

PRISCA Prenatal Risk Assessment*

SIEMENS

Maternal Fetal Health Screening

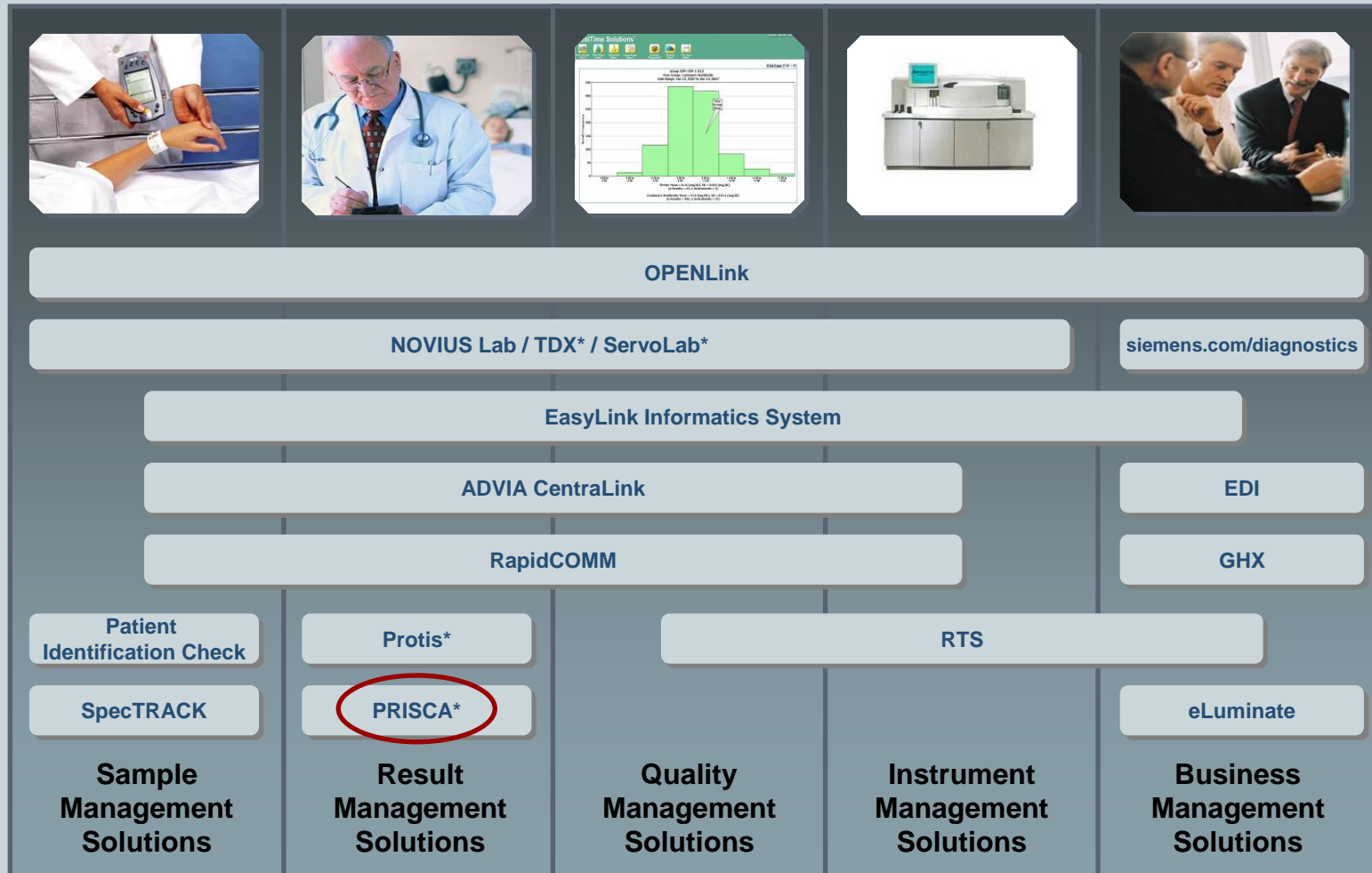
*Decision Support Tools for
Calculating and Reporting of
Maternal Screening Results*



**Note: Available outside the US Only*

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IT Solutions From Siemens



* Products only available outside USA

An Array of Supporting Services and Solutions

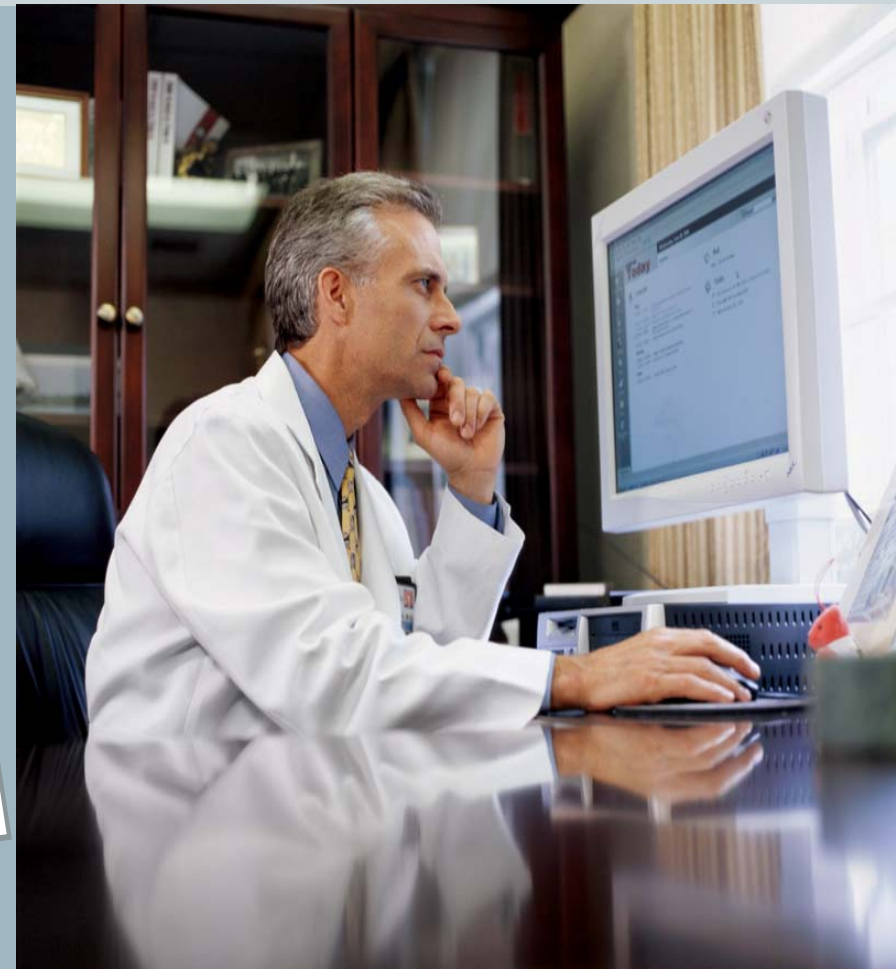


Maternal Screening Requires Decision Support Software

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Screening Program Parameters

1. Numerous “normal ranges” for various weeks of gestation
2. Numerous correction factors based on patient demographics
3. Incorporates lab results, patient history, and ultrasound
4. Multiple risk calculations and algorithms
5. Risk Factors determine next steps in care of patients



PRISCA Integrates Data from Multiple Healthcare Sources to Provide a Consolidated Patient Report

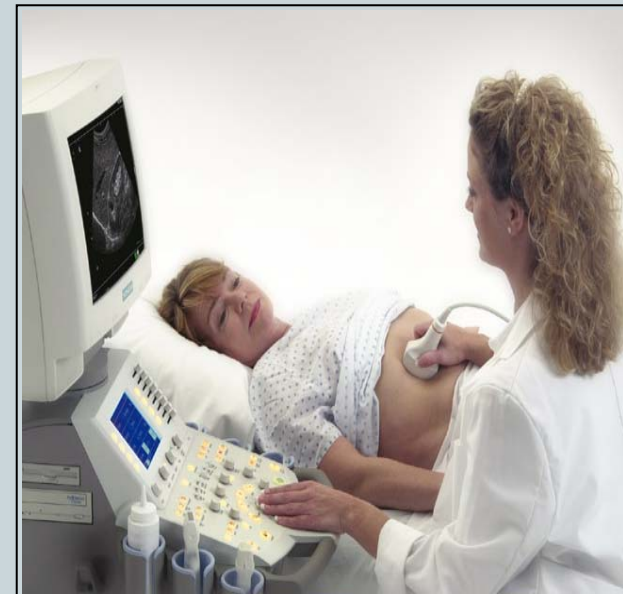
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**Patient
Demographics &
History**



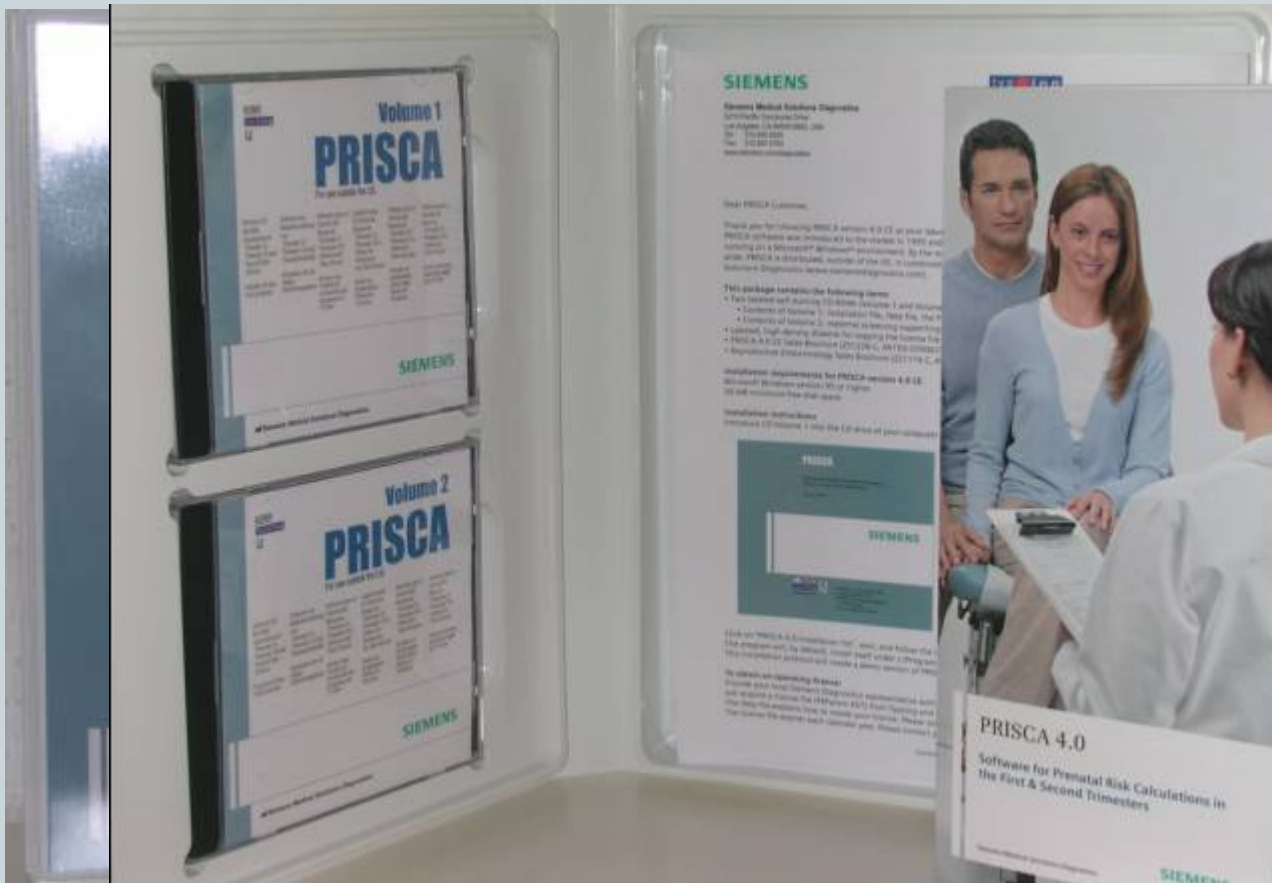
**Biochemical
Laboratory Results**



**Ultrasound
Measurements**

PRISCA 4.0

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PRISCA 4.0 is a CE certified software application for Maternal Screening Risk Calculation for Trisomy 21, Trisomy 18 and Neural Tube Defects.

PRISCA Support For Siemens Immunoassay Systems

SIEMENS



IMMULITE® 2500
Immunoassay System



IMMULITE® 2000
Immunoassay System



IMMULITE® 2000 XPi
Immunoassay System



IMMULITE® 1000
Immunoassay System

PRISCA Supports First Trimester Screening Approaches Combined with Ultrasound

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Measured at 9 weeks to 13 weeks and 6 days



**IMMULITE®
Systems**

Free β -hCG

Pregnancy Associated Plasma Protein (PAPP-A)

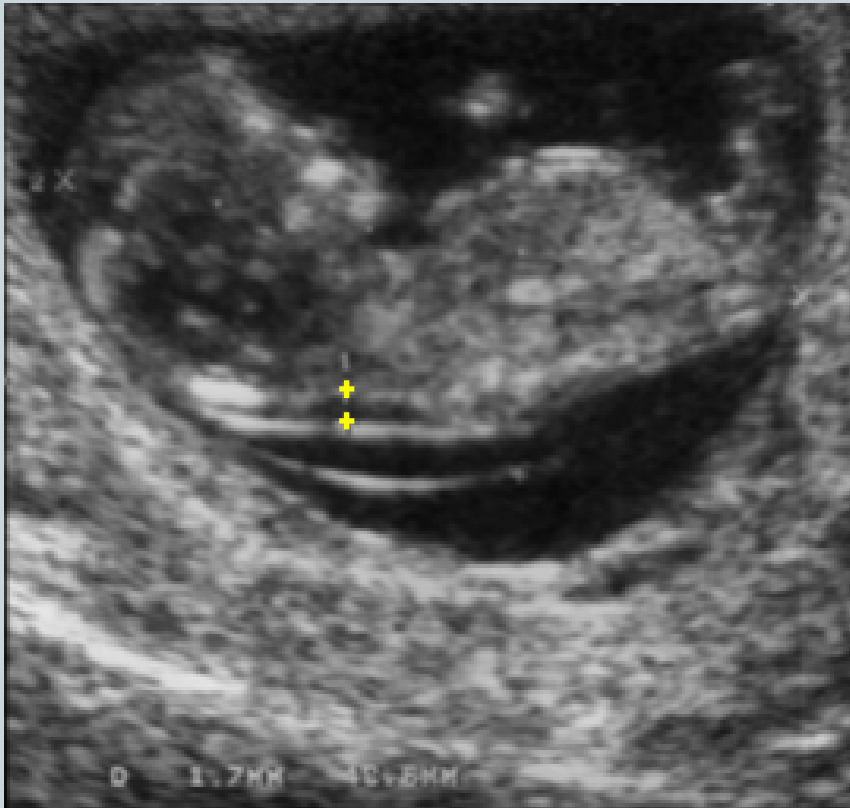


Gestational Age (Crown-Rump Length)

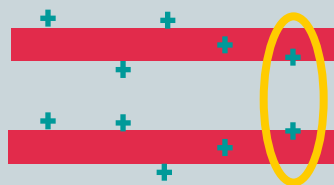
Nuchal Translucency

Nuchal Translucency Measurements

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- Gestation **9-13** wks
- CRL **45-84** mm
- Mid-sagittal view
- Image size **>75%**
- Neutral position
- Away from amnion
- Maximum lucency
- Calipers **on-to-on**



PRISCA Supports Second Trimester Screening Approaches Combined with Ultrasound

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**IMMULITE®
Systems**

Double Test (AFP and hCG)

Triple Test (AFP, hCG, and uE3)

Quadruple* Test (AFP, hCG, uE3, Inhibin A)



Gestational Age (Crown-Rump Length)

Nuchal Translucency

*Ability to enter Inhibin A results to enable quadruple testing requires PRISCA v 5.0 (in development)

Why 1st Trimester or 2nd Trimester Screening?

2nd Trimester

Well-established correction factors

Well-established algorithms

Extensive databases

Risks for Tr21, Tr18 and NTD

Specimen stability

1st Trimester

Earlier in pregnancy

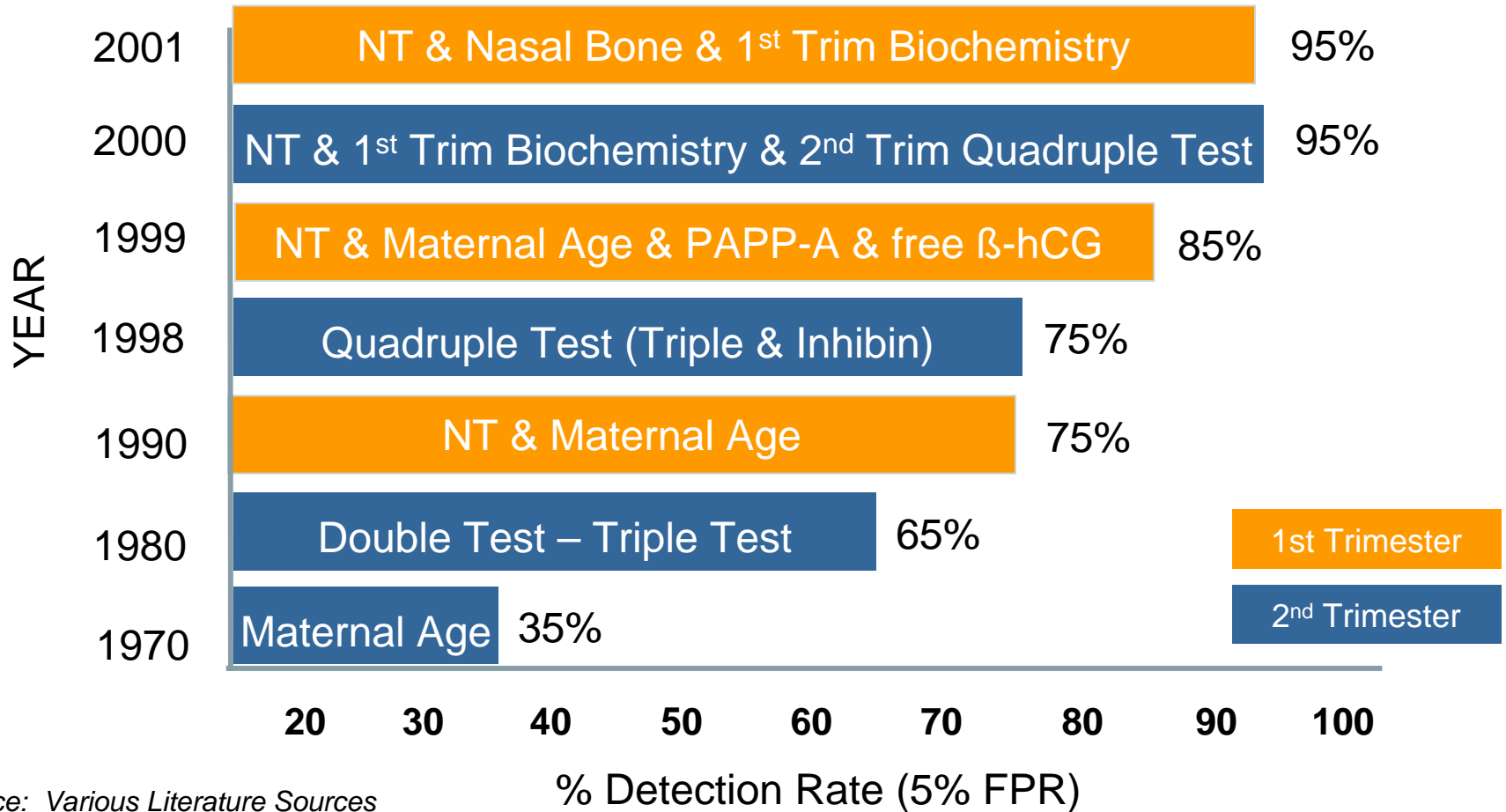
Higher detection rate with NT

Diagnostic Procedure by CVS

Correction factors
not well established

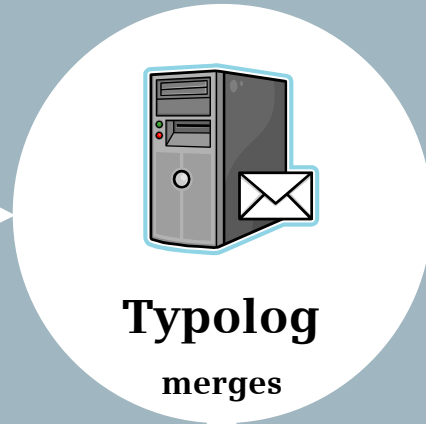
Lacks NTD screen by AFP

Summary of screening test performance



Source: Various Literature Sources

Shared Database for Quality Management



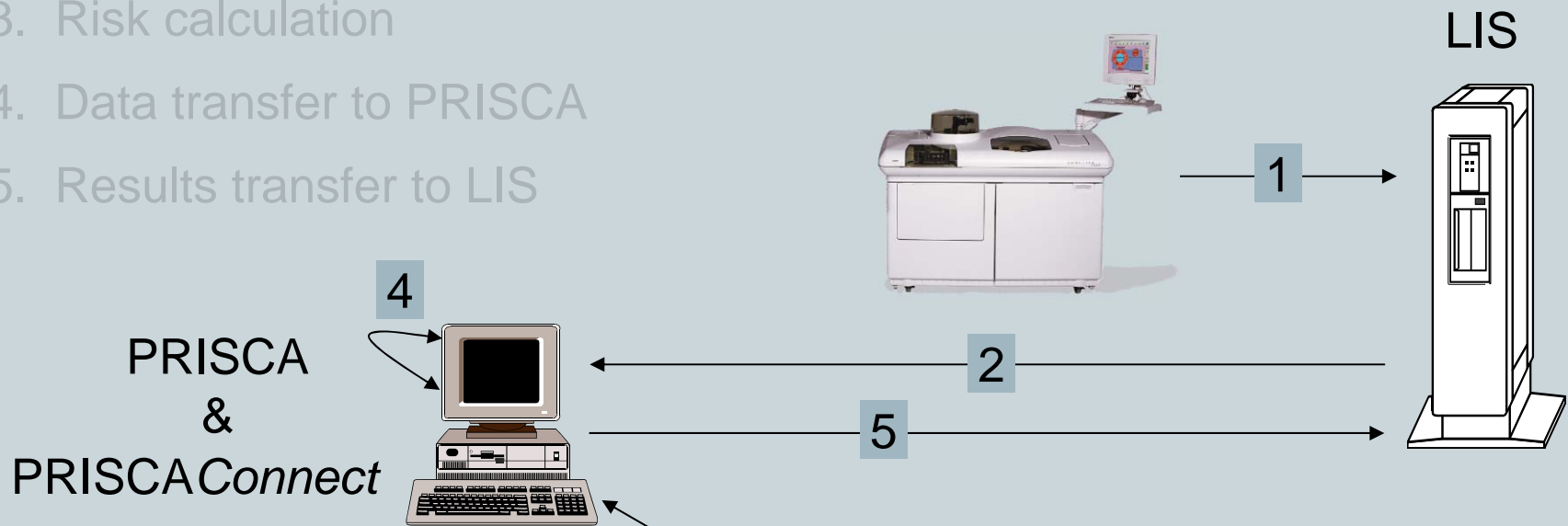
- **Basic statistics**
 - Medians, percentiles, regressions, standard deviations, confidence intervals
- **Interlaboratory Comparison**
 - Individual lab with all other labs
 - Tabular and graphical visualisation



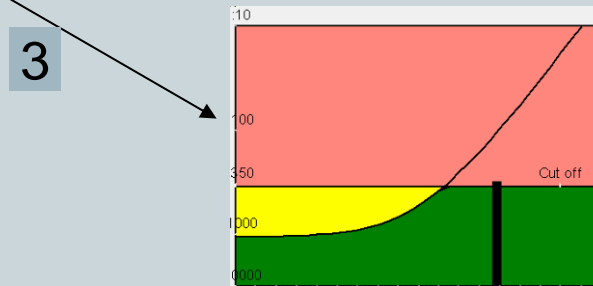
PRISCAConnect CE Software

– A fully automated solution for risk assessment

1. Bidirectional link instrument - LIS
2. Data transfer from LIS to PRISCAConnect
3. Risk calculation
4. Data transfer to PRISCA
5. Results transfer to LIS



Advantages:
Safety
Automation
Efficiency



PRISCAConnect Validation

- Newly calculated risks move into the validation grid.
- All records without problems move into the OK records grid
- Multiple options for validation
- Validate OK records and send back to LIS.

The screenshot shows the PRISCAConnect Version 1.0.1.72 interface. On the left, there are two progress bars: 'Total Progress' (4/4) and 'PRISCAConnect -> Unidex' (1/4). The main area is divided into two sections: 'OK Records' and 'Problem Records'.

OK Records Table:

Info	LastName	PatientCode	SampleCode	Trim	Bioch.Risk	Comb.Risk	NT
Check!	TEST004	PC004	SC004	2	87		
	TEST005	PC005	SC005	2	861		

Problem Records Table:

LastName	PatientCode	Step	Reason
TEST001	PC001	4	Risks in PRISCA not calculated
TEST002	PC002	4	Risks in PRISCA not calculated
TEST003	PC003	4	Risks in PRISCA not calculated

At the bottom, a red box highlights the validation controls: 'Validate', 'Validate All', 'Unvalidate', 'Unvalidate All', and 'Continue without sending'.

PRISCAConnect

- All other records move to the Problem records grid.
- Double-clicking a record gives further details about record

PRISCAConnect Version 1.0.1.72

Connect Continue Resend Exit

Progress

Total Progress: 4/4
PRISCAConnect -> Unidex: 1/4

OK Records

Info	LastName	PatientCode	SampleCode	Trim	Bioch.Risk	Comb.Risk	NT
Check!	TEST004	PC004	SC004	2	87		
	TEST005	PC005	SC005	2	861		

Validate Validate All Unvalidate Unvalidate All Continue without sending

Problem Records

LastName	PatientCode	Step	Reason
TEST001	PC001		4 Risks in PRISCA not calculated
TEST002	PC002		4 Risks in PRISCA not calculated
TEST003	PC003		4 Risks in PRISCA not calculated

PRISCAConnect Patient details

- Patient details screen supports operator need for additional information during validation or investigation of problem records

Patient Details

PRISCA Data		Download Data	
Lastname	TEST005	Lastname	TEST005
First name	Firstname05	First name	Firstname05
DOB	27.03.1983	DOB	27.03.1983
Patient code	PC005	Patient code	PC005
Sample Code	SC005	Sample Code	SC005
Date	25.09.2008	Date	04.07.2008

PRISCA		Download	
Ident	Value	Ident	Value
SDAT	25.09.2008	SDAT	25.09.2008
AFP	35,2	AFP	35,2
HCG	35	HCG	35
AR21	1081,86		
BR21	861		
GADS	6		
GWSM	17		

Print Close

PRISCAConnect Provides a New Level of Automation for Maternal Screening Programs

SIEMENS

- LIS Connectivity for automation of risk assessments
- Eliminates/minimizes manually entered data
- Reduces risk of error
- Improves lab workflow and efficiency
- Improves labor efficiency
- Easy to use in daily routine
- Allows lab to send results to LIS for printing, archiving, and delivery to clinicians
- Customized flexibility for reporting
- CE certification

PRISCAConnect



Automation of Prenatal Risk Assessment Programs

PRISCA Software Provides



Easy-to-Use Interface

Flexibility

Security

Quality Control

Automation

For Your Prenatal Screening Program

Easy-to-Use Interface

Main Input Screen

- Demographics

- Ultra sound

- Biochemistry

- 1st trimester
- 2nd trimester

- Results

PRISCA

Record Service Special Information Help

List Patient Details

Last name: LN01000
 First name: FN01000
 Patient ID: PC01000
 Sample ID: SC01000
 Physician:
 Date of birth: 25.05.81 Age: 25,26
 Weight: 70,1
 Smoking: no
 diabetes: no
 ethnic origin: Caucasian
 IVF pregnancy: no

Sonographer:
 Number of fetuses: 1
 CRL: Date:
 Gestation age (date of scan):
 Date of sampling: 29.08.06
 Gestation age on the date of sampling: 16 + 5
 determination method: unknown
 Nuchal translucency:
 MoM:

Risk calculation at sampling date
 Age risk: 1:1068
 Biochemistry risk: AFP - HCG - uE3 - Inh: 1:1933
 Biochem. risk + NT
 NTD risk: <1:10000
 Risk for Tr.18: >1:50

Markers	Value	Median	MoM	Corrected MoM
Free B. hCG		13,32		
PAPP-A				
AFP	12,80	36,68	0,35	0,36
HCG	7,20	21,27	0,34	0,35
uE3	0,69	3,18	0,22	0,22
Inhibin-A	76,40	228,72	0,33	0,36

New
 Delete
 Save
 Sort
 Find
 Report
 Batch
 Re-calculate
 1000/1000
 Help
 Close

Flexibility

The screenshot shows the PRISCA software interface. A red circle highlights the 'Service' menu, which is open and lists the following options: Settings, Medians, Weight regression, Statistics, Export, Referring Doctors, Password, and IMMULITE Download. The main interface is divided into several sections:

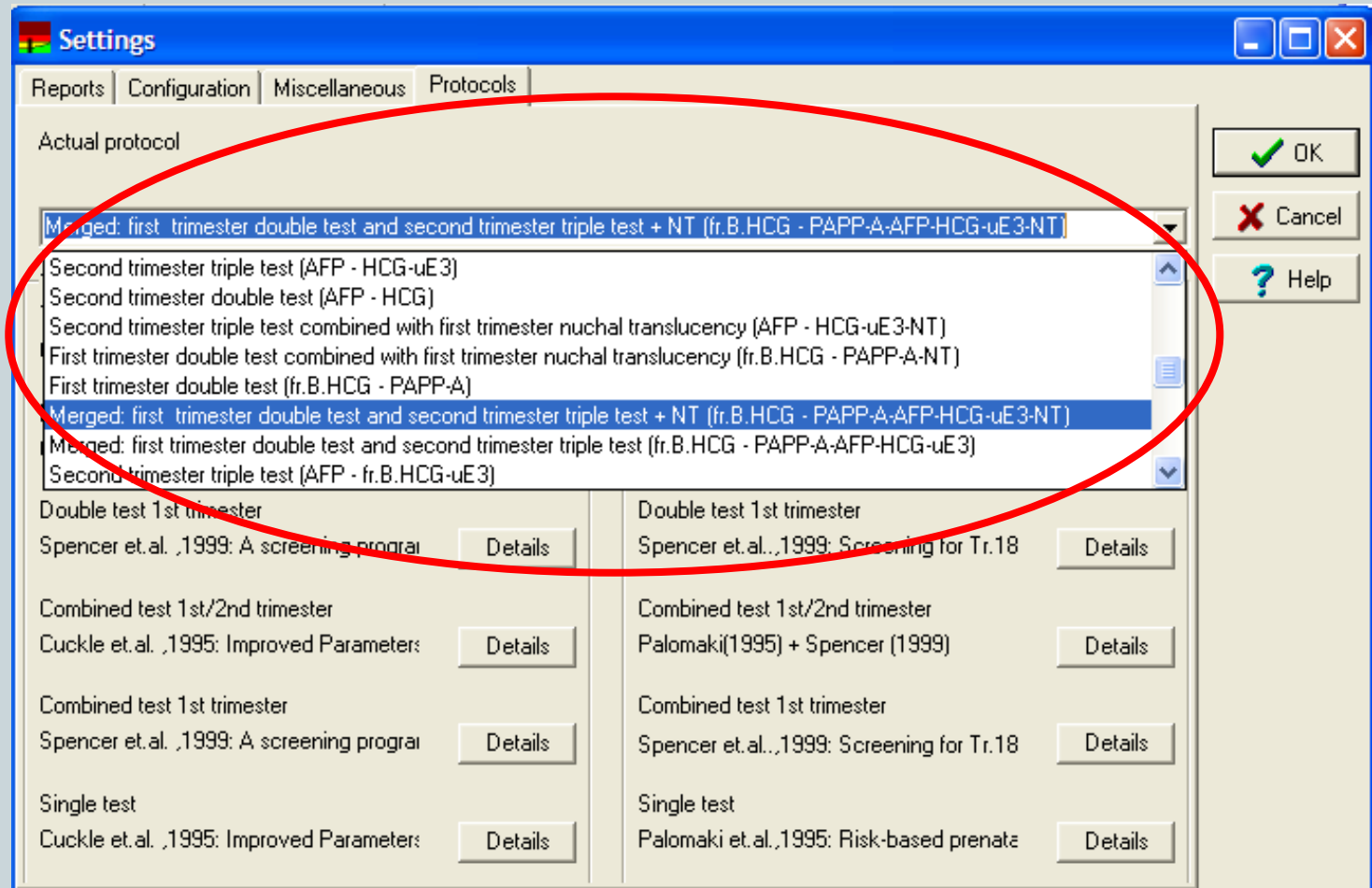
- Form Fields:** Includes fields for Sonographer, Number of fetuses (1), CRL, Date, Gestation age (date of scan), Date of sampling (16/07/07), Gestation age on the date of sampling (15 + 4), determination method (unknown), Nuchal translucency, and MoM.
- Demographics:** Includes fields for Last name, First name, Patient ID, Sample ID, Physician, Date of birth (24/11/77), Age (29,6), Weight (75), Smoking (yes), diabetes (unknown), ethnic origin (Caucasian), and IVF pregnancy (unknown).
- Table:** A table with 5 columns: Markers, Value, Median, MoM, and Corrected MoM. The data is as follows:

Markers	Value	Median	MoM	Corrected MoM
Free B. hCG		17,71		
PAPP-A				
AFP	20,00	25,88	0,77	0,81
HCG	54,00	27,67	1,95	2,65
uE3	6,15	8,22	0,75	0,79
- Risk Calculation:** Shows 'Risk calculation at sampling date' with 'Age risk 1:741' and 'Biochemistry risk AFP - HCG - uE3 1:210' (highlighted in red). Below this is 'Biochem. risk + NT' and 'NTD risk 1:5894'. At the bottom, 'Risk for Tr.18 <1.10000' is highlighted in green.
- Navigation:** A vertical toolbar on the right contains buttons for New, Delete, Save, Sort, Find, Report, Batch, Re-calculate, 4/4, Help, and Close.

Flexibility – Selection of a screening protocol

Select A Screening Protocol:

- 1st trimester
- 2nd trimester
- Single tests
- Combined



Flexibility - Determining the Gestation age

Gestation Age

Determination By:

- CRL
- Robinson & Fleming
- Own table
- By BPD
- Hadlock
- Own table
- Scan date
- Sample date
- Delivery date
- Conception date
- LMP

Data for the determination of the gestation age				
Name: FN1001 LN1001				
Patient ID: PC1001				
Method	Ultrasound data	Calculated gestational age week+days Scan date	Calculated gestational age week+days Sample Date	Select
For nuchal translucency screening: Enter CRL value				
CRL Robinson	57	12 + 1	14 + 3	<input checked="" type="radio"/>
CRL date	26.09.06			
For nuchal translucency screening: Enter CRL value				
CRL own table				<input type="radio"/>
CRL date				
BPD Hadlock				
BPD date				<input type="radio"/>
BPD own table				
BIP date				<input type="radio"/>
Use this option, if you do not know, if the scan method has was BPD or CRL. No nuchal translucency screening possible!				
Ultrasound date				<input type="radio"/>
Sample Date	12.10.06		14 + 3	<input type="radio"/>
Delivery date	09.04.07		14 + 3	<input type="radio"/>
Date of conception				<input type="radio"/>
Last Menstrual Period				<input type="radio"/>
		Cycle length	28	

Flexibility - Data overview page

Searching

Sorting

Selecting

Batch printing

Historical reports

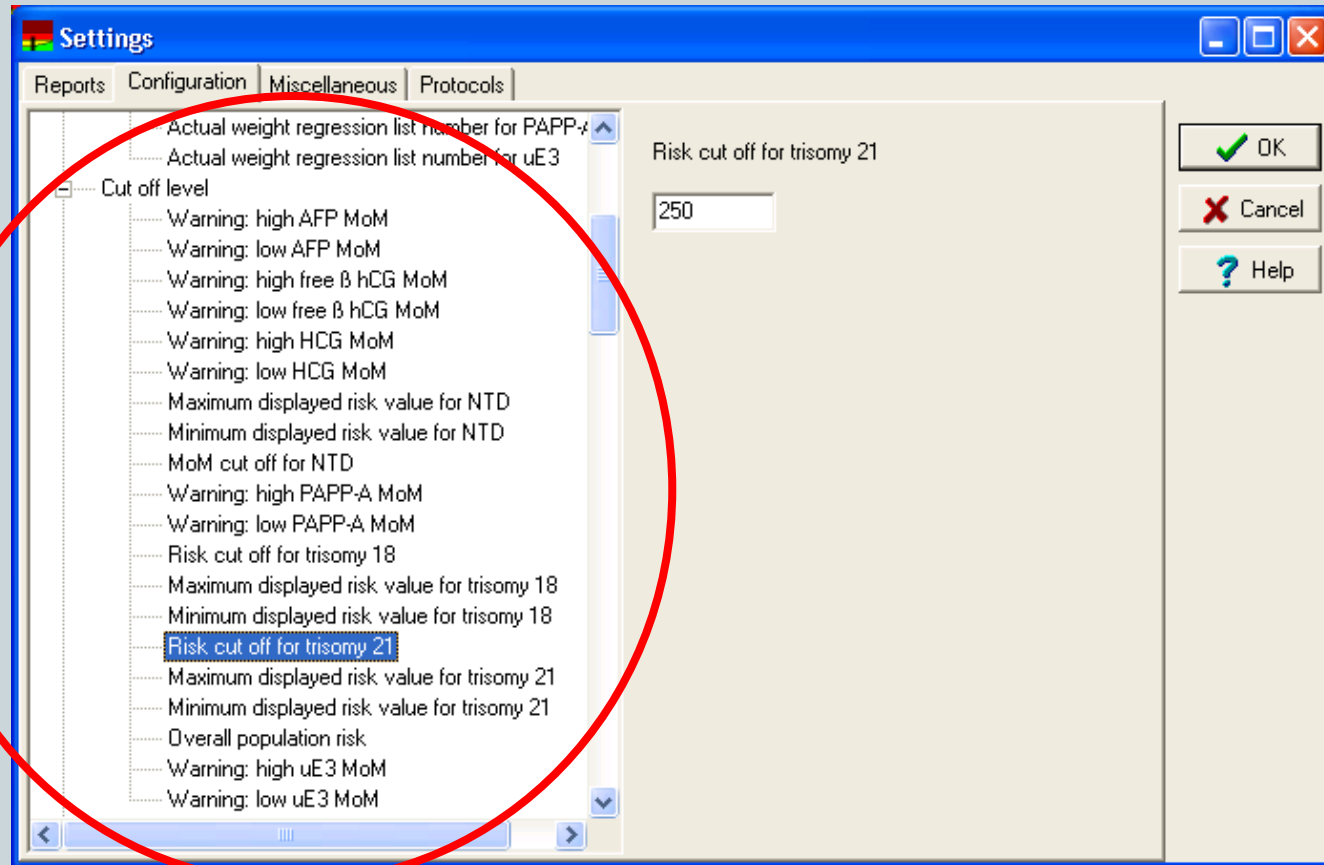
The screenshot shows the PRISCA software interface. At the top, there is a menu bar with 'Record', 'Service', 'Special', 'Information', and 'Help'. Below the menu bar, there are tabs for 'List', 'Patient', and 'Details'. A search bar is present with a dropdown menu set to '07.11.2006' and buttons for 'Select' and 'Deselect'. A 'Historical Reports' button is also visible. A status message on the right indicates 'No report printed', 'One report printed', and 'More than one report printed'. The main area contains a table with the following columns: Sample Date, Sample ID, Patient ID, Last name, First name, and Date of birth. The table lists 20 records. On the right side, there is a vertical toolbar with buttons for 'New', 'Delete', 'Save', 'Sort', 'Find', 'Report', 'Batch', 'Re-calculate', 'Help', and 'Close'.

Sample Date	Sample ID	Patient ID	Last name	First name	Date of birth
29/08/06	SC01000	PC01000	LN01000	FN01000	12/12/68
29/08/06	SC00999	PC00999	LN00999	FN00999	05/02/85
29/08/06	SC00998	PC00998	LN00998	FN00998	24/11/71
28/08/06	SC00997	PC00997	LN00997	FN00997	03/03/80
28/08/06	SC00996	PC00996	LN00996	FN00996	04/05/83
28/08/06	SC00995	PC00995	LN00995	FN00995	27/01/68
28/08/06	SC00994	PC00994	LN00994	FN00994	10/12/78
28/08/06	SC00993	PC00993	LN00993	FN00993	28/12/80
25/08/06	SC00992	PC00992	LN00992	FN00992	12/02/82
25/08/06	SC00991	PC00991	LN00991	FN00991	19/12/80
25/08/06	SC00990	PC00990	LN00990	FN00990	13/07/75
25/08/06	SC00989	PC00989	LN00989	FN00989	23/08/88
24/08/06	SC00988	PC00988	LN00988	FN00988	04/12/82
24/08/06	SC00987	PC00987	LN00987	FN00987	27/11/90
24/08/06	SC00986	PC00986	LN00986	FN00986	13/03/72
24/08/06	SC00985	PC00985	LN00985	FN00985	29/07/68
24/08/06	SC00984	PC00984	LN00984	FN00984	08/11/87

Flexibility - User defined settings

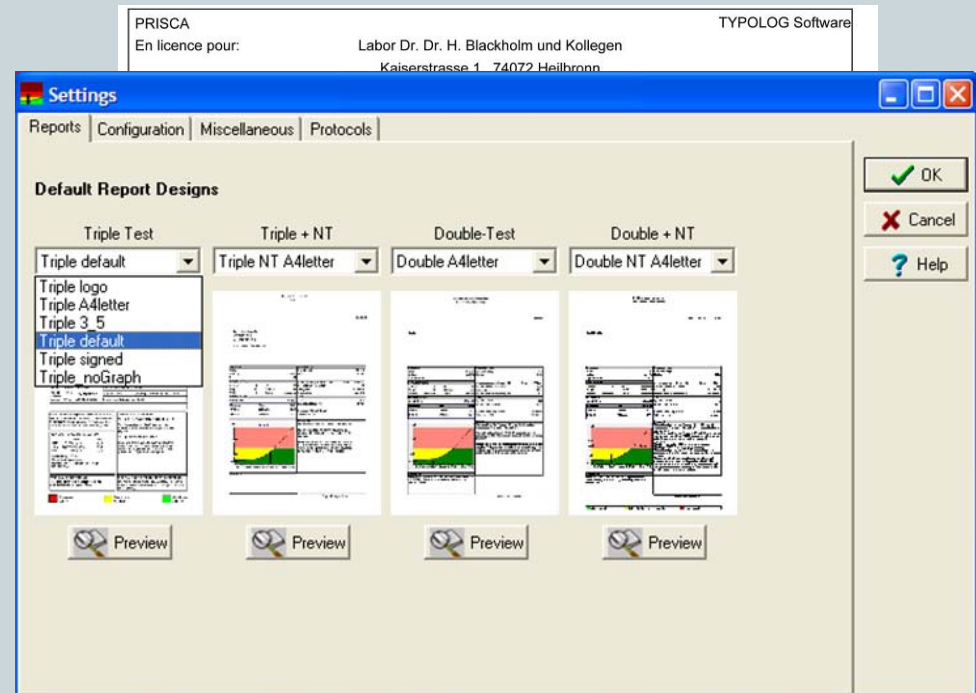
Adjustments to Local Conditions Are Possible:

- Cut Off levels
- Data ranges
- Units
- Language
- Display formats



Flexibility: Variety of Reports

- 19 Pre-defined Reports Available
- Different Default Report Settings for Different Doctors May be Assigned
- Special Reports Possible
- A Report Language Can Be Assigned to Each Referring Doctor



Le calcul de risque de Prisca depend de la precision des informations reçues du medecin prescripteur. Veuillez noter qu'il s'agit d'un calcul statistique SANS aucune valeur diagnostique !

RISQUE DE TRISOMIE 18
Le résultat pour la trisomie 18 est 1:326, ce qui représente un risque normal.

RISQUES A TERME (DOUBLE TEST + CLARTE NUCALE)

Date de l'échographie:	27/01/04	MoM:	0,6868311*
LCC	55 mm		
CN	1 mm	Trisomie 21:	<1:10000
Age gestationnel par LCC:	11 + 6	Trisomie 18:	<1:10000

Des risques combinés avec la CN supposent que toutes les mesures échographiques ont été faites selon le protocole du Fetal Medicine Foundation.
Le laboratoire décline toute responsabilité pour leurs impacts sur le calcul de risque !
No DTM frame, because AFP has not been measured!

■ inférieur au seuil
 ■ inférieur au seuil mais au-dessus du risque lié à l'âge
 ■ supérieur au seuil

Flexibility - Referring Physicians

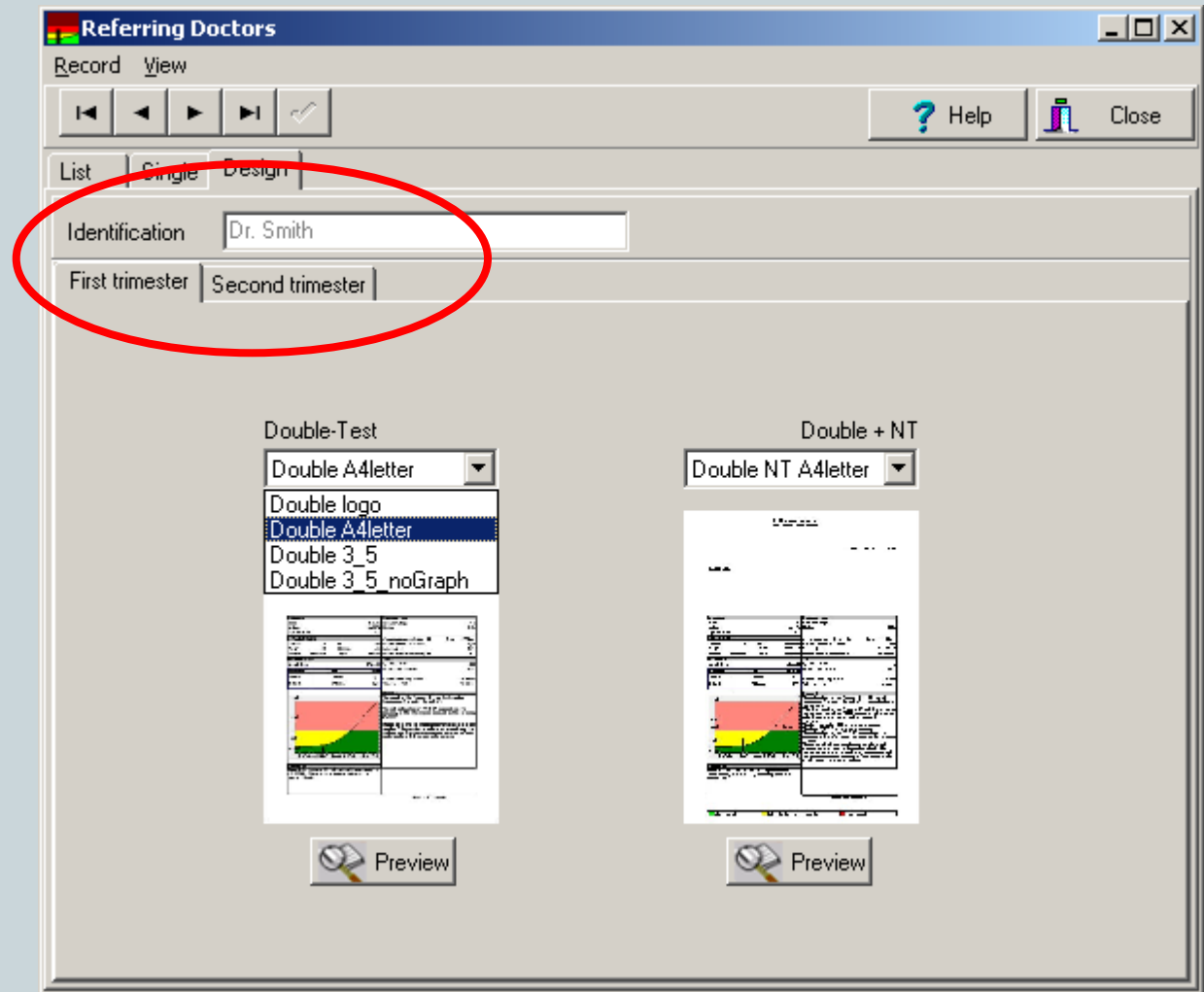
User-definable
list
of
referring
physicians

The screenshot shows a software window titled "Referring Doctors" with a blue title bar. Below the title bar is a menu bar with "Record" and "View". A toolbar contains navigation icons (back, forward, home, search) and a "Help" button with a question mark icon. Below the toolbar are three tabs: "List", "Single", and "Design", with "List" selected. The main area contains a form with the following fields:

- Identification: Dr. Harrison
- Title: Dr.
- Name: Peter Harrison
- Address: 1067, Orange Blvd.
- Address: Newport Beach, CA 96432
- Tel: (empty)
- Fax: (empty)
- Qualifications in measuring NT: FMF qualification course

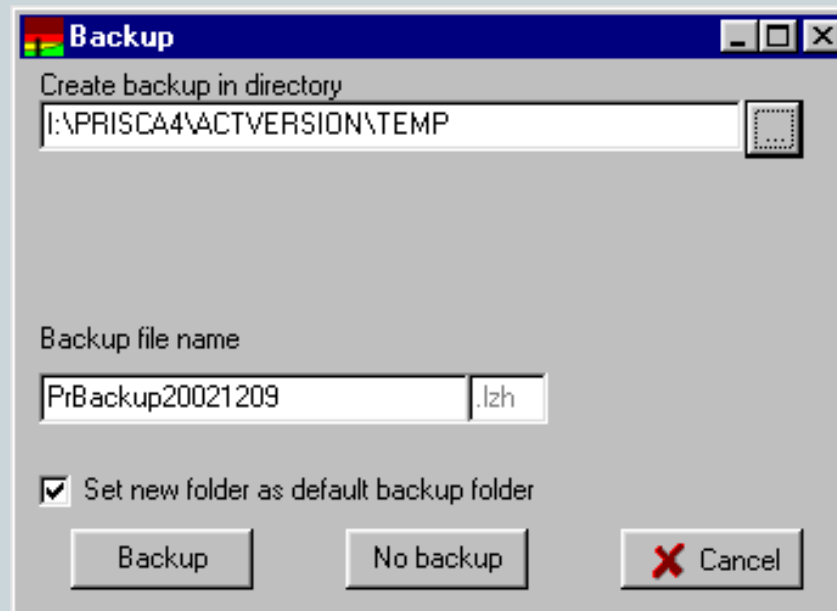
Flexibility - Referring Physicians

A report layout can be assigned to each of them



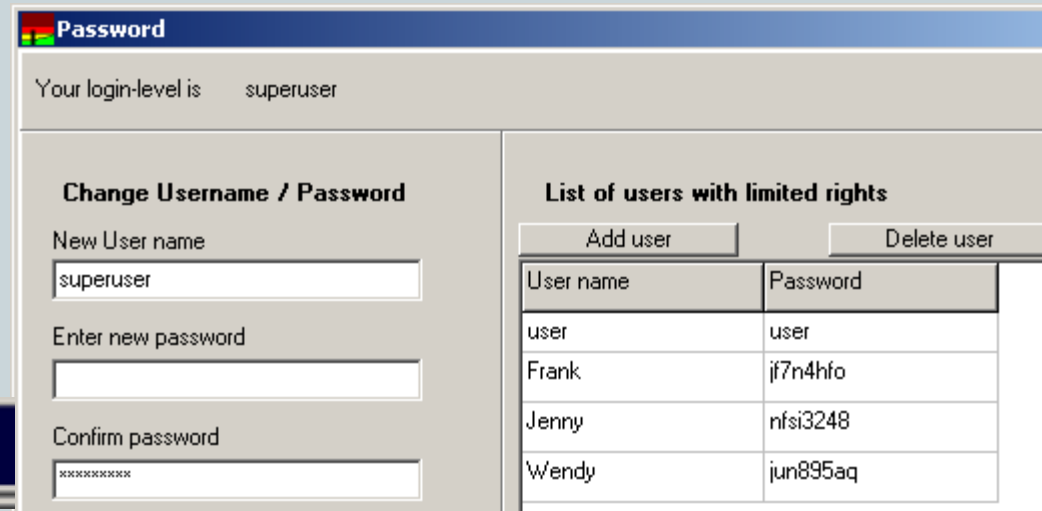
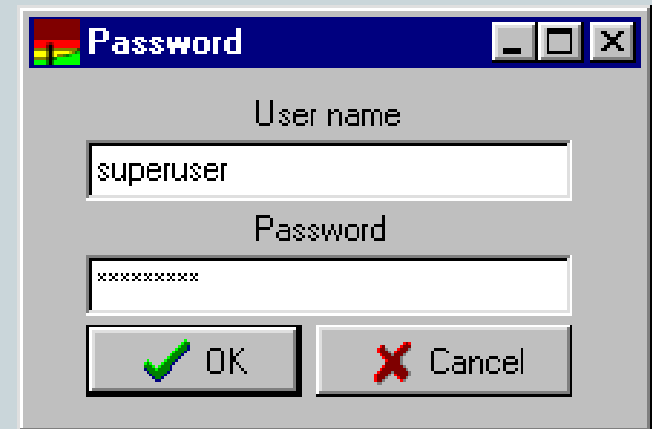
Security – Auto Backup Program

Automatic Backup Request During Each Program Termination



Security – Password Access

- Two Password Levels
 - Superuser for Unlimited Access
 - Users With Restricted Access
 - Users List Can be Created
 - Last Data Modification Assigned to Logged-In User



Last alterations by: superuser

Security - Reports Archive

Every printed report is archived automatically...

...and can be restored.

PRISCA

Record Service Special Information Help

List Patient

Search for 15.09.2004

in column Last name

Select Deselect Historical Reports

Sample Date	Sample ID	Patient ID	Last name	First name
12/09/04			Test	Test
10/09/04	TF9561	TF9561	PIMENTA	SUSANA
10/09/04	P3761	P3761	CORREIA	CRISTINA
09/09/04	FB3600	FB3600	CALAFATE	ELSA
08/09/04	P3732	P3732	CASTRO	M. MARGA
08/09/04	AB5034	AB5034	BERNARDO	SILVIA
08/09/04	LF3369	LF3369	SANTOS	SONIA
08/09/04	LF3367	LF3367	PEREIRA	TANIA

Historical Reports

Name: BERNARDO

Vorname: SILVIA

Patient ID: AB5034

Report Close

Name of the report	Date
4347_1.raf	09/09/04 18:10:10
4347_2.raf	13/09/04 16:16:32

Quality Control - Medians

- IMMULITE 2000® medians are well established for Caucasian populations.
- Medians can be entered automatically as an initial setup.

IMMULITE 2000 Parameters				
	AFP(IU/ml)	AFP(ng/ml)	HCG(IU/ml)	HCG(mIU/ml)
a	1.31087102	1.50149138	6.27480054	13.18255582
b	0.01817450	0.01817450	-0.02670495	-0.02670495
week	AFP(IU/ml)	AFP(ng/ml)	HCG(IU/ml)	HCG(mIU/ml)
14	23.25	28.14	35.79	35788
15	26.41	31.96	29.69	29686
16	29.99	36.29	24.62	24624
17	34.06	41.21	20.43	20426
18	38.68	46.81	16.94	16943
19	43.93	53.16	14.05	14054
20	49.89	60.37	11.66	11658
21	56.66	68.56	9.67	9670
22	64.35	77.86	8.02	8021

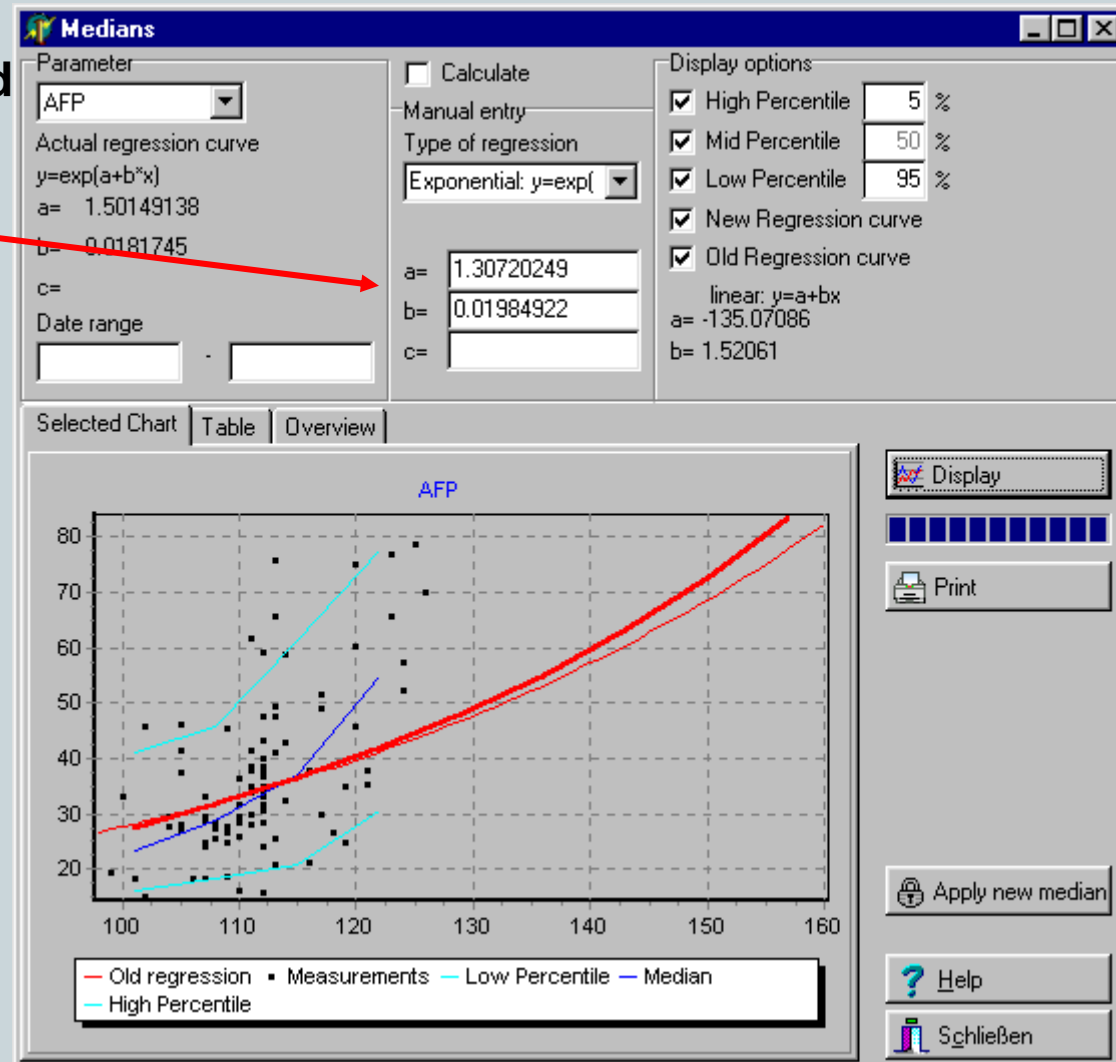
Median assistant

	Method	Units
AFP	IMMULITE 2000	IU/ml
HCG	IMMULITE 2000	IU/ml
uE3	IMMULITE 2000	ng/ml
PAPP-A	IMMULITE 2000	mIU/ml
FB HCG 1st trimester	IMMULITE 2000	ng/ml
FB HCG 2nd trimester	IMMULITE 2000	ng/ml

Medians – External medians

External medians can be entered manually

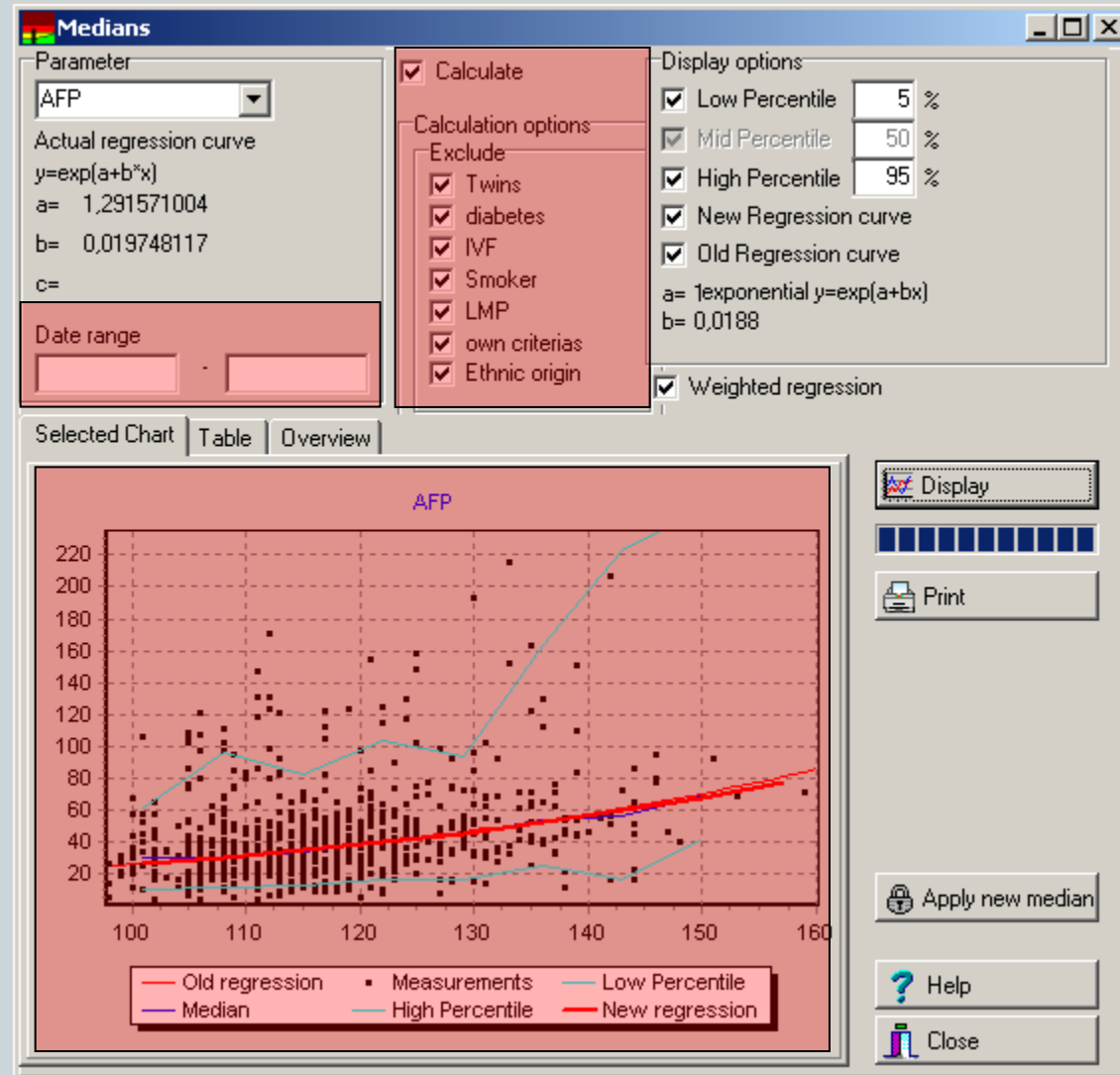
- **Defined as regression constants**
- **Constants can be calculated**
- **With 3rd party products (SPSS, Excel)**
- **With Shared Database**



Medians – Internal medians

Medians can be calculated based on the user's database

- Within certain date ranges
- Taking exclusion criteria into account
- Displaying percentiles and regression curves.



Medians – Internal medians

Tabular view of median calculation:

- Regression
- Percentiles
- Medians
- Number of measurements
- MoMs

The screenshot shows the 'Medians' software interface. The 'Parameter' is set to 'AFP'. The 'Actual regression curve' is $y = \exp(a + b \cdot x)$ with $a = 1,291571004$ and $b = 0,019748117$. The 'Date range' is empty. The 'Calculate' checkbox is checked. Under 'Calculation options', the 'Exclude' list includes: Twins, diabetes, IVF, Smoker, LMP, own criterias, and Ethnic origin. The 'Display options' are: Low Percentile (5%), Mid Percentile (50%), High Percentile (95%), New Regression curve, Old Regression curve, and Weighted regression. The regression parameters are $a = 1 \text{ exponential } y = \exp(a + b \cdot x)$ and $b = 0,0188$.

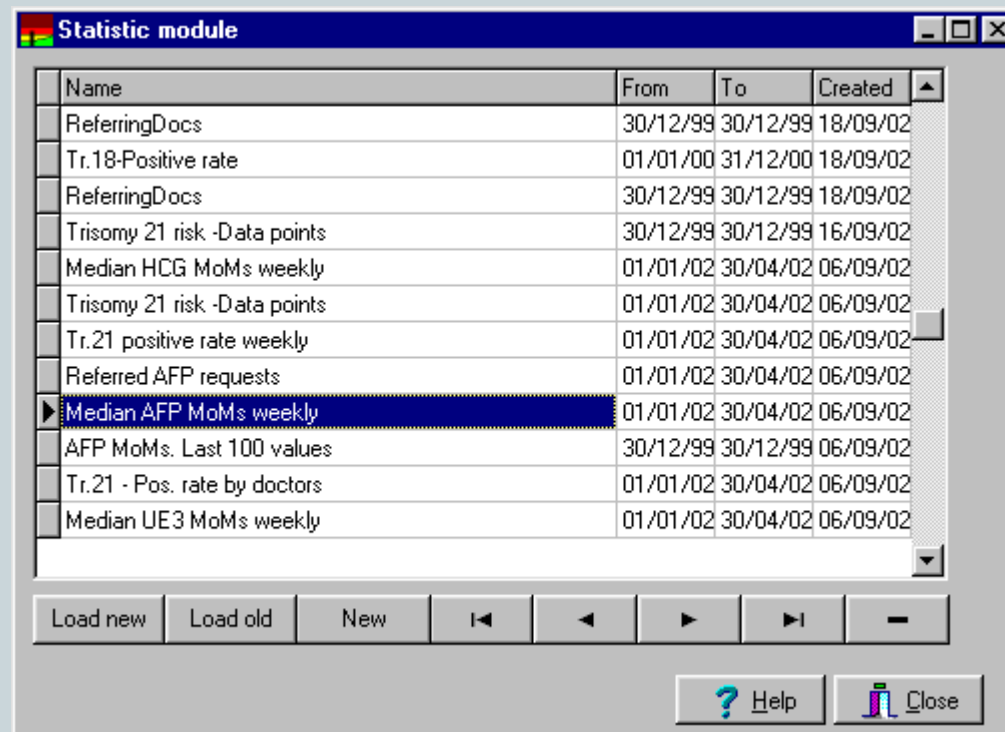
The 'Table' view shows the following data:

week	Regression	5 %	Median	95 %	#	MoM
14	27,05	10,95	30,50	61,10	51	0,89
15	30,85	11,83	30,65	96,45	226	1,01
16	35,19	12,81	34,10	81,90	242	1,03
17	40,13	16,80	40,50	103,84	159	0,99
18	45,77	16,10	45,30	93,98	73	1,01
19	52,21	25,46	53,95	163,03	42	0,97
20	59,55	16,84	56,80	222,30	17	1,05
21	67,92	41,72	69,20	247,80	5	0,98
22	77,47	80,78	170,60	260,42	2	0,45

Buttons on the right include: Display, Print, Apply new median, Help, and Close.

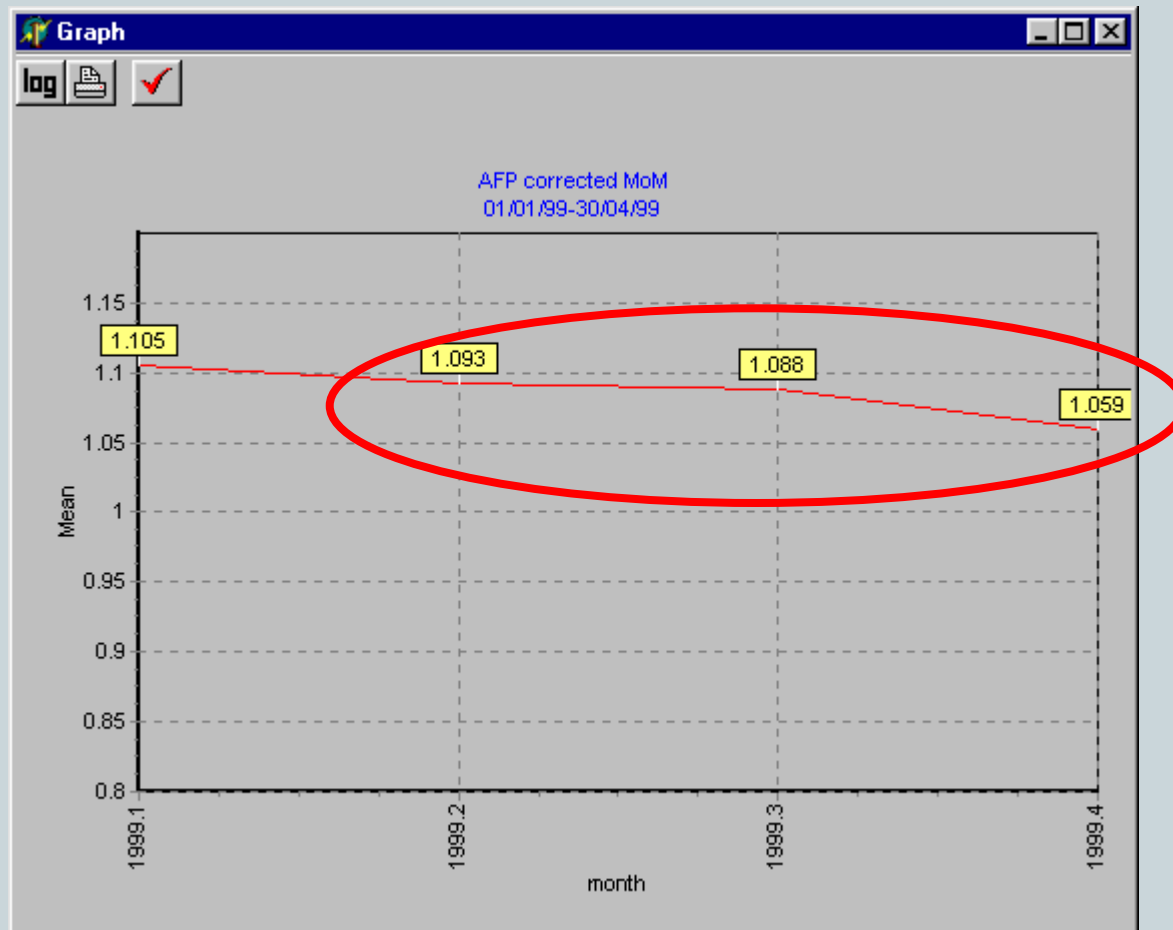
Quality Control - Statistics

- PRISCA 4.0 offers a Statistical Module with a Pre-defined List of Reports.
- These Reports can be Loaded.



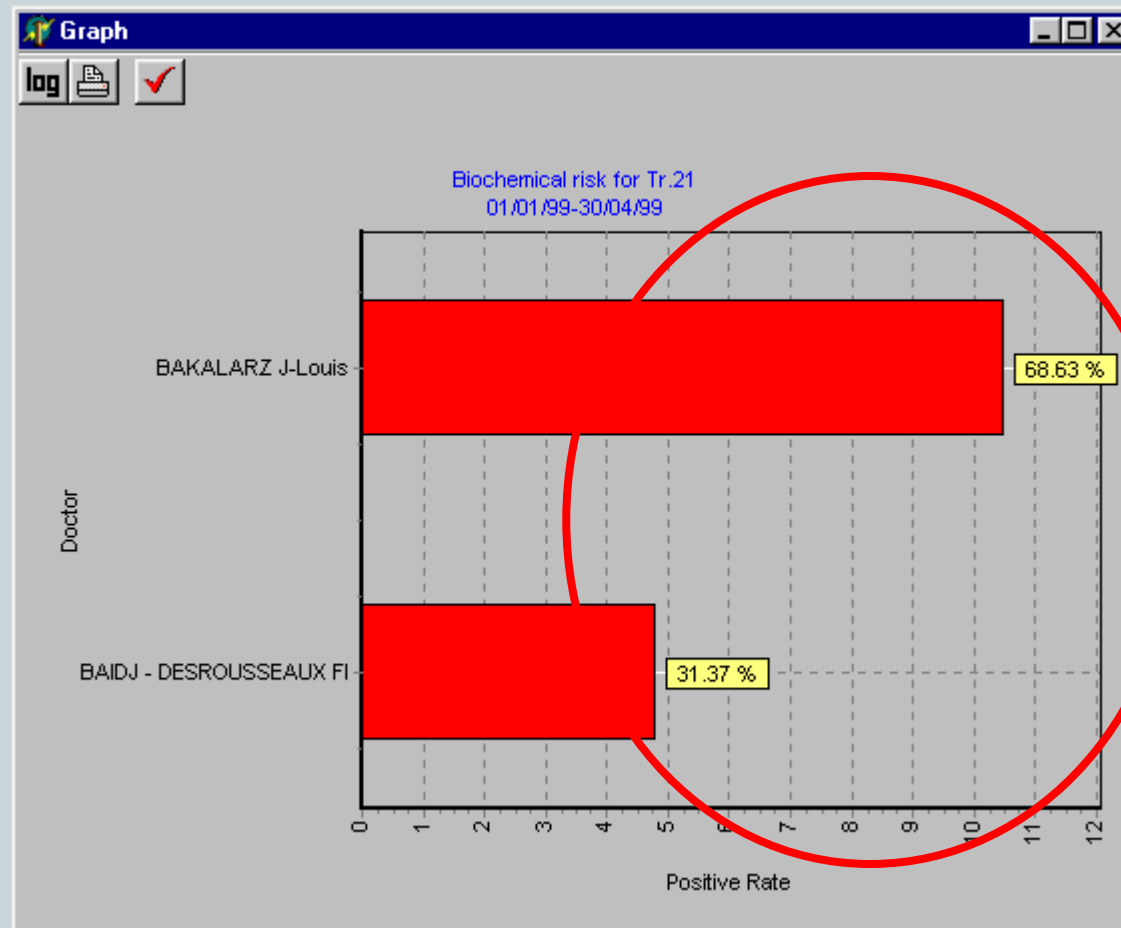
Statistics

- Control of the Median MoMs is an Early Warning System if There is a Shift in the Medians that needs Investigation



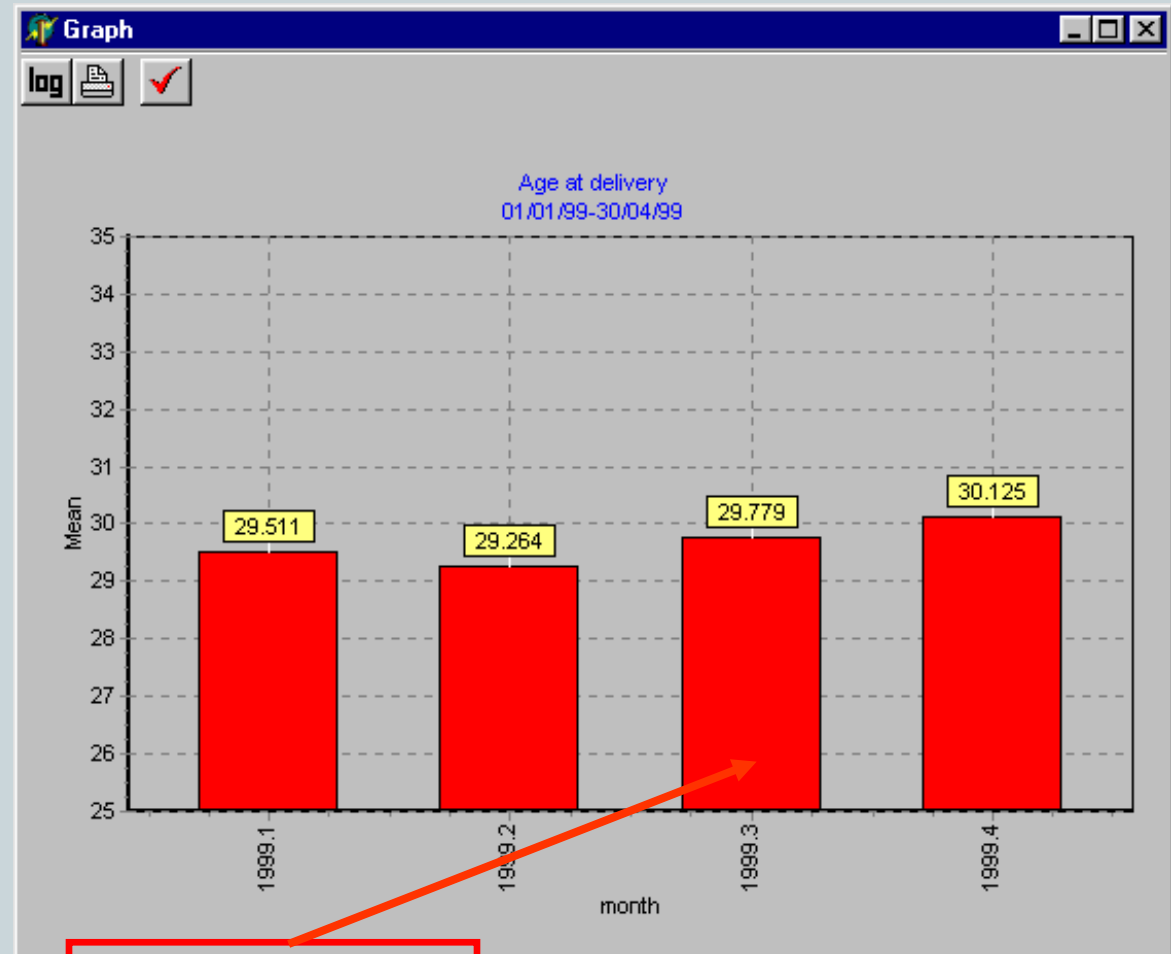
Statistics

- High positive rates for certain physicians might indicate problems in determination of the gestation age – medians...



Statistics

- Statistical reports are user configurable
- Example:
We want to investigate the development of the mean maternal age.
- We select:
- **Parameter** = Age at delivery
- **Date** = (desired date range)
- **Graph type** = vertical bar
- **Group** = Monthly
- **Calculation method** = mean



Click on "RUN"

Data export

If Built-In Statistics Do Not Meet All of Your Needs?

■ Patient data can be exported to...

MS EXCEL

MS Word

MS ACCESS

SPSS

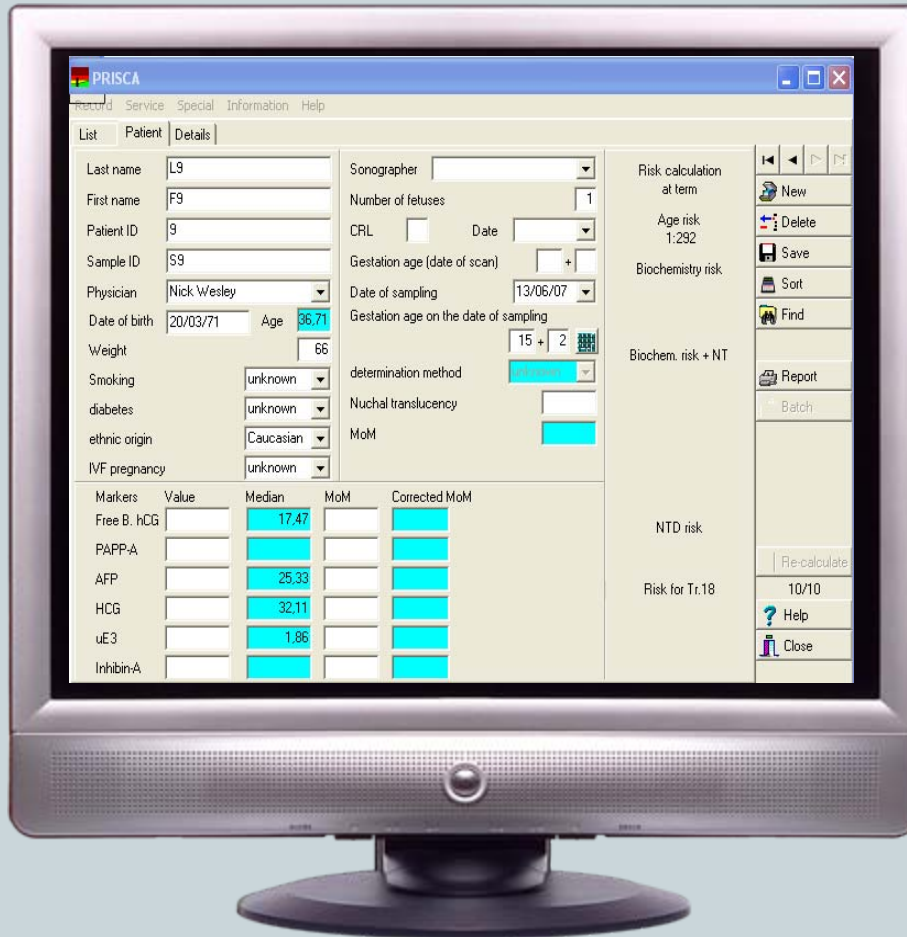
■ Within certain date ranges

■ With user definable columns

■ For Special Investigation

	A	B	C	D	E	F	G	H	I	J
1	LastName	FirstName	birthday	PatientCode	SampleDate	SampleCode	Age at sample	pregn. week	preg. day	Weight i
340	CAROFF	Cathy	28.12.1972		08.03.1999	9903195	26.20821918	15	3	
341	CARPI	Laurence	13.10.1972		11.02.1999	9902244	26.34794521	15	2	
342	CARRE	Nadine	22.10.1969		20.03.1999	9903447	29.42739726	16	0	
343	CARRE	Valérie	17.01.1967		08.04.1999	9904126	32.24383562	16	6	
344	CARRE	Véronique	14.01.1969		18.03.1999	9903418	30.19178082	15	0	
345	CARRER	Hélène	14.09.1962		01.03.1999	9903014	36.48493151	16	6	
346	CASSAN	Laëtitia	31.12.1970		29.01.1999	9901528	28.09863014	15	4	
347	CASTAGNET	Françoise	05.12.1970		27.01.1999	9901489	28.16438356	16	3	
348	CASTRIC	Marie-Andrée	09.02.1963		01.04.1999	9904038	36.16438356	15	6	
349	CAUDAL	Sylvie	01.02.1966		15.02.1999	9902278	33.06027397	15	6	
350	CAVAN	Marie-Noëlle	26.12.1969		06.01.1999	9901119	29.04931507	15	3	
351	CAVILLE	Chantal	22.12.1971		09.02.1999	9902160	27.15342466	15	4	
352	CAZE	Corinne	25.12.1964		08.01.1999	9901156	34.06027397	16	0	
353	CELLERIER	Rachel	22.03.1971		01.02.1999	9902061	27.88493151	15	2	
354	CELTON	Françoise	18.10.1965		19.03.1999	9903358	33.43835616	15	0	
355	CERBON	Christelle	18.01.1969		18.02.1999	9902391	30.10410959	16	1	
356	CHAOUCH	Armelle	12.08.1965		05.02.1999	9902150	33.50684932	15	3	
357	CHAPALAIN	Véronique	26.06.1967		09.03.1999	9903185	31.72328767	16	0	
358	CHAPERON	Rachel	11.02.1971		18.01.1999	9901331	27.95342466	15	5	
359	CHAPTAL	Germaine	07.01.1970		19.03.1999	9903375	29.21369863	16	6	

Coming Soon! PRISCA V. 5.0*



Correction for nasal bone assessment

Added 2nd Trimester Quadruple Test

More Flexible Center-Specific Medians

Improved NT Sonography Quality Control

More Flexible Determination of Gestational Age

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