clinicians who quickly identified the incorrect comments which made no difference to the patients' actual treatment.
64. The first level of quality assurance within SA Pathology was from IT staff who ticked off the changes which included the incorrect comments. The second level of approval was by laboratory staff, who also approved the changes. This was done despite no clinical expertise to judge the relevance of the comments to the correctly reported PSA level.
65. SA Pathology advised that it was introducing a new risk assessment process for IT changes that would involve more extensive testing and quality assurance processes in future, including clinical sign off.

## **General Management of SA Pathology**

66. It became apparent to the review as it progressed that SA Pathology has serious management issues. The handling of what was a potentially very serious issue with inaccurate PSA testing was initially contained at relatively low levels of the organisation and underestimated. Although senior management confirmed their receptiveness to problems, there was a notable lack of systems and effective quality control processes to identify problems and communicate them to senior levels where the importance of the problem could be evaluated and appropriate responses developed. Regular quality assurance processes occurred at levels where the clinical expertise necessary to evaluate the impact of issues was not available.

67. Most significantly there was an ill-defined reporting relationship between the technical staff and the clinical pathologists and scientists where the latter carried no direct accountability and responsibility, contributing to a lack of clinical expertise available when interpreting test results and examining the impact of quality assurance issues.
68. On this issue, the review was fortunate in that SA Pathology was undergoing a management review when the review team was in Adelaide conducting interviews. The person conducting the management review has enormous experience in the management and service delivery of pathology services. He spoke to the review and agreed with its concerns about the management and structure of SA Pathology. The management structure of SA Pathology is dysfunctional and purportedly differs from contemporary management structures in place in pathology laboratories throughout Australia. He has provided a report to the Chief Executive of SA Health which proposes substantial reform of the management structure of SA Pathology and which addresses the issues identified by this review.

## **The original PSA tests**

69. SA Pathology advised the manufacturer of inaccurate low level PSA readings and this advice included relevant data soon after the original complaint. On 5 April 2016, the manufacturer responded to SA Pathology advising that “similar to other commercially-available assays, the [relevant] Assay does not have an intended use for monitoring patients for PSA post-radical prostatectomy.” It further stated that since the assay was performing as designed and intended, the manufacturer would be taking no further action.
70. After the publicity in early April 2016, the Therapeutic Goods Administration was advised by SA Pathology of the problems with the original tests. The Therapeutic Goods Administration advised that it would monitor the situation but take no further action.
71. The Instructions for Use for the original assay say that its “intended use” is “as an aid in the detection of prostate cancer in men aged 50 years and older. This assay is further indicated as an aid in the management (monitoring) of patients with prostate cancer”. Further, in the “Summary and Explanation” section of the Instructions for Use, it says “PSA levels increase in men with cancer of the prostate, and after radical prostatectomy PSA levels routinely fall to the undetectable range. If prostatic tissue remains after surgery or metastasis had occurred, PSA appears to be useful in detecting residual and early recurrence of tumor. Therefore, serial PSA levels can help determine the success of prostatectomy, and the need for further treatment, such as radiation, endocrine or chemotherapy, and in the monitoring of the effectiveness of that therapy.” Further, on page 10, under “performance characteristics – analytical measuring range” the instructions state the assay “measures prostate-specific antigen concentrations from 0.01 – 100 ng/ml (ug/L)” and under “sensitivity” says the assay

“measures total PSA concentrations up to 100 ug/L with a minimum detectable concentration (analytical sensitivity of 0.01 ug/L.”

72. The manufacturer’s letter to SA Pathology that its assay was not intended for monitoring post-prostatectomy patients is inconsistent with the Instructions for Use provided by the manufacturer. Considering the information quoted above from the manufacturer’s Instructions for Use for the assay, the review has no criticism of SA Pathology in using the manufacturer’s test to report low PSA levels until it became aware of the bias in the assay at low levels, and at which time SA Pathology should have discontinued its use.
73. The manufacturer’s PSA tests have been used in a number of pathology laboratories around Australia. An issue with high level PSA results from the same manufacturer’s assay resulted in a warning issued by the Therapeutic Goods Administration in February 2016 to 14 Australian laboratories. The Commission has raised the issue of low end sensitivity in detail with the Therapeutic Goods Administration which is considering the appropriate action on its part.

## **Quality assurance in SA Pathology - failure to meet national standards**

74. Quite apart from manufacturers’ warranties or the view taken by regulators, laboratories retain their own responsibility to produce high quality, accurate results. The ISO 15189 standard for laboratory quality requires that every accredited laboratory: “4.2.5 .... regularly monitors and demonstrates proper calibration and function of instruments, reagents and analytical systems” and that “5.5.3 ...Each new version of examination kits with major changes in reagents or procedure be checked for performance and suitability for intended use”.
75. One of the major quality control tools for analysis is running a sample with a known concentration and ensuring that it is within acceptable limits. Although SA Pathology ran a low level PSA control every day, it failed to pick up the assay bias as (i) the level was not in the ultrasensitive range (<0.1 ug/L) and (ii) even though it did show several faults, the laboratory failed to respond appropriately. It is difficult to criticise SA Pathology for not running quality control in the ultrasensitive range when the review’s expert indicates that almost every other laboratory in the country was running the same non-ultrasensitive low PSA quality control sample >0.2 ug/L. According to the National Association of Testing Authorities’ Field Application Document, the quality control material used must cover the analytical concentrations encountered. Following prostate cancer treatment, low PSA results are frequently monitored and laboratories must run controls to assure this intended clinical use.

76. In regard to bench level scientists ignoring or accidentally disengaging Westgard rules, the supervisors of that service should consider that ISO 15189 states “5.6.1 It is important that the control system provide staff members with clear and easily understood information on which to base technical and medical decisions.” Supervising scientists must be confident in their quality control systems and be able to regularly audit their appropriate functioning. In SA Pathology it does not appear that bench level staff were able to assess the significance of potential warnings being generated by analytical systems, or that the mechanisms existed to bring these to the attention of more senior qualified staff but failed to do so.
77. Medical laboratories are expected to include interpretation services and, in delivering reports, make professional judgements, in this case, with respect to undetectable PSA following radical prostatectomy becoming detectable, indicating the potential recurrence of prostate cancer. In making these judgements, laboratories should have the applicable theoretical and practical background as well as recent experience.
78. It is a significant failure of laboratory internal controls that the positive analytical bias causing concerns regarding prostate cancer recurrence were noted by patients and clinicians before being noted by the laboratory releasing hundreds of these results. The number of undetectable PSA results being released decreased by 90% and the number of patients showing a detectable PSA ( $\geq 0.03$ ) following an undetectable PSA ( $< 0.03$ ) increased from 49% to 89% without anyone in the laboratory noticing the shift, regardless of its clinical implication.
79. Ideally, medically trained staff would check all reports leaving the laboratory, but in reality the volume of reports produced by large core laboratories, together with the other responsibilities of supervising pathologists mean that this is practically impossible. Therefore, systems must be implemented to screen reports for clinical alarms including the application of algorithms by trained staff or computer programs that look for major abnormalities and significant changes. This did not occur in the SA Pathology laboratories.
80. Responsibility to maintain quality in Australia lies with the supervising pathologist as the ‘Approved Pathology Provider’ under a formal agreement with the Health Insurance Commission stating they take personal responsibility for the rendering of services. It is vital that pathologists, the only medically qualified staff in a pathology laboratory, fulfil their bridging role for clinicians by ensuring that pathology services fulfil their clinical objective. This is done by remaining in close contact with both the laboratory and the clinicians which it serves. In discharging these vital obligations a pathologist must be supported by the administrative structure of the laboratory, ideally with each supervising pathologist represented at all senior administration meetings. This was not the case at SA Pathology.

## Recommendations

81. The terms of reference for this review ask it to “advise on improvements required relating to clinical governance systems and processes, incident management, professional standards and accountability within SA Pathology”. This incident reflects a number of significant clinical governance failings by the then senior management of SA Pathology.

### **Recommendation 1:** Formal apology and implementation of lessons learnt

That SA Pathology issue a public apology for distress and anxiety experienced by the patients because of the inaccurate PSA testing, and provide regular updates to the community on the implementation of lessons learnt from the incident and the new measures introduced to assure the quality control of clinical testing in SA Pathology laboratories.

### **Recommendation 2:** New management structure for SA Pathology

The Programme Director of South Australia Statewide Clinical Support Services engage an appropriately qualified and experienced person to implement an organisation structure for SA Pathology that: aligns appropriately skilled staff placement with the operational needs of the service; provides adequate clinical expertise to monitor and inform the production of results; clearly defines the responsibilities and accountabilities of staff; and ensures the requirements of referring clinicians are reflected in the work rules of the service.

**Recommendation 3:** Immediately ensure appropriate pre-analytical, analytical and post-analytical quality control procedures are operational within SA Pathology which meet national standards and are reinforced and regularly audited

It is the role and responsibility of the senior management of a pathology service to see that policies, procedures and practices are in place that ensure staff understand the quality control system in use, and that staff understand their role in relation to quality control including reporting requirements. This review recommends that an immediate review is undertaken to ensure appropriate quality control procedures are operational within SA Pathology and staff are regularly assessed to ensure their understanding and compliance with quality control procedures.

### **Recommendation 4:** National Accreditation

To confirm that SA Pathology meets national laboratory standards, the service, as soon as practical, seeks independent assurance of technical competence through accreditation by the National Association of Testing Authorities.

**Recommendation 5:** SA Pathology ensures that the Safety Learning System is fully implemented and that all incidents are logged in the Safety Learning System. Clinical staff are trained in open disclosure.

SA Pathology should cease using Q-Pulse as its exclusive incident reporting system and fully implement the state wide Safety Learning System (SLS) together with a program that ensures that staff understand how the system operates and the mandatory reporting requirements when clinical incidents are identified. SA Pathology should also review its open disclosure policy and how it will operate in the event of incidents involving patient results. SA Pathology should ensure that its systems allow for all relevant information to be provided to treating clinicians who will conduct the appropriate discussion with the patient.

**Central Adelaide Local Health Network**

**Independent Review into Prostate-Specific Antigen (PSA) testing of patients**

**Terms of Reference**

**1. Purpose;**

The Australian Commission on Safety and Quality in Health Care has been appointed to undertake an independent review of serious failures in reported test results for Prostate-Specific Antigen (PSA) testing of patients by the South Australian Pathology Service.

The review will investigate and report on:

- the reasons for falsely elevated PSA screening test results;
- the reasons for a further incident where patients were issued inaccurate written advice in relation to PSA screening test results; and
- the effectiveness of the subsequent investigations, mitigation responses, reporting and open disclosure of the incident to patients, referring clinicians and relevant authorities.

The review will identify the causes of the incidents, the response by South Australia Pathology and Central Adelaide Local Health Network, and advise on improvements required relating to clinical governance systems and processes, incident management, professional standards and accountability within South Australia Pathology.

**2. Scope**

The review will include but not be limited to:

- the technical aspects of the testing concerns
- when and how the incidents emerged
- the effectiveness of management action taken by SA Pathology to address the concerns
- the governance processes surrounding changes to equipment and automatically generated reports
- incident reporting
- the look back review
- adherence to policies and procedures
- information, communication and open disclosure to patients and referrers
- mitigation strategies employed and required to ensure testing and reporting are accurate

**3. Conduct**

- The Chief Executive SA Health will sponsor the review with the review team providing a report to the Chief Executive Officer of Central Adelaide Local Health Network (CALHN).
- The review team will comprise external health professionals with expertise in effective leadership, governance, and safety and quality. Other expertise may be co-opted as required.

#### **4. Review Team**

Skills required of the review team

- Review coordinator
- Senior Clinical Pathologist
- Senior Consultant Urologist
- Chief Executive Officer
- Expert in open disclosure and complaints management

#### **5. Methodology**

Information will be provided through:

- a) Meetings and interviews with key stakeholders
- b) Observation
- c) A call for papers and review of all materials relating to the incidents

#### **6. Stakeholders**

Stakeholders to be involved to include but not be limited to

- Patients and consumers
- Referring clinicians
- SA Pathology staff
- Previous Executive Director SA Pathology
- DHA Director Safety and Quality
- Group Director State-wide services
- Central Adelaide LHN Executive Team
- Chief Executive Officer, Central Adelaide LHN
- Chief Executive, SA Health

#### **7. Review Report**

A Review Report will document the findings and make recommendations to support continual improvement as described in 1. Urgent actions required will be identified as the review progresses and incorporated in the report with timeframes for completing other recommendations nominated for 3 months, 6 months and 12 months.

#### **8. Review Timeframe**

The Review will begin by 18 April 2016 with the report expected to be produced within 3 months subject to the review process itself.