

Publishing vaccine trial results – Does there have to be a delay?

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A recent survey of the time taken to publish randomised controlled vaccine trials indicated that this can be delayed by many years¹. The results of clinical trials can represent 'price sensitive information' and, according to the US Securities and Exchange Commission (SEC) rules, this information needs to be made public at the earliest possible opportunity. Usually, this is done by a press release of 'top line' results soon after the initial analysis. In contrast, the rigour of the academic publication process involves many time-consuming steps, and furthermore, the early release of top line results can prevent publication of the full dataset in the highest impact journals. The needs of commerce conflict with the needs of academia. Is there a way around this?

Our phase IIb efficacy trial of the first candidate TB vaccine evaluated in infants since BCG was last tested in the 1960s in ~3000 South African infants was a collaborative effort between two academic institutions, one in the UK and one in South Africa, a US based Pharmaceutical Company and a US based Product Development Partnership². All parties were committed to publishing the full trial results in a peer review journal as rapidly as possible and to ensure compliance with the SEC rules. Our timeline, detailed in Figure 1, shows that it is possible to publish the full results of a clinical vaccine trial ten working days after the investigators first see the analysis. What was the preparation which made this possible?

There were three key pieces which helped enable us to meet this unprecedented (we believe) timeline for publishing. Firstly, the lead authors had pre-prepared three shell versions of a Result section, corresponding to a positive, negative or equivocal result. The Introduction and Methods sections had also been drafted before the analysis had been conducted. The collaborative writing experience achieved by having the eight lead authors 'locked' in a room together was key to the success of this venture. Secondly, all co-authors had been primed to receive, and rapidly respond to, the paper, and asked to set time aside to do so. Thirdly, The Lancet had committed to publish these results, assuming sufficient quality and scientific rigor, regardless of the results. The senior author worked closely with the Fast Track editor who lined up peer reviewers to review this manuscript within 24 hours of the Lancet receiving the manuscript. The authors, the external reviewers and The Lancet kept their word and met the pre-agreed timelines.

The reporting of late phase clinical trials has become highly structured precisely to reduce the room for subjective interpretation. Therefore, the speed of reporting is simply down to organisation and commitment. We propose the above process as a feasible way of rapidly reporting important clinical vaccine trial results, which satisfies both commercial and academic requirements. Where there's a will, there's a way.

References

1. Manzoli L, Flacco ME, D'Addario M, Capasso L, De Vito C, Marzuillo C, et al. Non-publication and delayed publication of randomized trials on vaccines: survey. *BMJ* 2014;348:g3058.

2. Tameris MD, Hatherill M, Landry BS, Scriba TJ, Snowden MA, Lockhart S, et al. Safety and efficacy of MVA85A, a new tuberculosis vaccine, in infants previously vaccinated with BCG: a randomised, placebo-controlled phase 2b trial. *Lancet* 2013;381(9871):1021-8.

Figure 1: Timeline of key dates (all times are GMT):

Thursday 25th Oct 2012: Last patient, last visit;

Friday 30 November 2012: Statistical analysis plan locked;

Tuesday January 8th 2013: Database lock

December 2012: Discussions with the Lancet about publishing this paper before the trial results are known. A timeline for publishing is agreed with authors and the Lancet

Monday 21st January 8am: 8 investigators meet in hotel in Cape Town and are presented with the results of the execution of the statistical analysis plan. They have cleared diaries and agreed to stay there until the paper is fully written.

Thursday 24th January 4pm: Near final draft is sent to all other co-authors with instructions that all comments should be submitted by the time the senior author's overnight flight lands in the UK.

Friday 25th January am: Author comments are incorporated.

Friday 25th January 1pm: Paper is submitted through normal fast track system to Lancet.

Saturday 26th January 10pm: Comments from 6 peer referees are received.

Sunday 27th January: Responses to peer comments are prepared in skype calls with all authors

Monday 28th January am: Paper resubmitted to Lancet

Tuesday 29th January 6pm: Proofs received

Wednesday 30th January 8am: Proofs returned

Monday 4th February 9am: Press statement released, embargoed until noon

Monday 4th February 12 noon: Paper published online; Press conference at the Wellcome Trust in London