

An investigation to assess hook effects in Pregnancy Testing kits and devices

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Introduction

Pregnancy testing kits or devices are used routinely in the UK both by health care professionals in clinical settings and by patients for home use. Research showed that the stated hook effect cut off limits varied greatly between kits / devices.

Aims

To assess if there are any hook effects seen for Pregnancy Testing kits and devices (readers) registered on the Weqas Urine Pregnancy Testing EQA Programme (Proficiency Testing).

To assess if the observed hook effects match the manufacturers' claims.

To assess performance of Pregnancy Testing kits and devices at very high hCG concentrations.

Method

Urine was collected from healthy, non-pregnant female volunteers, filtered to 0.2µm and Gentamycin added to maintain sterility. Intact hCG was added to the urine to a concentration of 700,000 IU/L. The pool was sent out to 180 participants, selected to ensure similar numbers of results returned for each kit / device registered. Sites were selected according to the device in use and their high return rate. It was anticipated that this would equate to approximately 12 results per kit / device.

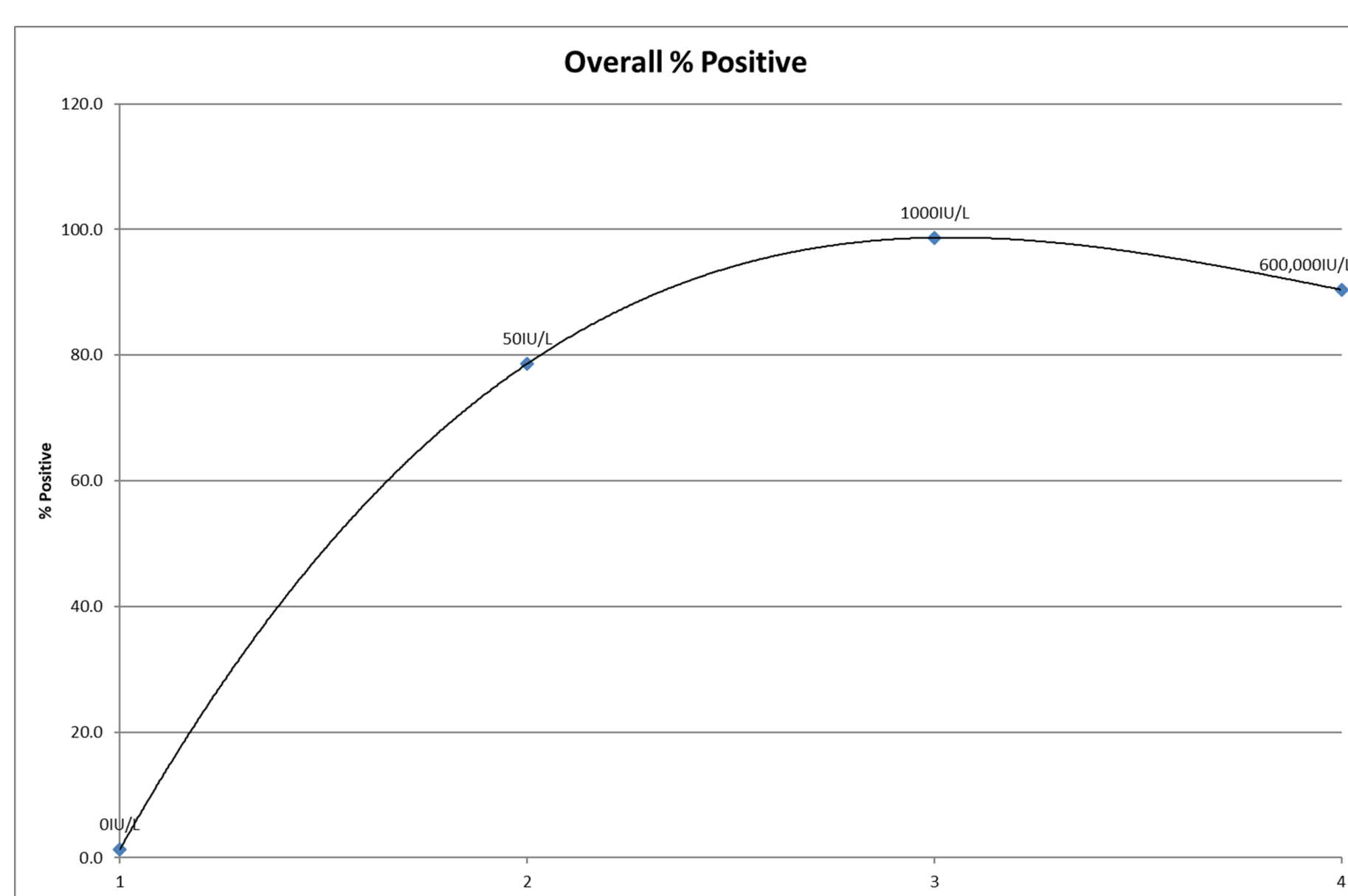
Pools were also distributed at concentrations of 50 IU/L and 1000 IU/L, plus a negative sample.

Participants were asked to analyse the samples in the same way as a patient or EQA sample, using their currently registered method.

Results

Overall % positive rates for each pool were 1.3% for the negative pool, 78.6% for the pool at 50 IU/L, 98.7% for the pool at 1000 IU/L and 90.4% for the pool at 700,000 IU/L.

Figure 1 Overall % positive rates for each pool



Three kits had significantly lower % positive rates for the 700,000 IU/L pool than the pool at 1000 IU/L. See Table 1.

Table 1 Overall % positive rates for each pool by kit / device

Instrument	% Positive			
	0IU/L	50IU/L	1000IU/L	600,000IU/L
Accusay hCG one step	0	80	100	100
Acon One Step	0	100	100	100
AIDE Diag One Step	0	83	92	83 (n=10)
Alere EASY hCG	1	71	99	92
Alere hCG	1	58	99	100
Alere hCG Combo	0	50	100	50
Alere TestPack Plus with OBC hCG Combo	0	67	100	100
SureStep One Step hCG	0	38	100	100
Check-mate	0	50	95	100
bioNexia	2	45	100	100
BioSign hCG DXpress	0	96	100	92
BioSign hCG Visual	4	50	100	90
First Response	0	100	100	100
One Step HCG	2	62	88	89
MEDICheck Dip & Read	0	58	96	63 (n=5)
QIC 2 STEP	0	100	100	100
Clinitek Status	2	97	100	100
Qupid One Step	0	88	100	100
SureScreen hCG GHCGC	0	46	99	64 (n=7)
SureScreen Midstream GHCGMS	0	100	100	100
Overall % Positive	1.3	78.6	98.7	90.4

The hook effect cut off limits ranged from >100,000 IU/L (Invitech Ltd One Step hCG) to >1,000,000 IU/L (Alere hCG Combo, Quadragech kits, Stanbio Qupid One Step).

Table 2 Hook cut off limits for kits / devices

Method	Instrument	Hook cut off
Accusay	Accusay hCG one step	approximately 500,000 mIU/mL
Acon One Step	One Step Device	<300,000 mIU/mL
AIDE Diagnostic (Nantong Egens Biotechnology)	AIDE Diag One Step Device	Not readily available
Alere	Alere EASY hCG	>250,000 mIU/mL
Alere	Alere hCG	> 500,000 mIU/mL
Alere	Alere hCG Combo	>1,000,000 mIU/mL (actual conc unconfirmed)
Alere	Alere TestPack Plus with OBC hCG Combo	Not readily available
Alere	SureStep One Step hCG	Not readily available
BHR Checkmate	Check-mate	approximately 200,000 mIU/mL
Biomerieux	bioNexia	Not readily available
Biomerieux	Vikia HCG-D	Not readily available
Biomerieux	Vikia-S One Step	Not readily available
BioSign hCG DXpress	BioSign hCG DXpress	approximately 500,000 mIU/mL
BioSign hCG DXpress	Miscellaneous	
BioSign hCG Visual	BioSign hCG Visual	Not readily available
Clonit	b-hCG Monostep	Not readily available
First Response	First Response	Not readily available
Invitech Ltd	One Step HCG	> 100,000 mIU/mL
NADAL	NADAL	Not readily available
Pasante hCG Test	MEDICheck Dip & Read	Not readily available
Quadragech	HCG CHECK 4	>1,000,000 mIU/mL (actual conc unconfirmed)
Quadragech	QIC 2 STEP	
Quidel	Quick Vue HCG Urine	>500,000 mIU/mL (actual conc unconfirmed)
Siemens	Clinitek Status	>600,000 mIU/mL
Stanbio	Qupid One Step	>1,000,000 mIU/mL (actual conc unconfirmed)
SureScreen	SureScreen hCG GHCGC	> 500,000 mIU/mL
SureScreen	SureScreen Midstream GHCGMS	Not readily available
VISITECT Pregnancy	VISITECT Pregnancy	

For those kits assigned as '>1,000,000 mIU/mL (actual conc unconfirmed)', the kit inserts stated either 'high levels of hCG 1,000,000 mIU/mL consistently gave positive results' or 'hCG up to and including 1,000,000 mIU/mL consistently gave positive results'.

Of the 157 results returned for the pool at 700,000 IU/L:

- 11 sites submitted a Negative result, across 6 kits / devices (7% of results).
- 4 sites submitted a weak positive result across 3 kits (2.5% of results).
- 142 sites submitted a positive result (90.5% of results).

Only 1 reader device (Biosign hCG DXpress) at 1 site submitted a negative result for the pool at 700,000 IU/L. Other sites using this device, and those using other devices, submitted a positive result for this pool.

Table 3 Instrument result summary for 700,000 IU/L pool

Negative		
Total Number	11	Percentage Returns
AIDE Diag One Step	2	18.18%
BioSign hCG DXpress	1	9.09%
MEDICheck Dip & Read	3	27.27%
One Step HCG	1	9.09%
Sure Screen Kit*	2	18.18%
SureScreen hCG GHCGC	2	18.18%
Weak Positive		
Total Number	4	Percentage Returns
Alere hCG Combo	1	25.00%
BioSign hCG Visual	1	25.00%
SureScreen hCG GHCGC	2	50.00%
Positive		
Total Number	142	Percentage Returns
Accusay hCG one step	4	2.82%
AIDE Diag One Step	10	7.04%
Alere EASY hCG	12	8.45%
Alere hCG	8	5.63%
Alere hCG Combo	1	0.70%
Alere TestPack Plus with OBC hCG Combo	2	1.41%
b-hCG Monostep	2	1.41%
bioNexia	13	9.15%
BioSign hCG DXpress	14	9.86%
BioSign hCG Visual	9	6.34%
Check-mate	3	2.11%
Clinitek Status	10	7.04%
First Response	2	1.41%
NADAL	1	0.70%
MEDICheck Dip & Read	5	3.52%
Acon One Step	1	0.70%
One Step HCG	8	5.63%
QIC 2 STEP	1	0.70%
Qupid One Step	12	8.45%
Sure Screen Kit*	2	1.41%
SureScreen hCG GHCGC	7	4.93%
SureScreen Midstream GHCGMS	1	0.70%
SureStep One Step hCG	11	7.75%
Vikia HCG-D	1	0.70%
VISITECT Pregnancy	1	0.70%

* Participant registered for Pasante kit, however commented 'Test performed on Sure Screen kit'

Discussion

From the 180 samples distributed, results were returned from 192 sites. This, unfortunately did not result in an even split across kits / devices but did allow for representation across a wide range of kits / devices. See Table 3.

Of the three kits that showed significantly lower % positive rates for the pool at 700,000 IU/L, one kit insert (SureScreen hCG GHCGC) did state a hook cut off limit of >500,000 IU/L. Data could not be found for the other two kits.

During the course of this study it became apparent that the hook effect cut off limits were not easily found for several manufacturers.

Users of the kit with the lowest stated hook effect limit of >100,000 IU/L submitted both positive and negative results (1 Negative, 8 Positive). The manufacturer's insert states 'can detect hCG at a range between 25 mIU/ml and 200,000 mIU/ml although the results were weaker above levels of 100,000 mIU/ml.'

Conclusions

This study identified that hook effects were present in some kits / devices evaluated.

The performance data in this study appears to support manufacturers' claims.

The small number of results obtained for some kits may not be representative of the kits' performance. It may be advantageous to repeat the study with a larger cohort of kits / devices.

The results demonstrate that it is imperative users are aware of the limitations of the kits in use, and ensure that they can easily identify hook effect cut off limits.