

DEVELOPMENT OF MEDICAL COUNTERMEASURE PRODUCTS IN AUSTRALIA: COULD PHARMACOMETRICS ADDRESS CAPABILITY AND CAPACITY GAPS?

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BACKGROUND

- Medical countermeasure (MCM) products are defined as diagnostics, vaccines and therapeutics for the protection of military and civilian personnel against chemical, biological and radiological (CBR) threats, emerging infectious diseases, and pandemics.
- Increasing on-shore capability in MCM product development is a priority for Australia.
- Australia has a small but experienced drug discovery and development community (Lester & Rayner, 2013).
- Pharmacometrics is the application of modelling and simulation (M&S) to inform product development and/or clinical decisions. The use of pharmacometric approaches has increased dramatically in drug development over the last 10 years.
- The main pharmacometric approaches include population pharmacokinetic (PK) +/- pharmacodynamic (PD) M&S, physiologically-based PK +/- PD M&S, and clinical trial M&S.
- Pharmacometric approaches have the potential to accelerate MCM product development.

OBJECTIVES

- To understand Australia's MCM product development capability and capacity.
- To identify new opportunities in the Australian MCM product development ecosystem for pharmacometrics.

METHODS

National capability audit (NCA) electronic survey

- In phase 1 of the NCA, an electronic survey of 145 questions based on the US Health and Human Services Broad Based Capabilities (BBC) Tool was opened to the Australian academic, industry, research institute, and government sectors.
- Invitations were sent to 454 individuals and broadcast via social media platforms. The survey was open from 22 MAR 2017 to 29 APR 2017 (38 days).
- The MCM capabilities assessed were: 1) manufacturing infrastructure 2) containment infrastructure 3) storage 4) research 5) evaluation and 6) commercial contracts. Capabilities were ranked as primary, secondary and emerging.
- Survey results were analysed using descriptive statistics.

NCA face to face interviews

- In phase 2 of the NCA, 30-min structured interviews were conducted to validate the findings of the electronic survey and to ascertain further details about capability and capacity.
- Technology readiness level (TRL)-guided 'impressions' of capability and capacity were established, de-identified, and presented using heat maps (individual) and summarized at an aggregate level (national).

Opportunities for pharmacometrics

- Results of the NCA were analyzed to identify gaps in the Australian MCM product development ecosystem that may benefit from pharmacometrics.

Bubbles = number of primary, secondary and emerging MCM capabilities in given areas

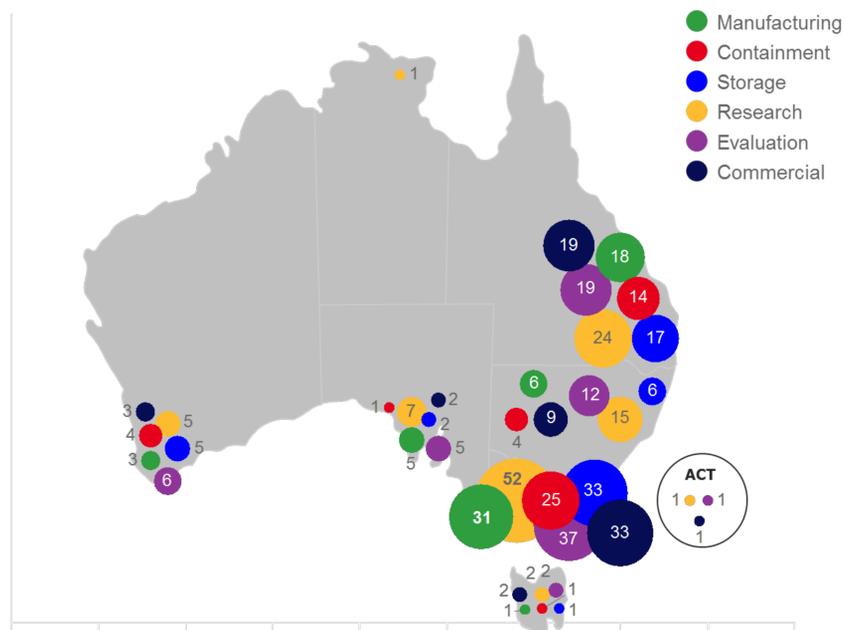


Figure 1 Geographic distribution of Australian MCM product development capabilities.



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RESULTS

NCA electronic survey

- There were 131 completed surveys. Most respondents were based on the east coast of Australia in Victoria, New South Wales and Queensland (87%). Thirty-nine percent were businesses, 37% were universities, 19% were research institutes, and 5% were government departments.
- Figure 1 shows the number of respondents with primary, secondary and emerging MCM capabilities.
- Two-thirds of respondents identified their primary and secondary positions on the MCM product development value chain as 'translational research/pre-clinical research'. The greatest concentration of activity was at TRL4 and earlier. Late-phase capabilities (i.e., clinical development and manufacturing) were weaker, and very few respondents identified market access as their primary position (5/131).

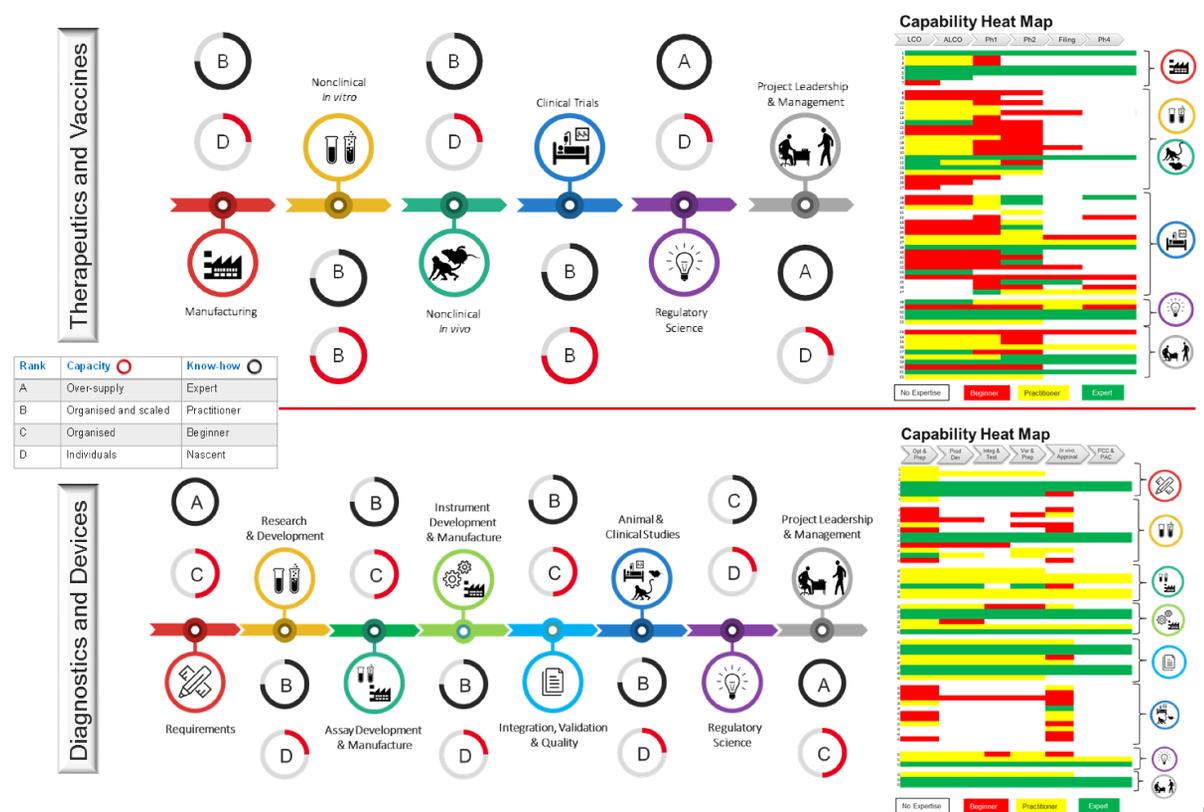


Figure 2 Aggregated national capacity and capability ('know-how') and individual interview heat maps for therapeutics and vaccines (top half) and diagnostics and devices (bottom half).

NCA face to face interviews and opportunities for pharmacometrics

- Interviews were conducted with 49 of the survey respondents (37%).
- Figure 2 shows that Australia has MCM product development know-how (predominantly A and B ratings in black circles) but capacity is limited (predominantly C and D ratings in red circles).
- Interviews confirmed strong BSL2/3+ *in vitro* capabilities (static & dynamic, genotypic & phenotypic), but minimal GxP examples in DMPK, immunoassay, bioanalysis, PD or safety. Importantly, GLP-compliant non-clinical *in vivo* services had limited diversity and availability.
- Australia's ABSL 3 and 4 facilities are not suitable for MCM product development.
- Leadership, program management, and regulatory science stewardship experience is lacking.
- The 2 areas of MCM product development that may benefit most from increased pharmacometrics were:
 - non-clinical *in vivo* PK ± PD and toxicology studies e.g., to replace/inform studies in larger animals that require high level containment, ABSL3/4;
 - and early clinical development e.g., phase 1 and phase 2a/b.

CONCLUSIONS

- Australia has a dispersed, relatively small but experienced drug discovery and development community with expertise relevant for MCM product development.
- Pharmacometric approaches could be utilised to address MCM capability and capacity gaps in Australia - non-clinical PK ± PD and toxicology and dose selection in early clinical studies.

REFERENCE

Lester, D and Rayner, CR (2013) Mapping Australia's Product Development Capability for Medical Countermeasures.