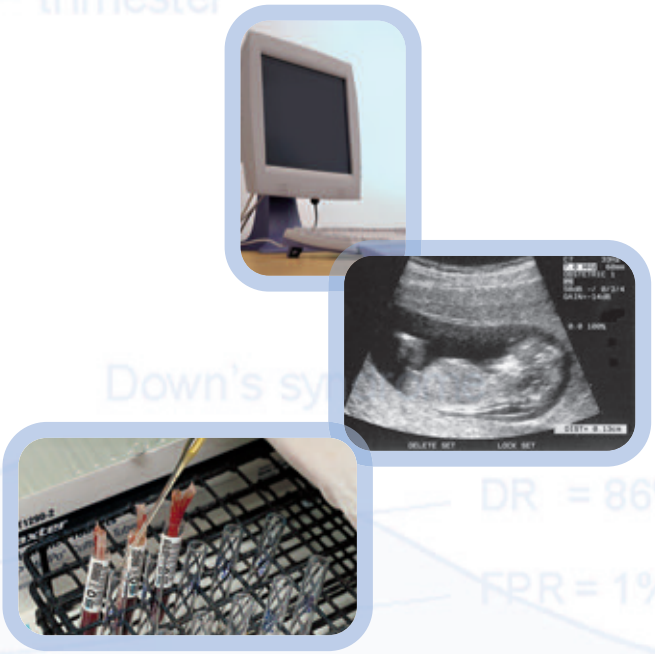
version7

antenatal screening software for down's syndrome & neural tube defects

For use in first trimester, second trimester and integrated screening for Down's syndrome

alpha™



alpha™

what is αlpha?

αlpha is the leading interpretive software for screening for Down's syndrome and neural tube defects. It is widely acknowledged as the best medical software of its kind and was the first software available for multiple marker Down's syndrome screening.

αlpha has pioneered the technology and set the standard for such software ever since.

αlpha philisophy : 7 key points

- Scientific basis of Down's syndrome risk estimation is in the public domain
- High quality professional service
- Risk estimation methodology is independent of assay reagents used
- New versions supplied without extra cost
- Advances in screening incorporated in new versions
- Quality assurance and programme monitoring facilities
- User flexibility without sacrificing screening integrity

αlpha is based on published scientific data and validated scientific methodology. The scientific basis for αlpha is in the public domain, and is available from the scientific literature.

αlpha uses a woman's age, the concentration of serum markers for Down's syndrome and neural tube defects, and other details of the pregnancy, to estimate the woman's risk of having a pregnancy with either of the two disorders.

αlpha uses serum markers in the second trimester of pregnancy (14 - 22 weeks gestation) and both serum and ultrasound markers in the first trimester of pregnancy 10 - 13 weeks gestation). It allows the use of up to 9 screening markers.

αlpha Version 7 is a major step forward incorporating the latest medical and scientific advances in antenatal screening for Down's syndrome and neural tube defects.

αlpha is supplied with the αlpha marker library providing comprehensive references on all statistical parameters used in risk estimation and with αlpha Outcome allowing users to follow up their screening programme and empirically validate it.

αlpha includes technical improvements that make the software more flexible and easier to use than ever before. Version 7 offers one of the most significant improvements to the software since αlpha was launched in 1988. No other software of its kind offers as wide a range of facilities or quality control features.

αlpha is licensed to interpret Integrated tests. The Integrated test is a major advance, providing safer and more effective Down's syndrome screening than ever before.

αlpha provides interpretations based on integrated and sequential screening protocols.

αlpha includes features designed to enhance screening performance, for example, the use of sonographer-specific medians for nuchal translucency measurement and features that make the monitoring and audit of screening better and easier to carry out.

αlpha has been used to screen over 9 million pregnancies in 47 countries. Probably no other medical software of its kind has been more widely used. The experience of this customer base is assurance of αlpha's quality and reliability.

αlpha's risk estimation has been validated; the Down's syndrome risk predicted by αlpha is in close agreement with the observed prevalence of Down's syndrome.

αlpha offers users and the women screened the most authoritative interpretation available from any Down's syndrome and neural tube defect screening software.

Customer support and service

- αlpha users receive thorough on-site training, and prompt support of the highest quality. Our priority is to help users achieve high quality screening with full technical and professional support.
- αlpha stays ahead of other software by being continually updated in the light of the latest scientific developments, and comments from users.

features

reporting

- Provides estimates of risk for Down's syndrome between 10 and 22 weeks and open neural tube defects (NTD) between 15 and 22 weeks using all recognized screening tests
- Uses screening parameters from the SURUSS study and Down's syndrome age related risk **new**
- Uses day specific parameters in the first trimester to achieve improved screening performance **new**
- Interprets Integrated test results - the safest and most effective screening test for Down's syndrome
- Allows screening for Down's syndrome in the first trimester using serum markers and nuchal translucency, either alone or in combination
- Interpretations can be made using a sequential testing protocol, with very high risk women having a first trimester screening result and nearly all the remaining women proceeding to have an Integrated test **new**
- User defined option to report Down's syndrome risk at term, or early second trimester or late first trimester
- Allows user to specify separate screening cut-off levels for different screening tests
- Provides diagnosis of open neural tube defects using amniotic fluid Alpha-fetoprotein (AF-AFP) and Acetylcholinesterase (AcheE) results
- Facility for identifying pregnancies with a high risk of trisomy 18 printing the risk, either at term or mid-trimester, using the same methodology used in Down's syndrome risk interpretation
- Option to identify pregnancies at high risk of Smith-Lemli-Opitz syndrome (SLOS)
- Allows for maternal age, gestational age, ultrasound measurements, ethnic group, maternal weight, past history of NTD and Down's syndrome
- Calculates gestational age from various fetal measurements including crown-rump length (CRL), biparietal diameter (BPD) and abdominal circumference (AC)
- Calculates gestational age from head circumference (HC) measurements **new**
- Separate median equations for gestational age estimated by dates and by scan, if desired
- Normal medians for the screening markers are derived from local data
- Nuchal translucency measurements adjusted for CRL
- αlpha offers the option of sonographer specific nuchal translucency medians to allow for systematic differences between measurements made by different sonographers. This simple measure provides a useful improvement in screening performance
- Option to include the result of an ultrasound nasal bone examination **new**
- Allows for differences in marker levels and maternal weight in up to five ethnic groups, either using separate medians and weight adjustments, or using correction factors
- αlpha adjusts serum marker levels in In vitro fertilization (IVF) pregnancies to correct the otherwise high false positive rate
- αlpha adjusts serum marker levels in smokers **new**
- Adjusts screening markers to avoid a high recurrent false positive rate **new**
- Maternal weight regression equation can be either log-linear or linear reciprocal **new**
- Screening results given for twin pregnancies and insulin dependent diabetic pregnancies
- Uses NT and serum markers in interpretation of twin pregnancies **new**
- Adjusts risk estimate for the age at which a previous pregnancy was affected with Down's syndrome **new**
- Option to specify gestational age range to use for second trimester samples **new**
- Option to identify anomalous marker patterns and warn user **new**
- Repeat testing is best avoided, but if done, it requires an interpretation which takes into account the previous result; αlpha does this
- Custom-designed report layouts are available on request
- The risk estimate can be shown graphically on the screening reports **new**
- Option to "cap" very high risk estimates or "trim" very low risk estimates **new**
- Option to include a digitized logo in report so that pre printed paper is not required **new**
- Option to include time of report in report **new**
- Stores patient information in a database which can be accessed to retrieve previous test results

monitoring

- αlpha provides what is probably the widest range of monitoring features including a facility to examine drift in the normal median values of the screening markers and set them to ensure that the expected screening performance is achieved
- One of αlpha's special features is the facility to estimate expected screening performance in terms of detection rate and false positive rate, based on the age distribution of the user's own screened population. This can be compared with the observed performance to monitor the screening programme
- αlpha can be used to determine the expected screening performance for any combination of screening markers. This is customized for the exact age distribution of women in the screening programme concerned. It can also be used to examine screening performance in different age groups screening performance based on the age distribution of pregnancies in England and Wales
- αlpha users can benefit from our free αlphacheck™ service. We will, at regular intervals, guide you through the steps involved in monitoring screening performance, and provide expert advice in correcting any problems identified. αlphacheck will help to ensure that the women you screen receive a service of the highest quality
- αlpha Outcome™ is available to allow users to record details of the presence or absence of birth defects for monitoring performance
- αlpha Outcome provides an empirical validation of the screening method, by tabulating the observed prevalence of Down's syndrome according to the risk predicted by αlpha
- Graph Monthly medians allows users to track their assay results over time and so detect assay drift
- For centres offering more than one type of screening test, separate statistical summaries can be produced for first trimester, second trimester and integrated screening results
- αlpha automatically creates audit trails of patient reports, changes to statistical information controlling the interpretation of screening and diagnostic results (e.g. median equations), and changes in screening policy (e.g. cut-off levels)
- Analyze-It™ which offers great flexibility and power to users who wish to perform statistical analyses using data from their screening database **new**
- Option to ignore smokers in monthly median results **new**

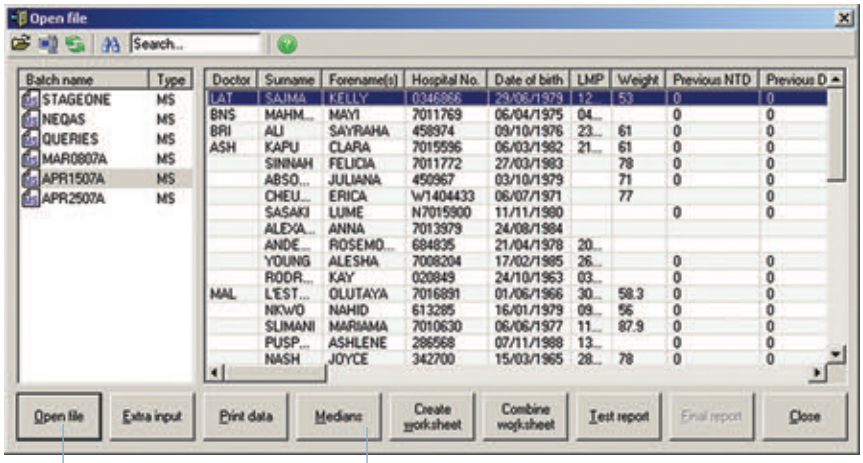
ease of use

- User-defined data entry facility - user can specify the entry items and the sequence of entry
- αlpha is supplied ready to use for screening for Down's syndrome with alpha-fetoprotein (AFP), unconjugated oestriol (uE_3), total human chorionic gonadotrophin (hCG) and inhibin A in the second trimester with nuchal translucency (NT), pregnancy associated plasma protein A (PAPP-A), hCG in the first trimester in any combination, and for AFP screening for NTD
- "What-if" facility to determine alternative interpretations for different screening data
- Export facility which allows users to select data for analysis using a statistical package of their choice
- Gestational age at date of sample is calculated and displayed on the data entry screen; easy identification of first and second trimester tests with an alert for those tests performed too early or too late
- Enhanced help facilities including context sensitive help and comprehensive alphabetical index of all available help topics
- The αlpha Marker Library summarises the statistical parameters (means, standard deviations and correlation coefficients) used and provides a list of references to relevant publications
- Facility to add local comments to reports
- Options to set-up reminder lists for Integrated test patients who are overdue for the second stage of the report and to automatically identify patients who are ready to report **new**
- Optional default features which avoid necessary repetitive data entry, saving time and cost
- NOT restricted to any one manufacturer's reagents or equipment - ensures user choice and flexibility
- Multi-user version available - different operations can be conducted at the same time on different workstations
- Reports in eleven languages - English, German, Italian, French, Greek, Spanish, Portuguese, Turkish, Russian, Czech and Slovak
- Option to automatically copy reports to 1, 2 or 3 specified doctors
- Interfacing αlpha with other software is now very simple. αlpha uses industry standard comma- or tab-separated files that are recognised by a wide variety of spreadsheets, databases and laboratory software
- Search feature means any patient record can be easily located in single operation
- "Wildcard" search facility can be used when the exact spelling of a patient's name is not known
- Intelligent auto complete facility to save unnecessary key strokes when entering doctors, sonographers or their addresses
- A comprehensive printed user manual is provided.
- Facility to merge patient data with output from analytical instrumentation **new**
- Fully compatible with Microsoft Windows™ using the style of user interface familiar to Windows users **new**

data entry and reporting

Data Entry Screen

The open file screen provides an overview of unreported patients



Open a batch file for editing

Check medians and MoM values for a batch of patients before reporting

DATA ENTRY

- Fast and user-friendly
- Report preview facility
- On-line help facility
- Maintains lists of doctors, sonographers and addresses
- Can be tailored to user's requirements

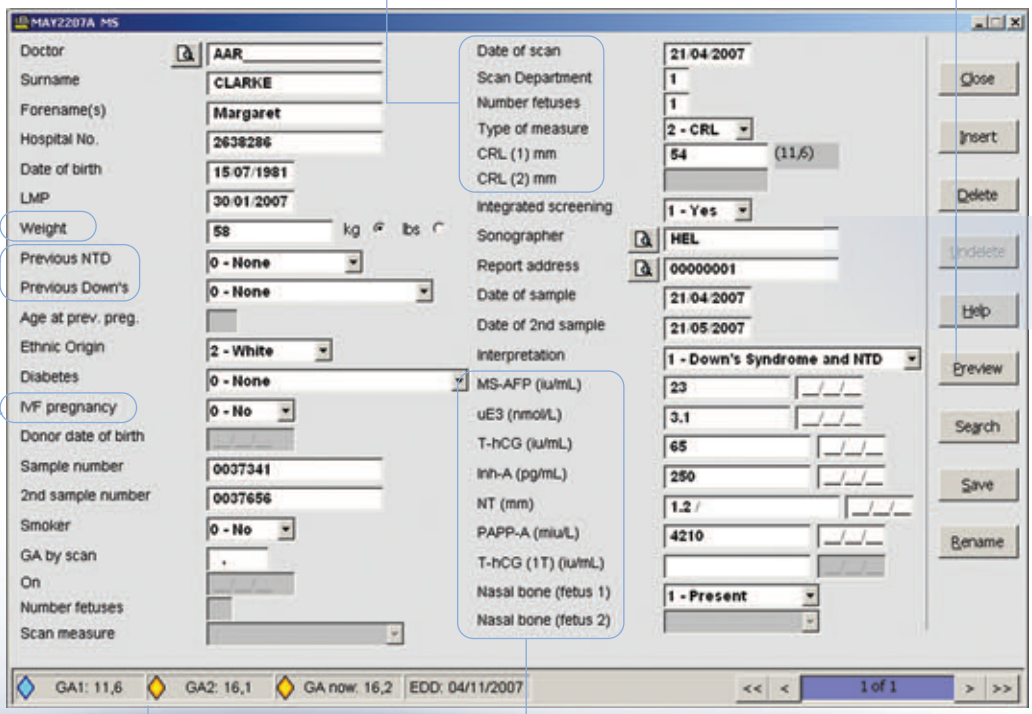
Interpretation based on either LMP dates or ultrasound scan: scan is used when available

Report preview allows you to inspect the interpretation at the time of data entry

Maternal weight used to adjust MoM values of serum markers

αlpha takes previous history of Down's syndrome and NTD into account, and adjusts the final risk estimate accordingly

MoM values corrected in IVF pregnancies. If the egg is donated, age risk is based on donor's date of birth. Gestation based on the egg collection - date, if known



Colour-coded indicator for gestational age

αlpha offers users flexibility in the choice of screening markers. Both first and second trimester markers can be used

REPORTING:

- Uncluttered yet provides all the necessary information needed for an interpretation
- Reports can be printed in ten languages
- Customised report layouts on request

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Magnolia

NEURAL TUBE DEFECT AND DOWN'S SYNDROME SCREENING **Reported 12:04 22 May 07**

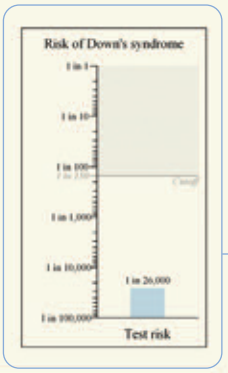
Surname	:	CLARKE
Forename(s)	:	Margaret
Hospital No.	:	2638286
Date of birth	:	15/07/81
LMP	:	30/01/07
EDD	:	04/11/07
Date of sample	:	21/04/07
Date of 2nd sample	:	21/05/07
Sample number	:	0037341

CLINICAL DETAILS AND TEST RESULTS

Previous NTD	:	None		
Previous Down's	:	None		
Insulin dependent diabetes	:	None		
Maternal age at EDD	:	26 years		
Scan measurement (CRL)	:	54 mm on 21/04/07		
Gestation at date of 1st sample	:	11 weeks 4 days (by dates) 11 weeks 6 days (by CRL scan)		
Gestation at date of 2nd sample	:	15 weeks 6 days (by dates) 16 weeks 1 days (by CRL scan)		
Gestation used	:	Scan estimate (CRL)		
Weight	:	58 kg		
Ethnic Origin	:	Caucasian		
MS-AFP level	:	23 iu/mL	;	0.80 MoM
uE3 level	:	3.1 nmol/L	;	0.91 MoM
Total hCG level	:	65 iu/mL	;	1.64 MoM
Inhibin-A level	:	250 pg/mL	;	1.71 MoM
Nuchal measurement	:	1.2 mm	;	0.99 MoM
PAPP-A level	:	4210 miu/L	;	1.94 MoM
Fetal nasal bone	:	Present		

INTERPRETATION

Screening result : Screen negative
Risk of Down's : 1 in 26,000 (at term)

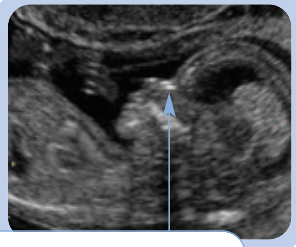


COMMENTS FROM MAGNOLIA MEDICAL CENTRE

The detection rate for the Integrated test is approximately 86% at a false positive rate of 1%

A screen negative result does not exclude the possibility of Down's syndrome or a neural tube defect, because screening does not detect all affected pregnancies

This is an Alpha report



Automatically copy reports to up to 3 doctors

Report address can be positioned for window envelopes

αlpha adjusts MoM values in diabetic women according to whether or not the MoM values have been corrected for maternal weight

Option to use presence or absence of nasal bone as a marker

Corrects for differences in marker levels and maternal weight in up to 5 ethnic groups. Names of ethnic groups can be specified by the user

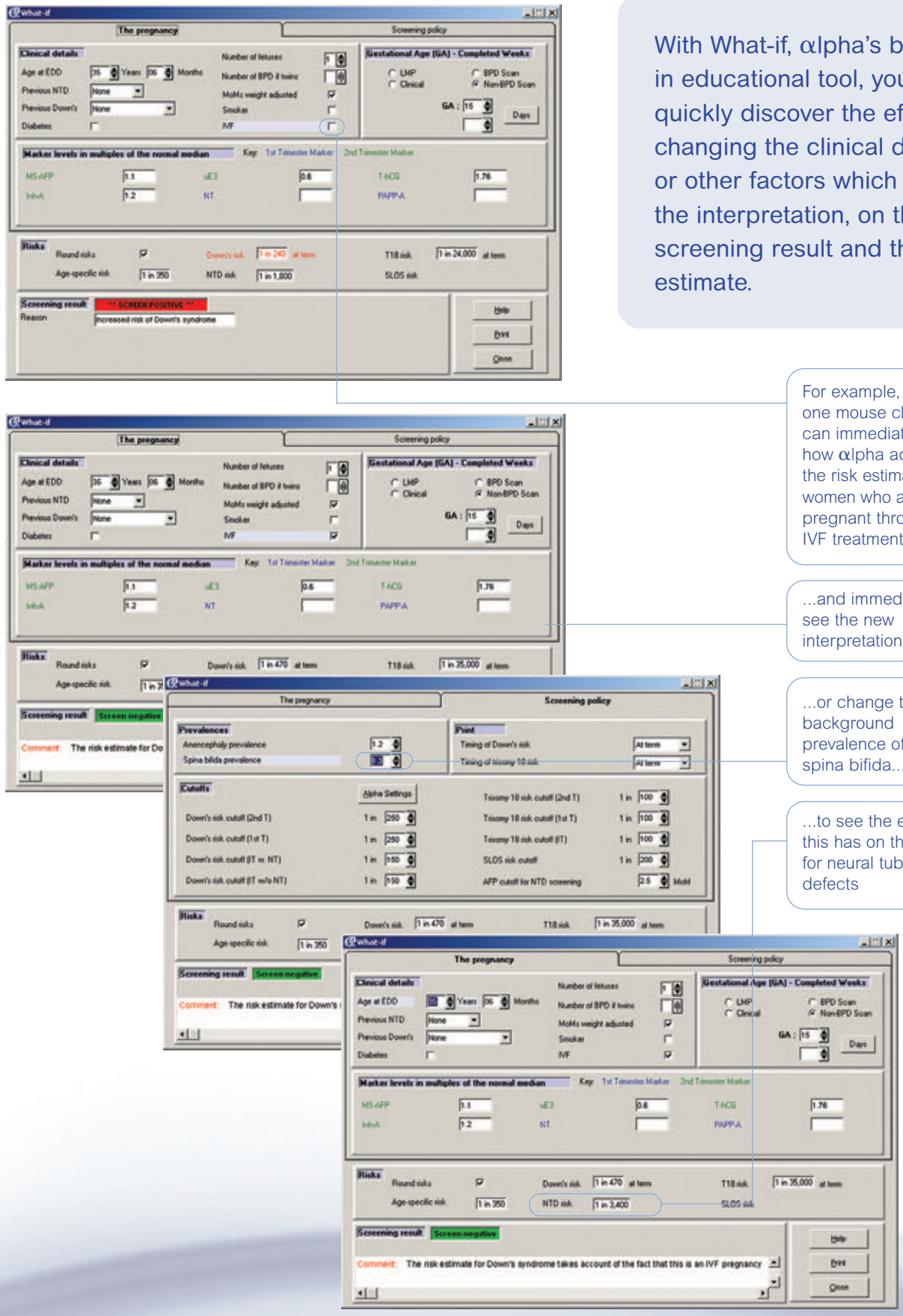
"Riskometer" can be added if desired

Explanation of "screen positive" and "screen negative" results printed automatically if user requires

Locally defined messages can be added to reports

αlpha™

what-if



With What-if, αlpha's built in educational tool, you can quickly discover the effect of changing the clinical details, or other factors which affect the interpretation, on the screening result and the risk estimate.

For example, with one mouse click, you can immediately see how αlpha adjusts the risk estimate in women who are pregnant through IVF treatment...

...and immediately see the new interpretation....

...or change the background prevalence of spina bifida...

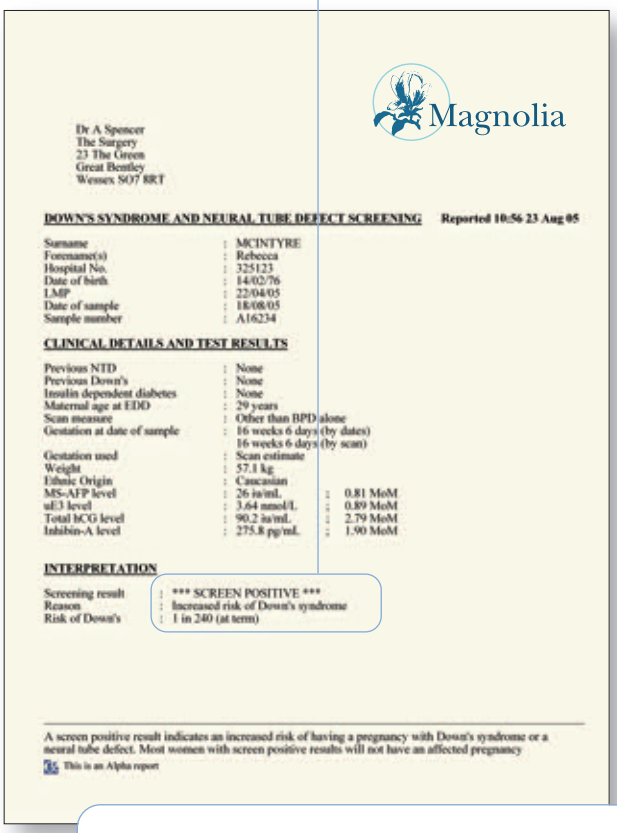
...to see the effect this has on the risk for neural tube defects

adjustment to avoid high recurrent false positive rate

A woman who has a false-positive screening result in one pregnancy is more likely to have one in a subsequent pregnancy than women in general. αlpha can help to avoid this problem by adjusting screening markers in women without a previously affected pregnancy who have been screened in a previous pregnancy with results in the αlpha database.

The screening report for the current pregnancy is positive.

The screening report for the previous pregnancy is also positive.



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DOWN'S SYNDROME AND NEURAL TUBE DEFECT SCREENING Reported 10:56 23 Aug 05

Surname	: MCINTYRE		
Forename(s)	: Rebecca		
Hospital No.	: 325123		
Date of birth	: 14/02/76		
LMP	: 22/04/05		
Date of sample	: 18/08/05		
Sample number	: A16234		

CLINICAL DETAILS AND TEST RESULTS

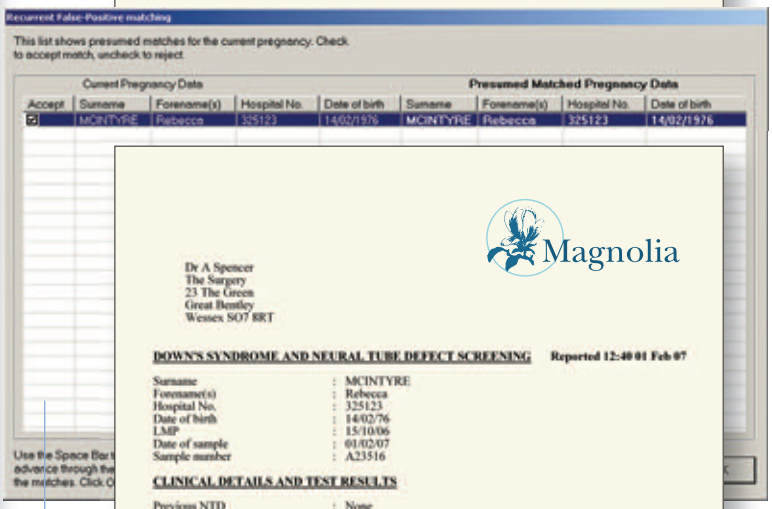
Previous NTD	: None		
Previous Down's	: None		
Insulin dependent diabetes	: None		
Maternal age at EDD	: 29 years		
Scan measure	: Other than BPD alone		
Gestation at date of sample	: 16 weeks 6 days (by dates) 16 weeks 6 days (by scan)		
Gestation used	: Scan estimate		
Weight	: 57.1 kg		
Ethnic Origin	: Caucasian		
MS-AFP level	: 26 iu/mL	:	0.81 MoM
uE3 level	: 3.64 nmol/L	:	0.89 MoM
Total hCG level	: 90.2 iu/mL	:	2.79 MoM
Inhibin-A level	: 275.8 pg/mL	:	1.90 MoM

INTERPRETATION

Screening result	:	*** SCREEN POSITIVE ***
Reason	:	Increased risk of Down's syndrome
Risk of Down's	:	1 in 240 (at term)

A screen positive result indicates an increased risk of having a pregnancy with Down's syndrome or a neural tube defect. Most women with screen positive results will not have an affected pregnancy

This is an Alpha report



Recurrent False-Positive matching

This list shows presumed matches for the current pregnancy. Check to accept match, uncheck to reject.

Current Pregnancy Data				Presumed Matched Pregnancy Data			
Accept	Surname	Forename(s)	Hospital No.	Date of birth	Surname	Forename(s)	Hospital No.	Date of birth
☑	MCINTYRE	Rebecca	325123	14/02/1976	MCINTYRE	Rebecca	325123	14/02/1976

Use the Space Bar to advance through the matches. Click O

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DOWN'S SYNDROME AND NEURAL TUBE DEFECT SCREENING Reported 12:40 01 Feb 07

Surname	: MCINTYRE		
Forename(s)	: Rebecca		
Hospital No.	: 325123		
Date of birth	: 14/02/76		
LMP	: 15/10/06		
Date of sample	: 01/02/07		
Sample number	: A23516		

CLINICAL DETAILS AND TEST RESULTS

Previous NTD	: None		
Previous Down's	: None		
Insulin dependent diabetes	: None		
Maternal age at EDD	: 31 years		
Scan measure	: Other than BPD alone		
Gestation at date of sample	: 15 weeks 4 days (by dates) 15 weeks 4 days (by scan)		
Gestation used	: Scan estimate		
Weight	: 57 kg		
Ethnic Origin	: Caucasian		
MS-AFP level	: 25 iu/mL	:	0.94 MoM
uE3 level	: 1.91 nmol/L	:	0.65 MoM
Total hCG level	: 101.2 iu/mL	:	2.07 MoM
Inhibin-A level	: 261.1 pg/mL	:	1.71 MoM

INTERPRETATION

Screening result	:	Screen negative
Risk of Down's	:	1 in 910 (at term)
Comment	:	The risk estimate for Down's syndrome takes account of MoMs in a previous pregnancy

A screen negative result does not exclude the possibility of Down's syndrome or a neural tube defect, because screening does not detect all affected pregnancies

This is an Alpha report

When screening, αlpha will automatically find previous pregnancies for this patient and allow the user to confirm that an adjustment should be made

The marker levels in the previous pregnancy are used to adjust the levels in the current pregnancy to calculate a modified risk estimate. The screening result is now negative.

the Integrated test

The Integrated Test is a method of screening for Down's syndrome which uses measurements obtained during the first and second trimesters to provide a single estimate of the risk of having a pregnancy with Down's syndrome.

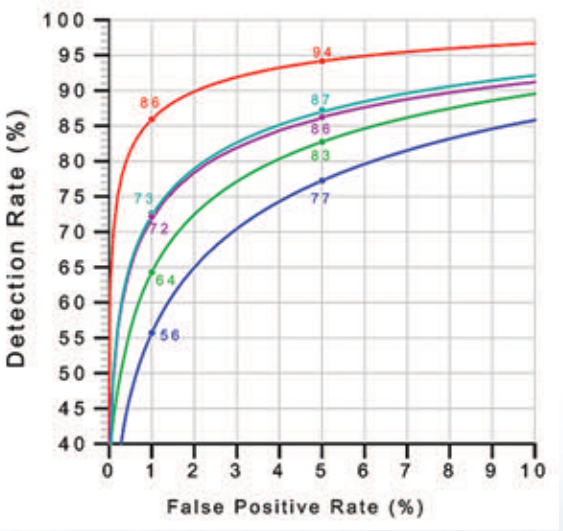
αlpha version 7 is licensed to interpret Integrated test screening results.

1st trimester
PAPP-A + NT
(10-13 weeks)

2nd trimester
AFP + uE3 +
hCG + inhibin-A
(14-22 weeks)

SAFER, MORE EFFECTIVE SCREENING

The Integrated test offers screening that is safer and more effective than currently used tests because high detection rates can be achieved with much lower false-positive rates than existing tests. For example, using the Integrated test in place of the triple test, the detection rate is higher (86% compared with 77%) and the false-positive rate is lower (1% compared with 5%).†



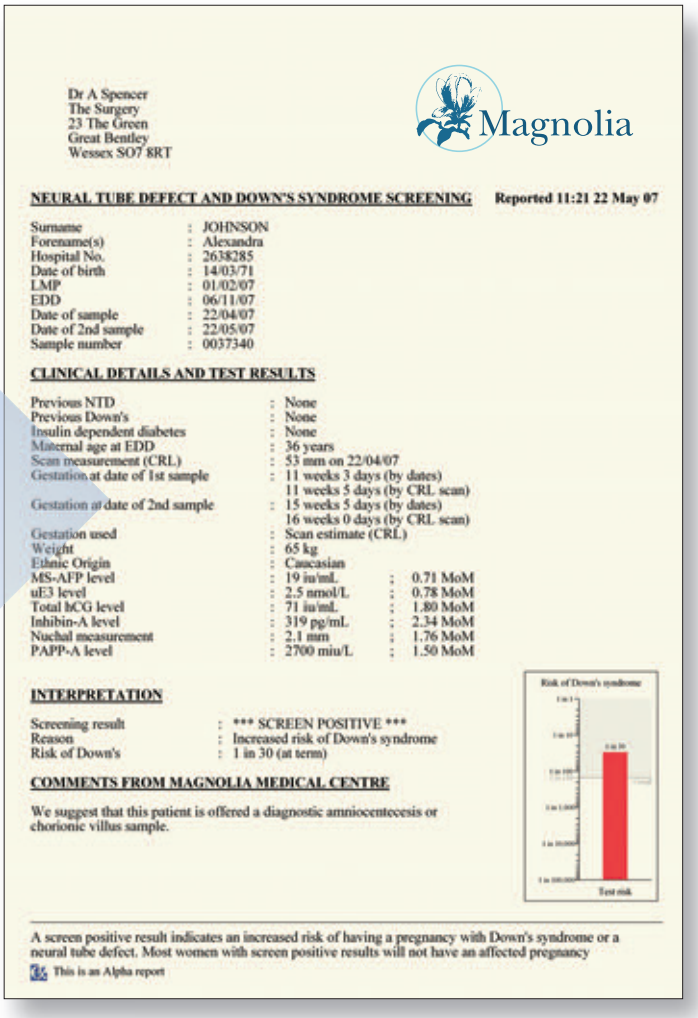
Integrated test	Nuchal Translucency and PAPP-A in the first trimester, AFP, uE_3, hCG and inhibin-A in the second trimester
Serum Integrated test	PAPP-A in the first trimester, AFP, uE_3, hCG and inhibin-A in the second trimester
Combined	Nuchal Translucency, PAPP-A and hCG in the first trimester
Quadruple	AFP, uE_3, hCG and inhibin-A in the second trimester
Triple	AFP, uE_3, hCG in the second trimester

† Based on parameters cited in: -

Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM (2003). First and second trimester antenatal screening for Down's syndrome: the results of the Serum, Urine and Ultrasound Screening Study (SURUSS). J Med Screen 10, 56-104.

Wald NJ, Rodeck C, Rudnicka AR, Hackshaw AK (2004). Nuchal translucency and gestational age. Prenat Diagn 24, 150-151

Based on the age distribution of maternities in England and Wales 1996-98



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NEURAL TUBE DEFECT AND DOWN'S SYNDROME SCREENING **Reported 11:21 22 May 07**

Surname	: JOHNSON
Forename(s)	: Alexandra
Hospital No.	: 2638285
Date of birth	: 14/03/71
LMP	: 01/02/07
EDD	: 06/11/07
Date of sample	: 22/04/07
Date of 2nd sample	: 22/05/07
Sample number	: 0037340

CLINICAL DETAILS AND TEST RESULTS

Previous NTD	: None		
Previous Down's	: None		
Insulin dependent diabetes	: None		
Maternal age at EDD	: 36 years		
Scan measurement (CRL)	: 53 mm on 22/04/07		
Gestation at date of 1st sample	: 11 weeks 3 days (by dates) 11 weeks 5 days (by CRL scan)		
Gestation at date of 2nd sample	: 15 weeks 5 days (by dates) 16 weeks 0 days (by CRL scan)		
Gestation used	: Scan estimate (CRL)		
Weight	: 65 kg		
Ethnic Origin	: Caucasian		
MS-AFP level	: 19 iu/mL	:	0.71 MoM
uE3 level	: 2.5 nmol/L	:	0.78 MoM
Total hCG level	: 71 iu/mL	:	1.80 MoM
Inhibin-A level	: 319 pg/mL	:	2.34 MoM
Nuchal measurement	: 2.1 mm	:	1.76 MoM
PAPP-A level	: 2700 miu/L	:	1.50 MoM

INTERPRETATION

Screening result	: *** SCREEN POSITIVE ***
Reason	: Increased risk of Down's syndrome
Risk of Down's	: 1 in 30 (at term)

COMMENTS FROM MAGNOLIA MEDICAL CENTRE

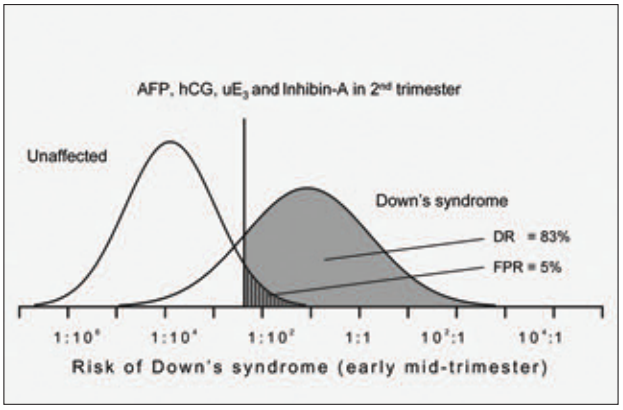
We suggest that this patient is offered a diagnostic amniocentecesis or chorionic villus sample.

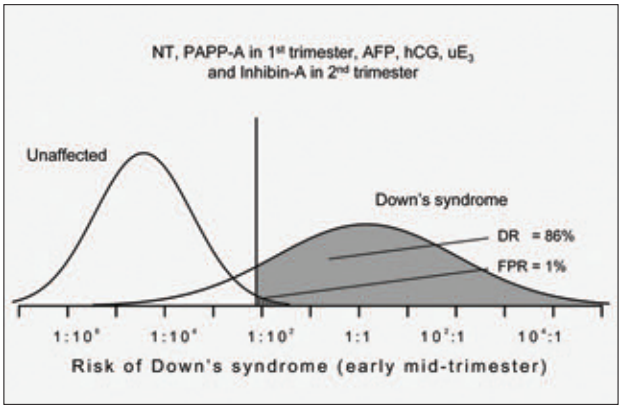
A screen positive result indicates an increased risk of having a pregnancy with Down's syndrome or a neural tube defect. Most women with screen positive results will not have an affected pregnancy

This is an Alpha report

MORE DISCRIMINATORY THAN ANY OTHER METHOD OF SCREENING

The Integrated test is more discriminatory than other screening tests because there is a smaller overlap between the distributions of risk in affected and unaffected pregnancies, as shown in the diagrams below (quadruple test above, integrated test below).





Screening	FPR(%)	DR(%)	OAPR
Integrated test	1	86	1 : 7
serum integrated test	5	87	1 : 36
Combined	5	86	1 : 36
Quadruple	5	83	1 : 38
Triple	5	77	1 : 43

FPR = false positive rate
DR = detection rate
OAPR = odds of having an affected pregnancy given a positive result

BENEFITS OF THE INTEGRATED TEST

- The safest and most effective method of screening for Down's syndrome
- Achieves a high detection rate with much lower false-positive rate than other screening tests
- Preserves AFP screening for open neural tube defects
- Identifies pregnancies at high risk of trisomy 18, using first and second trimester serum markers
- Requires fewer diagnostic procedures per case of Down's syndrome detected than other screening tests, as shown right

sequential testing

αlpha can be used to interpret sequential testing which allows early completion of screening for women with very high risk pregnancies identified in the first trimester. A high risk cut-off is set for the first trimester test so there is a low false positive rate. Nearly all women proceed to the full Integrated test.

- User specified risk cut-off levels for first trimester and second trimester
- Information on pregnancies that are not positive in the first trimester are held for use in an integrated test

In a small proportion of pregnancies, the first trimester screening test indicates that this is a very high-risk pregnancy and so the screening test is then completed in the first trimester. If required, hCG can also be measured in the first trimester

All other women screened have an Integrated test

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DOWN'S SYNDROME SCREENING Reported 12:11 03 Mar 07

Surname	: SEDDON	
Forename(s)	: Hayley	
Hospital No.	: 26354138	
Date of birth	: 02/07/66	
LMP	: 20/12/06	
Date of sample	: 03/03/07	
Sample number	: A12638	

CLINICAL DETAILS AND TEST RESULTS

Previous NTD	: None	
Previous Down's	: None	
Insulin dependent diabetes	: None	
Maternal age at EDD	: 41 years	
Scan measurement (CRL)	: 55 mm on 02/03/07	
Gestation at date of sample	: 10 weeks 3 days (by dates) 12 weeks 0 days (by CRL scan)	
Gestation used	: Scan estimate (CRL)	
Weight	: 62.3 kg	
Ethnic Origin	: Caucasian	
Nuchal measurement	: 2.7 mm	: 2.18 MoM
PAPP-A level	: 3241 miu/L	: 1.49 MoM

INTERPRETATION

Screening result	: *** SCREEN POSITIVE ***
Reason	: Increased risk of Down's syndrome
Risk of Down's	: 1 in 35 (at term)
Comment	: This test does not screen for neural tube defects

A screen positive result indicates an increased risk of having a pregnancy with Down's syndrom
women with screen positive results will not have an affected pregnancy

This is an Alpha report

Magnolia

Dr A Spencer
The Surgery
23 The Green
Great Bentley
Wessex SO7 8RT

DOWN'S SYNDROME AND NEURAL TUBE DEFECT SCREENING Reported 11:19 06 Apr 07

Surname	: O'BRIEN	
Forename(s)	: Kelly	
Hospital No.	: 26382831	
Date of birth	: 07/11/77	
LMP	: 10/12/06	
Date of sample	: 03/03/07	
Date of 2nd sample	: 05/04/07	
Sample number	: A23546	

CLINICAL DETAILS AND TEST RESULTS

Previous NTD	: None	
Previous Down's	: None	
Insulin dependent diabetes	: None	
Maternal age at EDD	: 29 years	
Scan measurement (CRL)	: 52 mm on 01/03/07	
Gestation at date of 1st sample	: 11 weeks 6 days (by dates) 12 weeks 0 days (by CRL scan)	
Gestation at date of 2nd sample	: 16 weeks 4 days (by dates) 16 weeks 5 days (by CRL scan)	
Gestation used	: Scan estimate (CRL)	
Weight	: 54 kg	
Ethnic Origin	: Caucasian	
MS-AFP level	: 32 iu/mL	: 1.00 MoM
uE3 level	: 4.1 nmol/L	: 1.03 MoM
Total hCG level	: 52 iu/mL	: 1.51 MoM
Inhibin-A level	: 123 pg/mL	: 0.82 MoM
Nuchal measurement	: 1.2 mm	: 1.02 MoM
PAPP-A level	: 2412 miu/L	: 0.96 MoM

INTERPRETATION

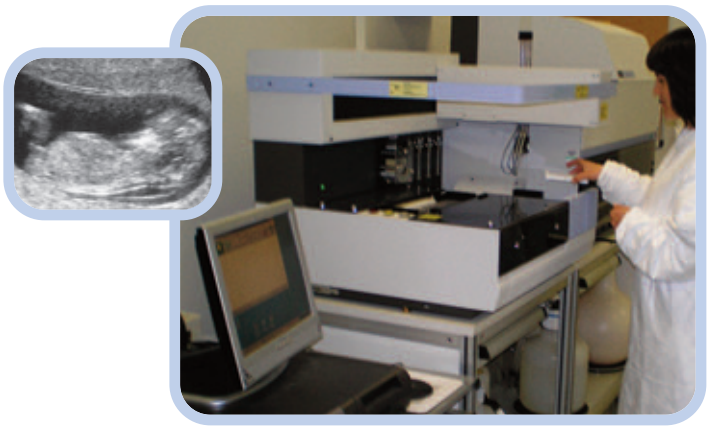
Screening result	: Screen negative
Risk of Down's	: 1 in 33,000 (at term)

A screen negative result does not exclude the possibility of Down's syndrome or a neural tube defect, because screening does not detect all affected pregnancies

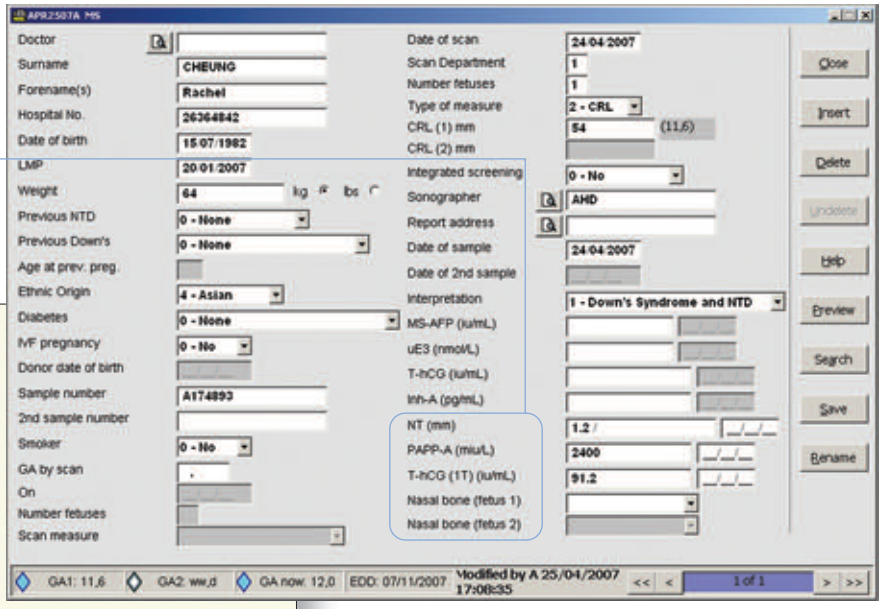
This is an Alpha report

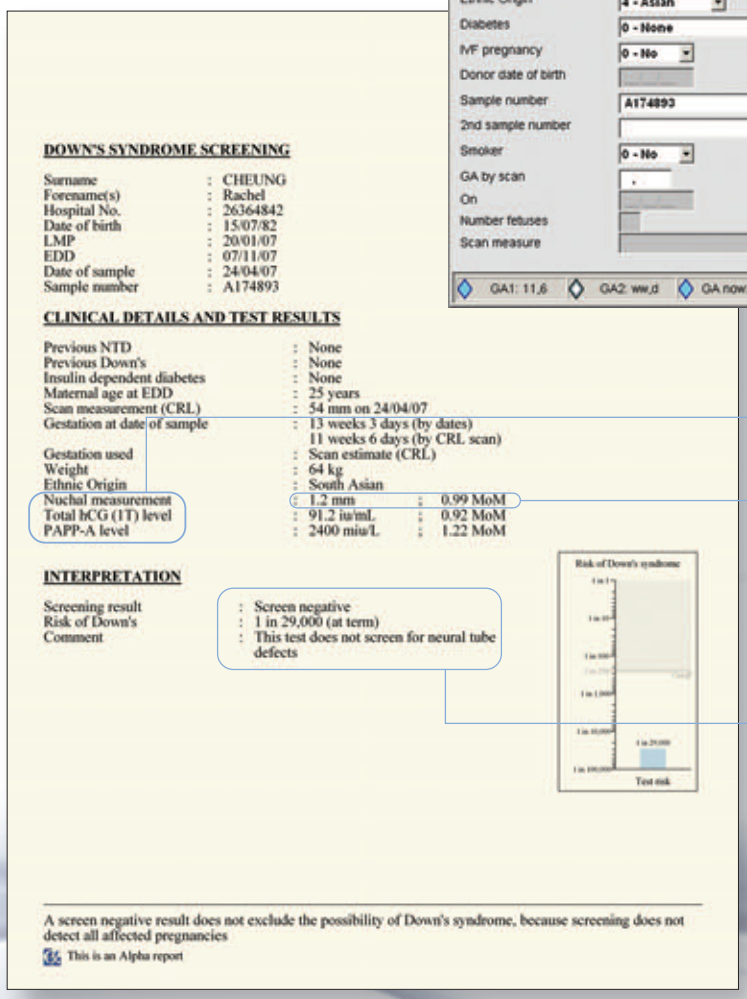
first trimester screening with αlpha

First trimester – the combined test at 10 to 13 weeks



Screening for Down's syndrome in the first trimester using serum markers and nuchal translucency, either alone or in combination





DOWN'S SYNDROME SCREENING

Surname	:	CHEUNG
Forename(s)	:	Rachel
Hospital No.	:	26364842
Date of birth	:	15/07/82
LMP	:	20/01/07
EDD	:	07/11/07
Date of sample	:	24/04/07
Sample number	:	A174893

CLINICAL DETAILS AND TEST RESULTS

Previous NTD	:	None		
Previous Down's	:	None		
Insulin dependent diabetes	:	None		
Maternal age at EDD	:	25 years		
Scan measurement (CRL)	:	54 mm on 24/04/07		
Gestation at date of sample	:	13 weeks 3 days (by dates) 11 weeks 6 days (by CRL scan)		
Gestation used	:	Scan estimate (CRL)		
Weight	:	64 kg		
Ethnic Origin	:	South Asian		
Nuchal measurement	:	1.2 mm	:	0.99 MoM
Total hCG (1T) level	:	91.2 iu/mL	:	0.92 MoM
PAPP-A level	:	2400 miu/L	:	1.22 MoM

INTERPRETATION

Screening result	:	Screen negative
Risk of Down's	:	1 in 29,000 (at term)
Comment	:	This test does not screen for neural tube defects

A screen negative result does not exclude the possibility of Down's syndrome, because screening does not detect all affected pregnancies

This is an Alpha report

Allows flexibility in the choice of serum and ultrasound markers

Nuchal translucency measurements are adjusted for crown-rump length and expressed as MoM values

Down's syndrome risks are estimated using the same multi-variate methodology which has been validated in second trimester screening

epidemiological monitoring

Monitoring and Improving the Performance of Screening

MONITORING THE FALSE POSITIVE RATE

Reports generated in requested period		
Type of report	**Number**	**Percent**
First maternal serum tests	3610	100.0%
Repeat maternal serum tests	0	0.0%
Updated maternal serum results	0	0.0%
Total	**3610**	**100.0%**

First maternal serum tests			
Screening result	**Reason**	**Number**	**Percent**
Positive	Increased risk of Down's syndrome	239	6.6%
	Increased risk of Down's and previous NTD	2	0.1%
	Increased risk of Down's and raised AFP	2	0.1%
	Raised AFP	44	1.2%
	Previous Down's only	2	0.1%
	Previous NTD only	15	0.4%
Uninterpretable	Test done too early	15	0.4%
	Test done too late	6	0.2%
	Grand multiple pregnancy	1	0.0%
Negative		3284	91.0%
Total		**3610**	**100.0%**
Increased risk of trisomy 18 was reported in 28 first tests (0.78%)			

Age	N	%	Cum %
<=15	7	0.19	0.19
16	8	0.22	0.42
17	35	0.97	1.39
18	46	1.27	2.66
19	72	2.00	4.66
20	121	3.35	8.01
21	128	3.55	11.55
22	140	3.88	15.43
23	138	3.82	19.26
24	210	5.82	25.08
25	226	6.26	31.34
26	251	6.95	38.29
27	262	7.26	45.55
28	294	8.15	53.70
29	267	7.40	61.10
30	255	7.07	68.16
31	249	6.90	75.06
32	202	5.60	80.66
33	154	4.27	84.93
34	145	4.02	88.94
35	122	3.38	92.32
36	93	2.58	94.90
37	41	1.14	96.04
38	48	1.33	97.37
39	41	1.14	98.50
40	21	0.58	99.09
41	15	0.42	99.50
42	10	0.28	99.78
43	6	0.17	99.94
44	2	0.06	100.00
45	0	0.00	100.00
46	0	0.00	100.00
47	0	0.00	100.00
48	0	0.00	100.00
49	0	0.00	100.00
50	0	0.00	100.00
51	0	0.00	100.00
52	0	0.00	100.00
53	0	0.00	100.00
54	0	0.00	100.00
>=55	0	0.00	100.00
-	3609	100.00	-

Median age specified

αlpha's monitoring features allow you to determine the observed positive rate in your population...

...and compare it with the expected false-positive rate for a population with the same age distribution as your own, at specified cut-offs (1 in 300 in this example)

Expected number of Down's syndrome term pregnancies in the absence of screening and selective abortion, based on the age distribution of the screened population	5.58
Equivalent birth prevalence	1.55 per 1000

αlpha tabulates and plots the age distribution of women screened. This is used to generate the table of expected screening performance

Quad test (MS-AFP, uE3, T-hCG and Inh-A with maternal age)												
Gestation	**Based on dates**						**Based on scan**					
Weight adjustment	**Unadjusted**			**Adjusted**			**Unadjusted**			**Adjusted**		
Risk cut-off (term)	**DR (%)**	**FPR (%)**	**OAPR**	**DR (%)**	**FPR (%)**	**OAPR**	**DR (%)**	**FPR (%)**	**OAPR**	**DR (%)**	**FPR (%)**	**OAPR**
1 in 100	58.9	2.3	1:25	59.1	2.3	1:25	66.2	2.1	1:20	67.2	2.1	1:20
1 in 150	66.0	3.6	1:35	65.9	3.6	1:35	71.1	3.0	1:27	71.9	2.9	1:26
1 in 200	70.3	4.7	1:43	70.2	4.7	1:43	75.2	4.1	1:35	75.9	4.0	1:34
1 in 250	73.7	5.9	1:51	73.7	5.9	1:52	78.0	5.0	1:42	78.6	4.9	1:41
1 in 300	76.4	7.0	1:59	76.3	7.0	1:59	80.0	5.8	1:47	80.4	5.7	1:46
1 in 350	78.5	8.0	1:66	78.4	8.1	1:66	81.4	6.6	1:52	81.9	6.5	1:51
1 in 400	80.1	9.0	1:72	80.0	8.9	1:72	82.8	7.3	1:57	83.2	7.2	1:56
1 in 450	81.3	9.8	1:78	81.4	9.9	1:78	83.9	8.1	1:62	84.4	8.0	1:61
1 in 500	82.5	10.7	1:83	82.5	10.7	1:84	85.0	8.9	1:68	85.4	8.7	1:66

MONITORING MEDIANS

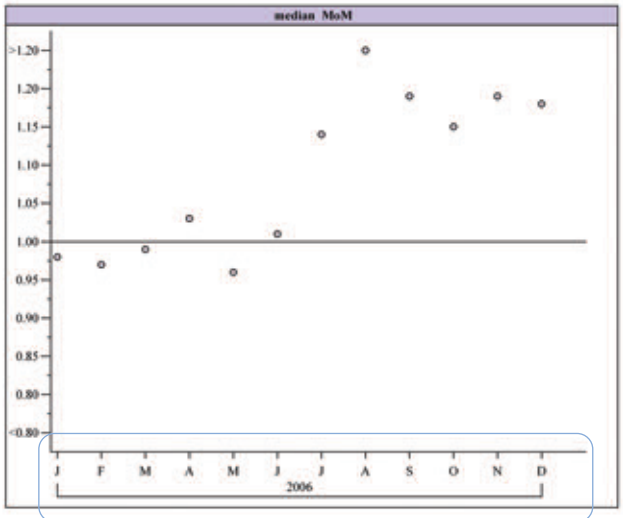
Gestational age			Median T-hCG	
Completed weeks	Median days	Number	Units	MoM
14	103.5	4	21.00	0.426
15	111.0	113	42.00	1.205
16	114.0	1176	34.95	1.161
17	121.0	215	31.00	1.240
18	129.0	77	24.00	1.160
19	136.0	35	25.00	1.289
20	142.5	26	23.4	1.294
21		0		
22	158.0	2	21.00	1.251
14 - 22		1648		1.175 *
			10th centile	0.564
			90th centile	2.405
* = value falls outside 95% confidence interval around 1.0 MoM			S.D. (log10 MoM)	0.246

Gestation-specific tabulations allow you to evaluate the stability of the medians, and to inspect the change in the serum marker levels with increasing gestational age

Month	Number	Median reported MoM
Jan 2006	291	0.980
Feb	293	0.970
Mar	336	0.990
Apr	355	1.030
May	277	0.960
Jun	282	1.010
Jul	262	1.140 *
Aug	273	>1.200 *
Sep	313	1.190 *
Oct	261	1.150 *
Nov	317	1.190 *
Dec	225	1.180 *
	3485	1.070 *

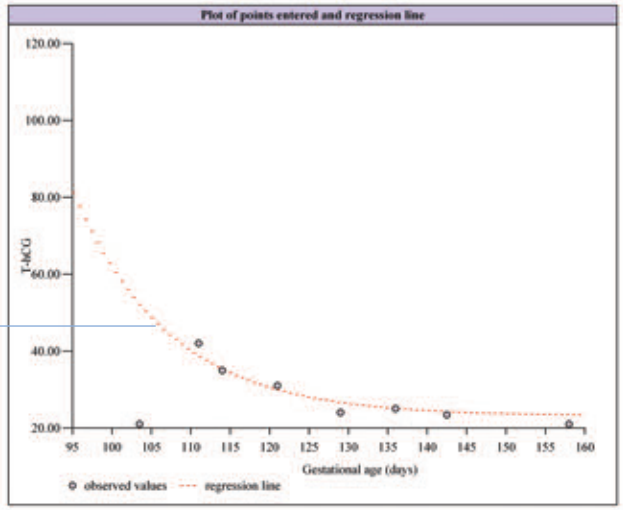
αlpha highlights median MoM values which fall outside the 95% confidence interval around 1.0 MoM. The 2006 values illustrated are too high

Selected options	
Date range	From 01/01/06 to 31/12/06
Codes	Include all codes



αlpha provides a graphical indication of median MoM values from month to month so that long-term trends and fluctuations in marker levels can be monitored

Weighted regressions can be generated automatically from the tabulated data. αlpha calculates the coefficients for the regression equation which determines the normal median marker level at each gestational age

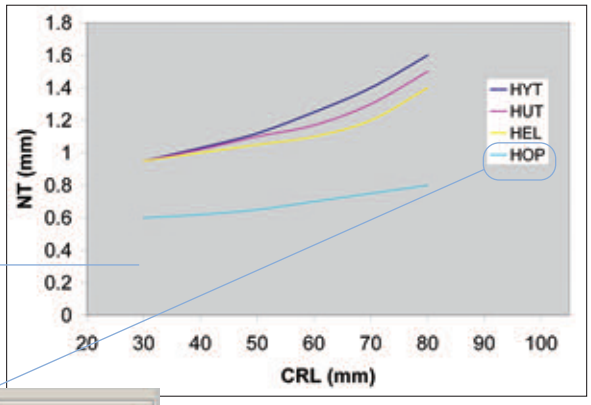


Regression line equation
Median T-hCG = A + B * e**(-0.08268* (GA(days) -100))
A = 23.10205
B = 38.44347

quality control of nuchal translucency measurement

Sonographer-specific nuchal translucency medians

αlpha has a number of features that help the user quantify and monitor nuchal translucency (NT) measurements for individual sonographers, and where appropriate, allow for systematic measurement differences between sonographers, so improving screening performance

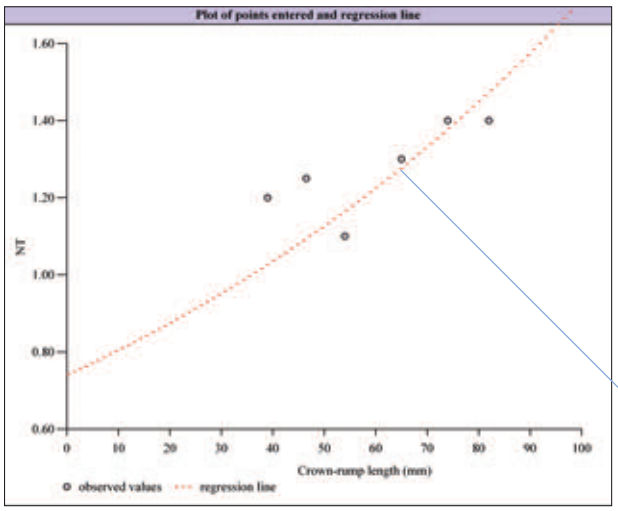


There may be systematic differences in NT measurements made by different sonographers

4 matching sonographers

Code	Sonographer name
HOP	Rachel Hopkins
HEL	Stewart Helford
HUT	Maurice Hutchins
HYT	Janice Hyatt

αlpha allows the user to record the identity of the sonographer for each NT measurement



Regression line equation
Median NT = A * B**CRL(mm)
A = 0.741082
B = 1.008428
This represents a 11.5% increase in median NT per week.

CRL(mm)	Number of samples	Expected median NT	Observed median NT
39	1	1.028	1.200
46.5	12	1.095	1.250
54	55	1.166	1.100
65	78	1.279	1.300
74	39	1.379	1.400
82	8	1.475	1.400

NT medians	A	B
Median equation: NT / CRL (Overall)	0.4663890	1.0179050
Median equation: NT / CRL (AHD)	0.6834107	1.0104560
Median equation: NT / CRL (BCN)	0.9452036	1.0106340
Median equation: NT / CRL (HUT)	0.7410820	1.0084280

Selected options	
Date range	From 01/01/04 to 28/02/07
GA estimated by	Scan if available, dates otherwise
Ethnic groups	Overall
Codes	Requested sonographer codes: HUT

Crown-rump length (mm)			Median NT	
Group	Median	Number	Units	MoM
<20		0		
20 -		0		
30 -	39.0	1	1.20	1.288
40 -	46.5	12	1.25	1.155
50 -	54.0	55	1.10	0.937
60 -	65.0	78	1.30	0.881
70 -	74.0	39	1.40	0.779
80 -	82.0	8	1.40	0.713
90 -		0		
>100		0		
		193		0.879 *
			10th centile	0.682
			90th centile	1.217
			S.D. (log10 MoM)	0.098

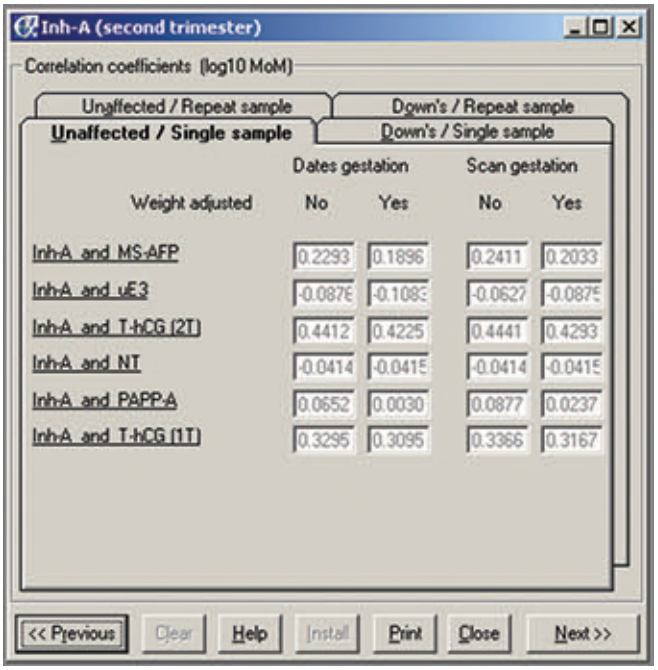
Sonographer-specific regressions of NT according to crown-rump length (CRL) measurement provide an indication of the rate of increase of the median NT measurement with gestational age

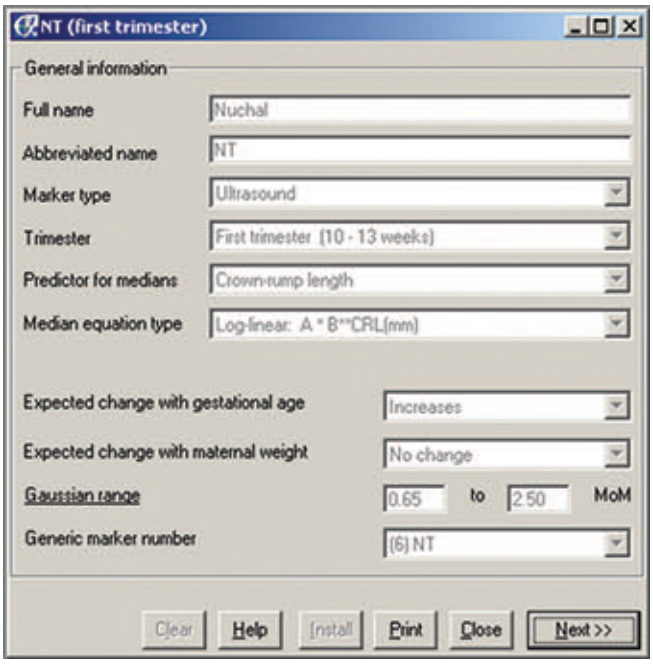
Sonographer-specific tabulations of NT measurements include an estimate of the standard deviation of NT MoM values, which can be compared with published estimates. This gives an indication of whether the precision of NT measurement is as expected

Coefficients of the normal median NT equation can be specified for each sonographer. αlpha automatically selects the appropriate coefficients for calculating the NT MoM, based on the sonographer code entered by the user

the αlpha marker library

αlpha is supplied ready to use for screening for Down's syndrome with AFP, uE3, hCG and inhibin A in the second trimester with NT, PAPP-A, hCG in the first trimester in any combination, and for AFP screening for NTD

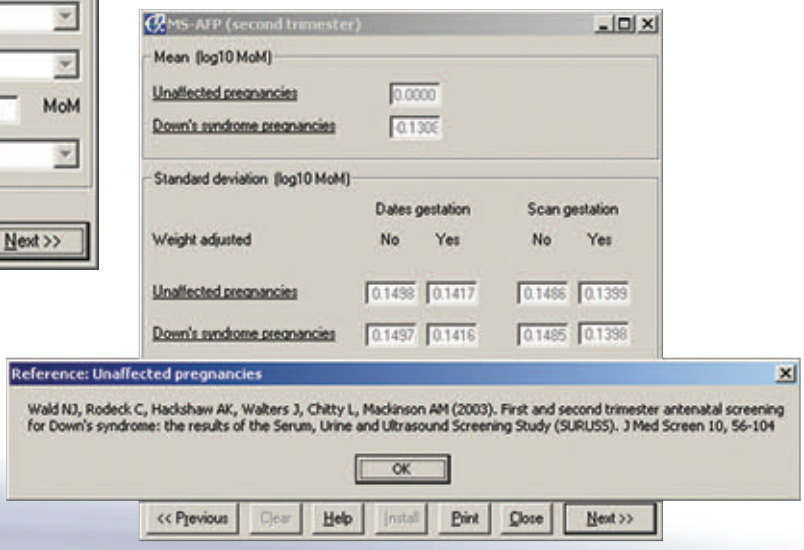




Statistical parameters relating to the markers are shown in the αlpha Marker Library

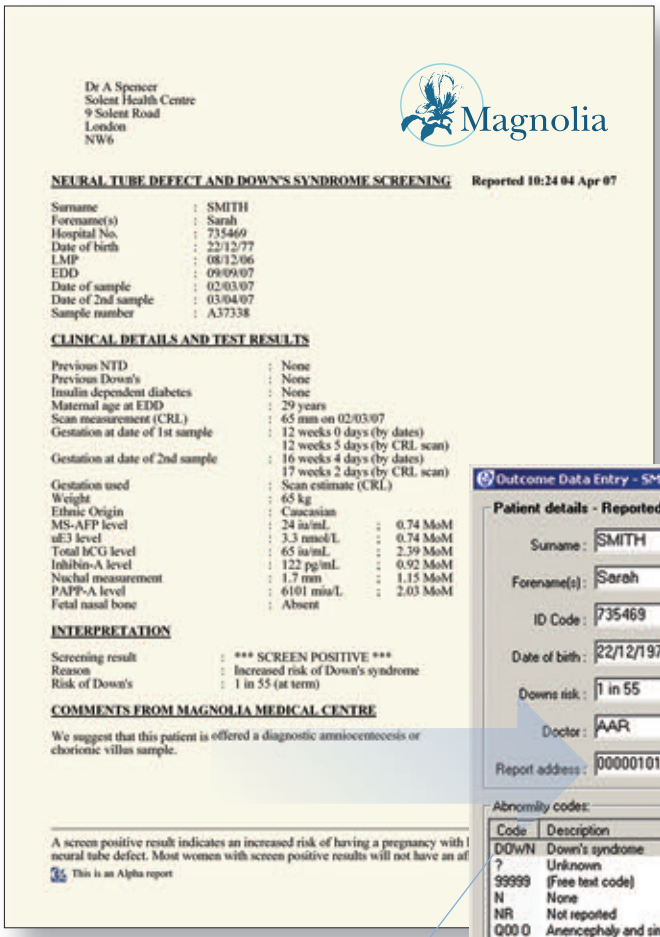
The αlpha Marker Library also serves as a valuable source of information relating to the screening markers, includes on-line help screens and a bibliography with key references

αlpha uses the latest statistical parameters for improved screening performance.



αlpha outcome

αlpha Outcome is now an integral part of αlpha. It gives users the ability to access the αlpha database and specify the outcomes of all pregnancies screened. It is a valuable management tool.



Dr A Spencer
Solent Health Centre
9 Solent Road
London
NW6

Magnolia

NEURAL TUBE DEFECT AND DOWN'S SYNDROME SCREENING Reported 10:24 04 Apr 07

Surname	SMITH
Forename(s)	Sarah
Hospital No.	735469
Date of birth	22/12/77
LMP	08/12/06
EDD	09/09/07
Date of sample	02/03/07
Date of 2nd sample	03/04/07
Sample number	A37338

CLINICAL DETAILS AND TEST RESULTS

Previous NTD	None	
Previous Down's	None	
Insulin dependent diabetes	None	
Maternal age at EDD	29 years	
Scan measurement (CRL)	65 mm on 02/03/07	
Gestation at date of 1st sample	12 weeks 0 days (by dates) 12 weeks 5 days (by CRL scan)	
Gestation at date of 2nd sample	16 weeks 4 days (by dates) 17 weeks 2 days (by CRL scan)	
Gestation used	Scan estimate (CRL)	
Weight	65 kg	
Ethnic Origin	Caucasian	
MS-AFP level	24 iu/mL	0.74 MoM
uE3 level	3.3 nmol/L	0.74 MoM
Total hCG level	65 iu/mL	2.39 MoM
Inhibin-A level	122 pg/mL	0.92 MoM
Nuchal measurement	1.7 mm	1.15 MoM
PAPP-A level	6101 miu/L	2.03 MoM
Fetal nasal bone	Absent	

INTERPRETATION

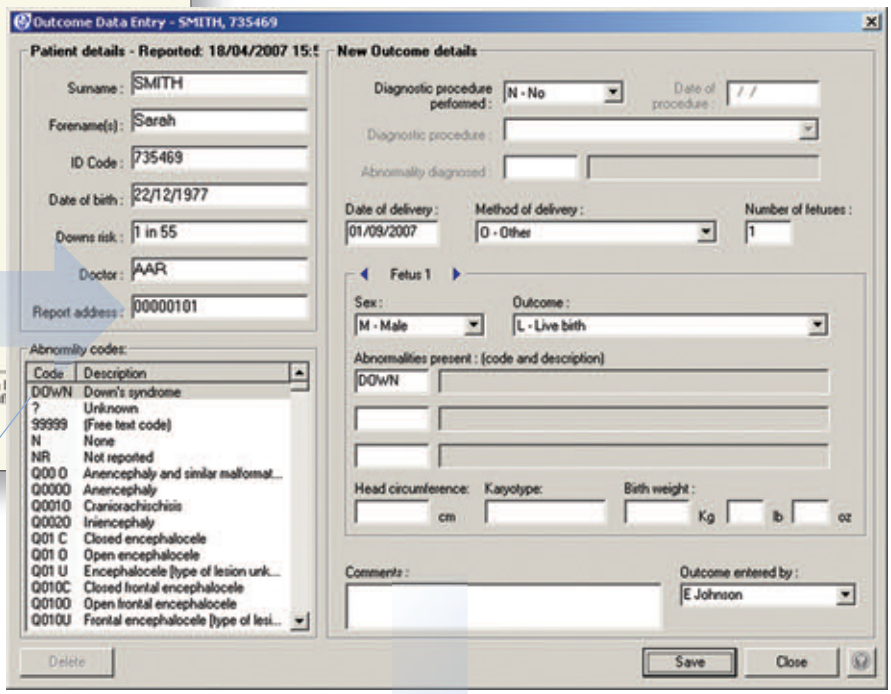
Screening result	*** SCREEN POSITIVE ***
Reason	Increased risk of Down's syndrome
Risk of Down's	1 in 55 (at term)

COMMENTS FROM MAGNOLIA MEDICAL CENTRE

We suggest that this patient is offered a diagnostic amniocentecesis or chorionic villus sample.

A screen positive result indicates an increased risk of having a pregnancy with neural tube defect. Most women with screen positive results will not have an af

This is an Alpha report



Outcome Data Entry - SMITH, 735469

Patient details - Reported: 18/04/2007 15:5

Surname: SMITH
Forename(s): Sarah
ID Code: 735469
Date of birth: 22/12/1977
Downs risk: 1 in 55
Doctor: AAR
Report address: 00000101

Abnormality codes:

Code	Description
DOWN	Down's syndrome
?	Unknown
99999	(Free text code)
N	None
NR	Not reported
Q00.0	Anencephaly and similar malformat...
Q0000	Anencephaly
Q0010	Craniorachischisis
Q0020	Iniencephaly
Q01.C	Closed encephalocele
Q01.O	Open encephalocele
Q01.U	Encephalocele [type of lesion unk...
Q010C	Closed frontal encephalocele
Q0100	Open frontal encephalocele
Q010U	Frontal encephalocele [type of lesi...

New Outcome details

Diagnostic procedure performed: N - No
Date of procedure: / /
Diagnostic procedure:
Abnormality diagnosed:
Date of delivery: 01/09/2007
Method of delivery: 0 - Other
Number of fetuses: 1

Fetus 1

Sex: M - Male
Outcome: L - Live birth

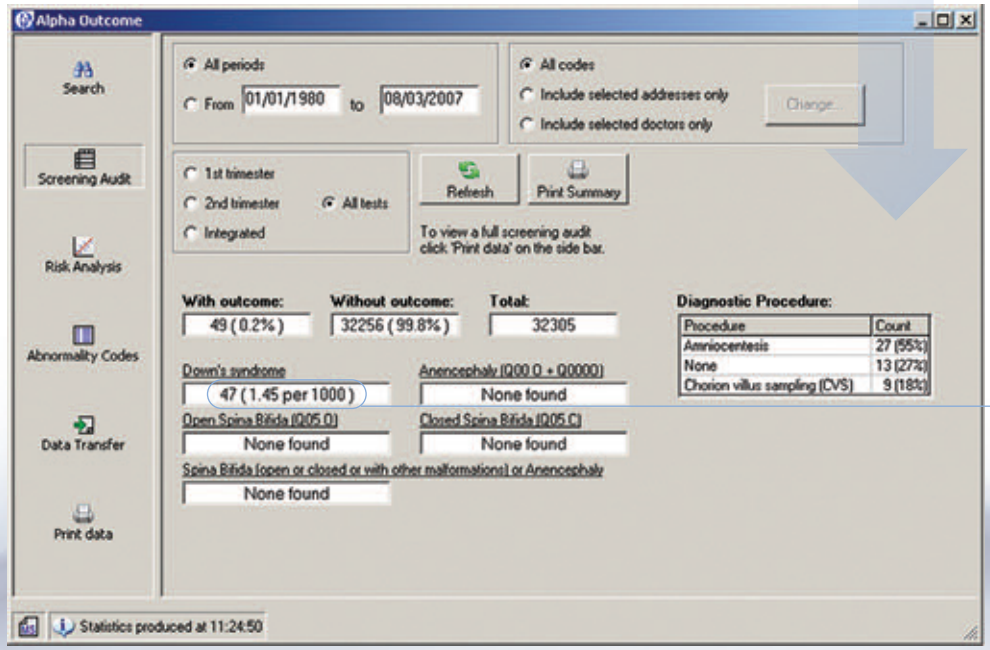
Abnormalities present: (code and description)
DOWN

Head circumference: cm
Karyotype:
Birth weight: Kg lb oz

Comments:
Outcome entered by: E Johnson

Delete | Save | Close

Record the presence of birth defects using the10th Edition of the International Classification of Diseases (ICD codes)



Alpha Outcome

Search
Screening Audit
Risk Analysis
Abnormality Codes
Data Transfer
Print data

All periods
From 01/01/1980 to 08/03/2007

All codes
Include selected addresses only
Include selected doctors only
Change...

1st trimester
2nd trimester
Integrated
All tests

Refresh
Print Summary

To view a full screening audit click 'Print data' on the side bar.

With outcome:	Without outcome:	Total:
49 (0.2%)	32256 (99.8%)	32305

Diagnostic Procedure:

Procedure	Count
Amniocentesis	27 (55%)
None	13 (27%)
Chorion villus sampling (CVS)	9 (18%)

Down's syndrome: 47 (1.45 per 1000)
Anencephaly (Q00.0 + Q0000): None found
Open Spina Bifida (Q05.0): None found
Closed Spina Bifida (Q05.C): None found
Spina Bifida (open or closed or with other malformations) or Anencephaly: None found

Statistics produced at 11:24:50

Produce summaries of pregnancies with specified abnormalities

validating method using alpha outcome

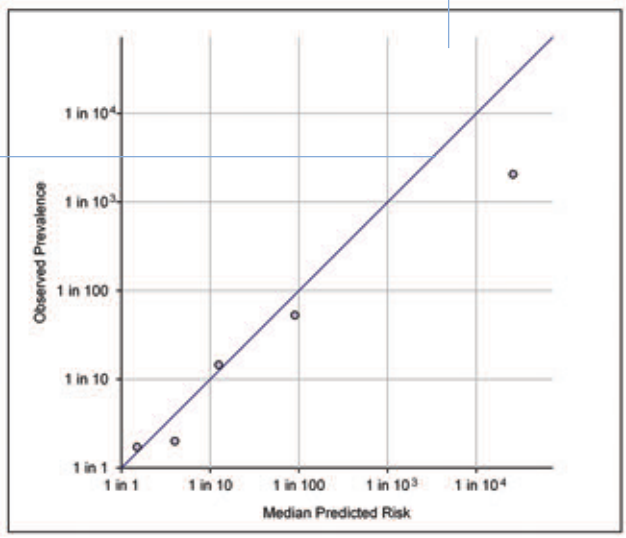
Studies have demonstrated that risk estimates for Down's syndrome produced by αlpha are accurate. Now αlpha users can perform this validation for themselves provided a sufficiently large number of women have been screened. The technique is a complete validation of the screening method.

With αlpha Outcome, it is possible to tabulate and plot a graph of the observed prevalence of Down's syndrome according to the median risk in groups of pregnancy ranked by the predicted risk

The diagonal line represents perfect agreement between the predicted risk of Down's syndrome and the birth prevalence of Down's syndrome in the absence of screening

In a single step, this provides an overall validation of the screening method

Recent studies have shown that there is close agreement between the risk of Down's syndrome predicted by αlpha and the observed birth prevalence of Down's syndrome in the absence of screening



Predicted risk at mid trimester		Observed frequency		
Category	Median	Down Syndrome (DS)	Unaffected	Observed prevalence*
>1 in 2	1 in 1.5	7	5	1 in 1.71
1 in 5 -	1 in 4	5	5	1 in 2
1 in 20 -	1 in 12.5	2	27	1 in 14.5
1 in 140 -	1 in 90	3	155	1 in 52.7
<1 in 140	1 in 26000	3 (3.9)[1]	8024	1 in 2060
All	1 in 24000	20 (20.9)[1]	8216	1 in 394

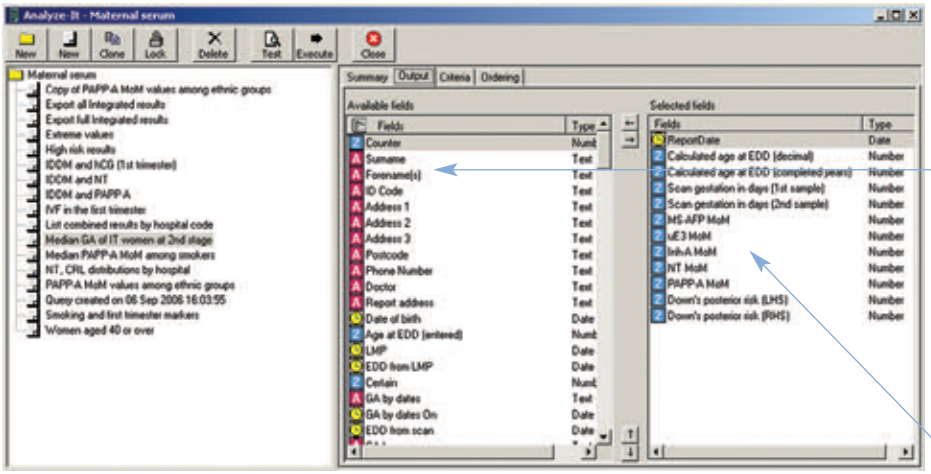
Detection Rate	False Positive Rate	OAPR*
85 %	2.4 %	1 : 12

* OAPR = The odds of being affected given a positive result.
* 1 in (DS + Unaffected) / DS
[1] Allowing for the spontaneous fetal loss of affected pregnancies from mid-trimester to term.

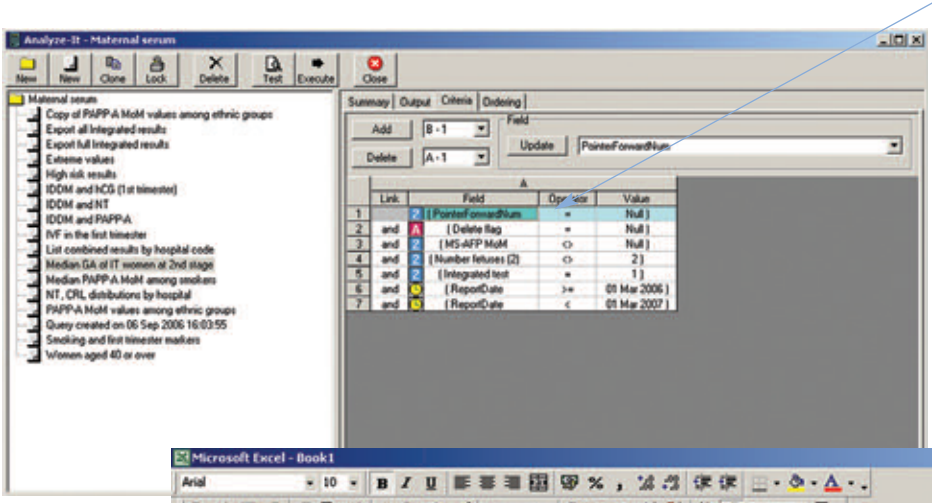
analyze-it™

- Analyze-it enables users to produce tabulations of their screening data directly from αlpha
- Analyze-it is flexible so that users can define exactly what subsets of the data they wish to tabulate, for example all diabetic women with PAPP-A MoMs above 3.0 who weigh over 70kg

In addition αlpha's data transfer options provide the user with an easy and flexible method of transferring selected items to most other popular databases and spreadsheets if required

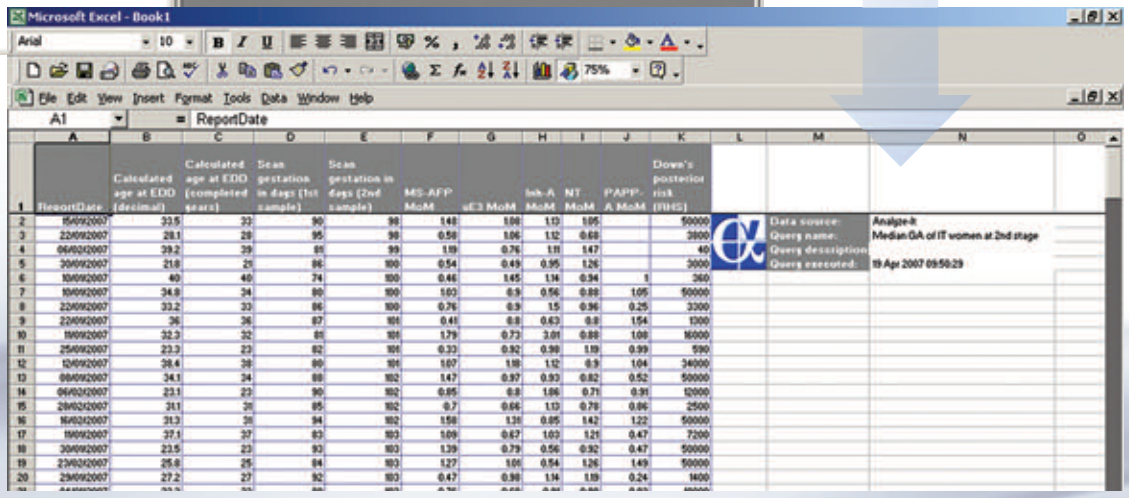


αlpha displays a list of the database fields available for transfer, including patient data, clinical details, test results, MoMs and risks



You select the fields which you want to transfer and include any special criteria. In this example, all women screened with the Integrated test in a certain date range are exported

αlpha transfers the selected data directly to Microsoft™ Excel to provide you with the tabulation you require



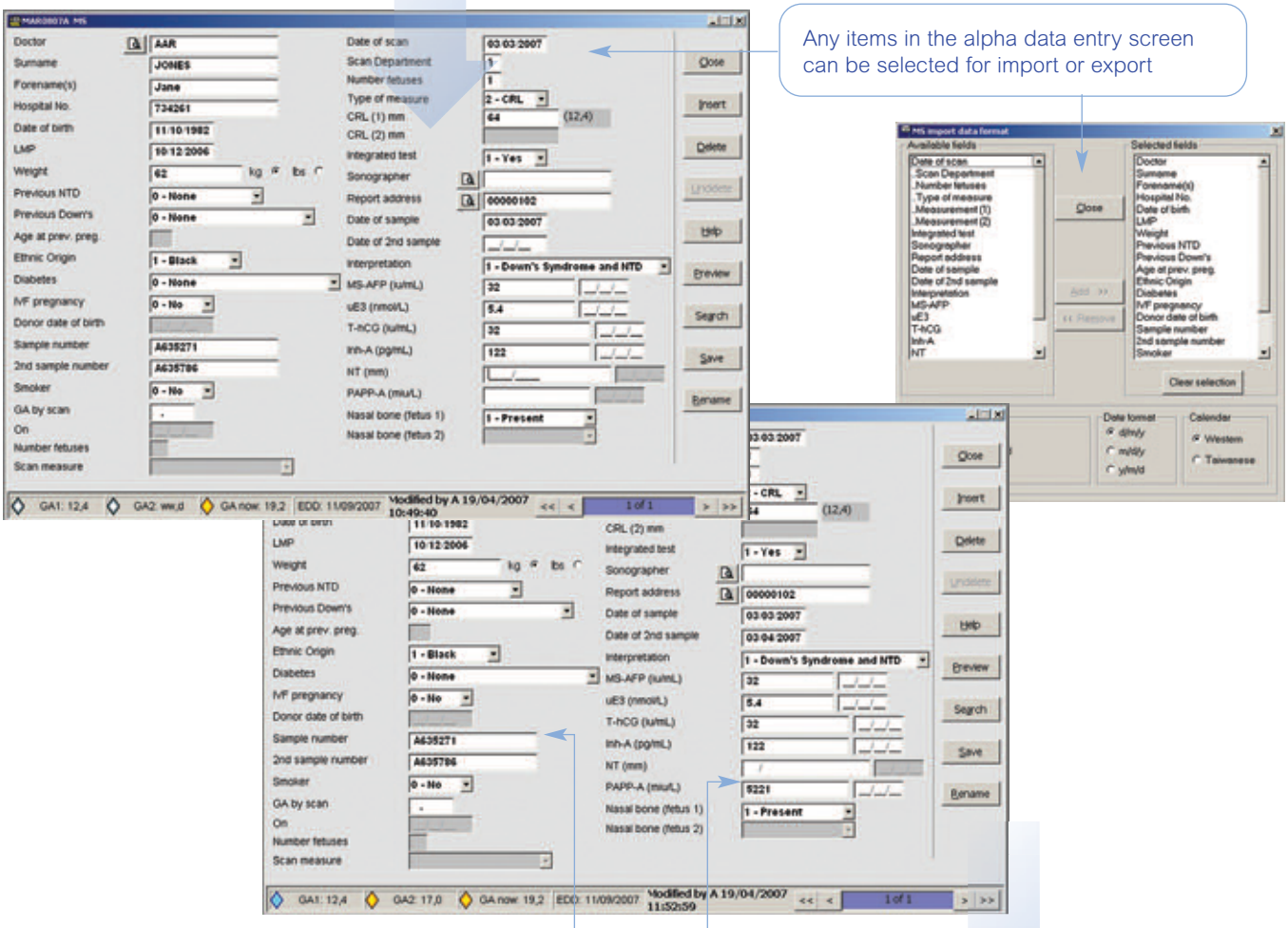
interfacing αlpha with lab systems

αlpha provides many ways to import and export data from laboratory information systems and import data from laboratory equipment

- Import patient data from other systems
- Import test results from laboratory equipment and laboratory management systems
- Export patient data to laboratory management systems

Data can be imported from a comma separated variable text file

AAR,JONES,734261,11/10/82,10/12/86,62,0,0,0,1,0,A635271,A635786,0



If required, output from an assay machine can be automatically merged with the data, using the sample number to identify the patient

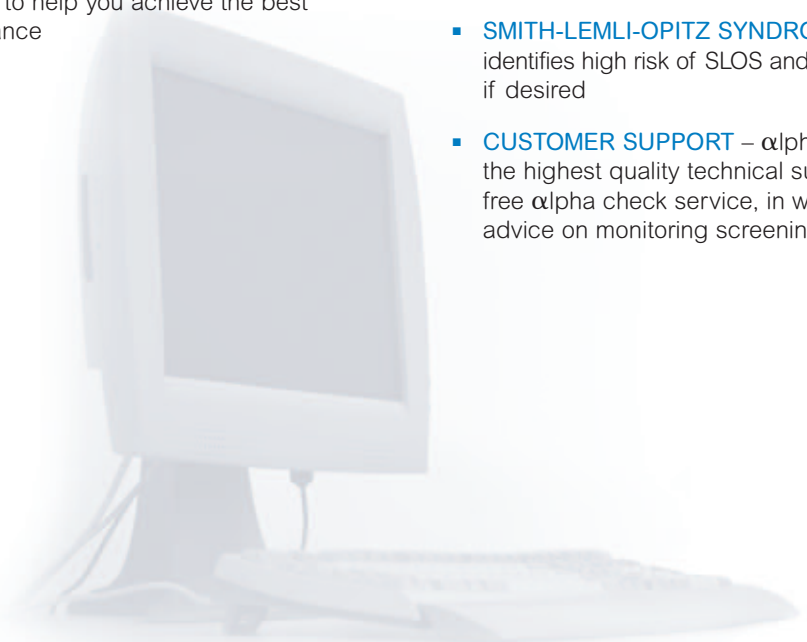
CODE	CONC
A635270	3343
A635271	5221
A635272	5232
A635273	3425
A635274	5234
A635275	4532
A635276	5323

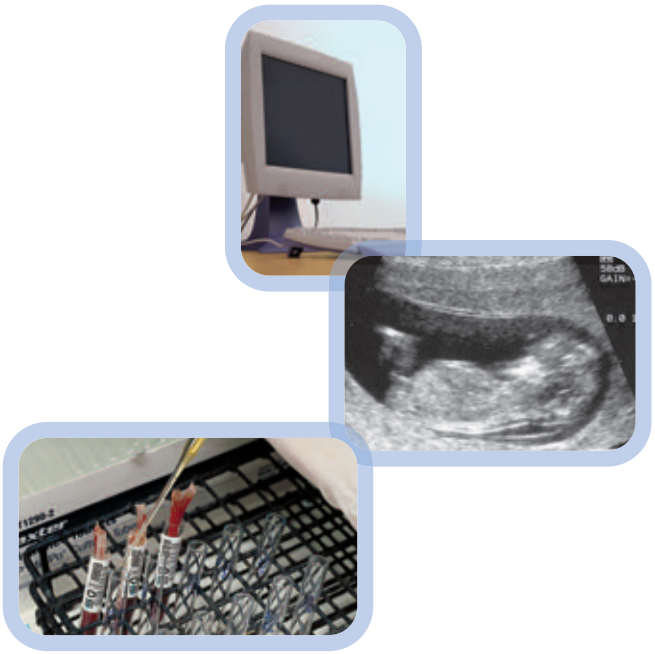
JONES,1.21,1.3,0.23,1.23,2212,2200

The screening results can be exported to a text file when the patient is reported.

what makes αlpha special?

- TRACK RECORD – αlpha, was originally developed by Professors Wald and Cuckle and launched in 1988. Professor Wald has continued to direct its development. It is now the world's leading software for Down's syndrome and NTD screening. Over 9 million women in 47 countries have been screened using αlpha
- SCIENTIFIC BASIS – αlpha is based on published scientific data and validated statistical methodology
- LEADER IN ITS FIELD – αlpha typically incorporates advances in screening ahead of its competitors
- INTEGRATED TEST – αlpha is licensed to use the Integrated Test, which uses screening markers from the first and second trimesters to give a single screening result. This is the safest and most effective screening method available
- SEQUENTIAL SCREENING – αlpha is licensed to perform sequential screening
- MONITORING – αlpha offers the best range of monitoring features to help you achieve the best screening performance
- FIRST TRIMESTER COMBINED TEST – αlpha allows screening using nuchal translucency and serum markers, either alone or in combination, between 10 and 13 weeks of pregnancy
- RECURRENT FALSE POSITIVES - αlpha is the only software to adjust for marker levels in previous pregnancies to reduce the recurrence of false positives
- EMPIRICALLY VALIDATED – Studies have shown that the risk of Down's syndrome produced by αlpha is accurate. The average risk in groups of pregnancies ranked by risk is in close agreement with the prevalence observed in practice
- OUTCOME – αlpha Outcome allows you to compare the risk of Down's syndrome predicted by αlpha with the observed prevalence in your population, providing an empirical validation of the screening method
- TRISOMY 18 – αlpha identifies high risk of trisomy 18 and prints the risk estimate, if desired
- SMITH-LEMLI-OPITZ SYNDROME (SLOS) – αlpha identifies high risk of SLOS and prints the risk estimate, if desired
- CUSTOMER SUPPORT – αlpha users benefit from the highest quality technical support, including our free αlpha check service, in which we provide expert advice on monitoring screening performance





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