Validation & Verification under ISO/IEC 17025:2005

What does this mean for forensic DNA software?

Dr C N Maguire

14th July 2016

So, what is ISO 17025?

General requirement for the competence of testing and calibration laboratories

Includes Forensic Science providers/laboratories in many jurisdictions

Requires:

- Accreditation body that will attest to the lab's technical competence
  - UKAS, NATA, ANAB (ANSI-ASQ)

- Adherence and operation under documented quality system

- Scope of Accreditation

What does this mean for a forensic science laboratory?

Lots of documentation including:

- Quality Manual
- Administrative procedures
  - Sample integrity, Chain of Custody,
- Staff Competency programmes including training and continuous improvement
- Casework procedures
  - Reagent preparation - traceability
  - Analytical methods – Limits of detection
  - Interpretation of Results
- Court presentation

What does this mean for DNA profiling ?

STR Analysis is becoming more sensitive & complex DNA profiles more prevalent

Requires more advanced modelling methodologies

Requires software solutions

DNA mixtures – LRmix, Lab Retriever, STRmix, TrueAllele, LiRaHD,

Relationship Analysis – GPS-ibd, Boneparte, *familias*, eDNA, DNA-View

Court challenges – LCN, DNA mixtures

STRmix – Validated or not accepted?

Probabilistic genotyping software – advance mathematical (MCMS) modelling

Contents lists available at ScienceDirect

Forensic Science International: Genetics

journal homepage: www.elsevier.com/locate/fsig

A series of recommended tests when validating probabilistic DNA profile interpretation software

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ABSTRACT

There has been a recent push from many jurisdictions for the standardisati
interpretation methods. Current research is moving from threshold-based inter
towards continuous interpretation strategies. However laboratory uptake of
probabilistic models is slow. Some of this reluctance could be due to the pe
calculations to replicate the software answers and the lack of formal internal valida

STATE OF NEW YORK
ST. LAWRENCE COUNTY COURT

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PEOPLE OF THE STATE OF NEW YORK:

– against – : NOTICE OF MOTION TO PRECLUDE

ORAL NICHOLAS HILLARY, : Indictment No. 2015-15

Defendant. Hon. Felix J. Catena

----------X

PLEASE TAKE NOTICE, that upon the annexed affirmation of EARL S. WARD and the accompanying memorandum of law, the undersigned will move the County Court of St. Lawrence County on the 1st Day of July, 2016, at 9:30 a.m., or as soon thereafter as counsel may be heard, for an Order granting the following relief:

1. Precluding the prosecution from offering expert testimony as to the use of, or any results produced by, the forensic software tool STRmix because the use of this software for probabilistic genotyping is not generally accepted in the relevant scientific and legal

STRmix – Validated or not accepted?

Probabilistic genotyping software – advance mathematical (MCMS) modelling

Validation of software for use in forensic analysis

Model Validation: Is the model sound and fit for purpose?

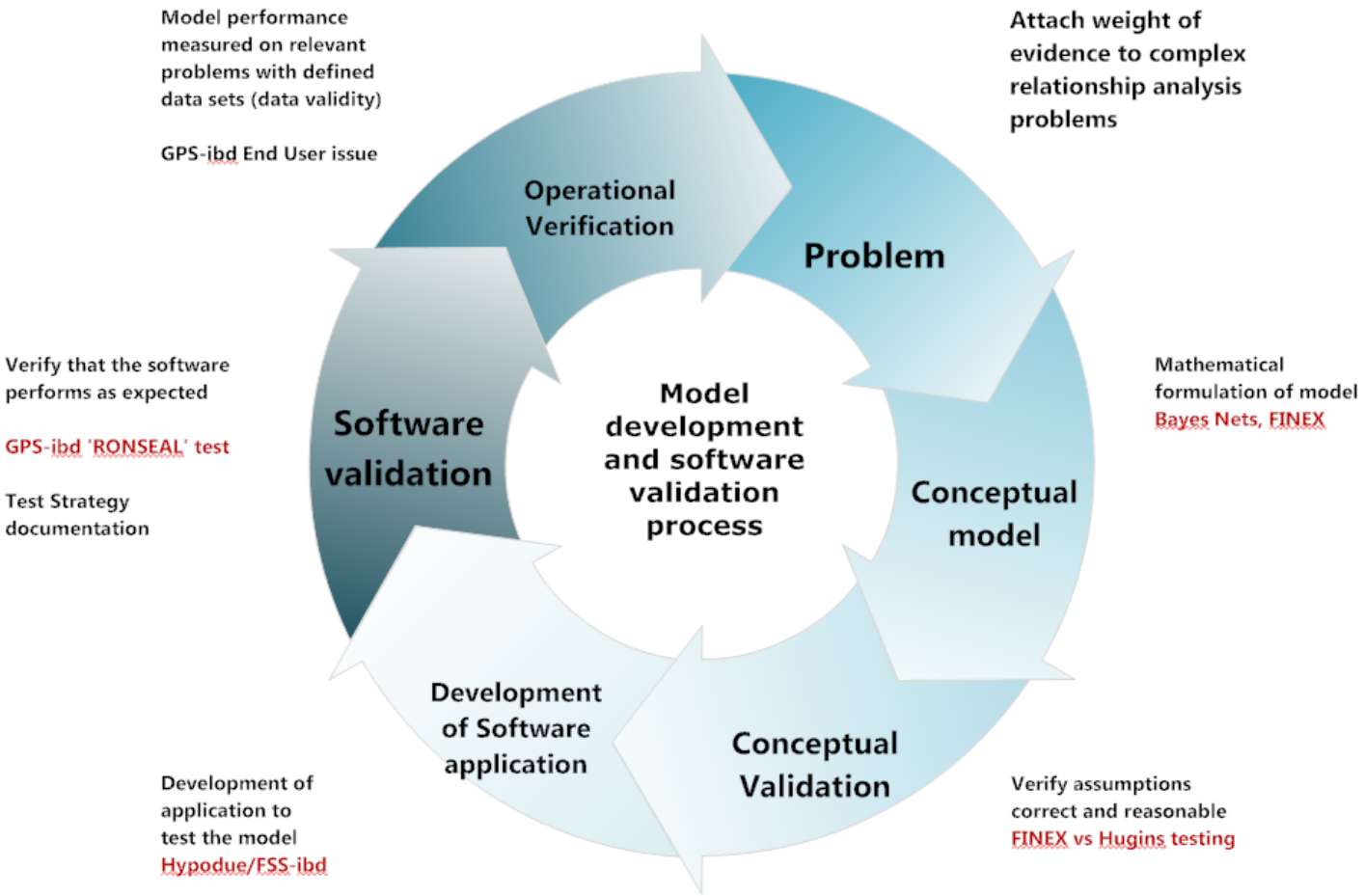
- Conceptual validation – the mathematics and underlying assumptions are correct
- Operational validation – development of 'computerised model' for testing

Software Validation: Does the application follow the mathematical concepts in the model?

- Define the specifications of the software
- Test the analytical capabilities of the software
- Verify the code base
- Compare with other applications or 'long-hand' calculations

Operational Verification – real life testing

After Haned et al, Science and Justice 56 (2016) 104-108



After Haned et al, Science and Justice 56 (2016) 104-108 Fig 1

GPS-ibd evolutionary timeline

- FINEX: Forensic Identification by Networked EXpert systems (2004–2005)
  - **Dr Robert Cowell – City University** ; used to teach the principles of Bayes Nets
- Hypodue (2005–2006)
  - Dr Robert Cowell (development of GUI)
  - **Dr Chris Maguire & Dr Tim Clayton (FSS)** domain knowledge to introduce mutation model and Fst corrections
- FSS-ibd (introduced Nov 2006)
  - Built by **VidaVia Media SL** and introduced into FSS casework – civil and court-ordered paternity tests; Immigration casework; Criminal cases (including incest); coronial work (including Mispers and DVI); Familial Searching NDNADB
- FSS DNA Lineage (re-branding 2010); never introduced before FSS closure
  - Extensive testing & validation of functionality. **Functionality unchanged by re-branding**
- GPS-ibd – collaboration between City University and VidaVia Media SL
  - Extensive re-testing & validation of functionality. **Functionality unchanged by re-branding**

GPS-ibd evolutionary timeline – supporting documentation

VALIDATION REVIEW CHECKLIST

For FSS-ibd Software Project

The Forensic Science Service®

Complete
To Be Completed
Confirmation Req'd

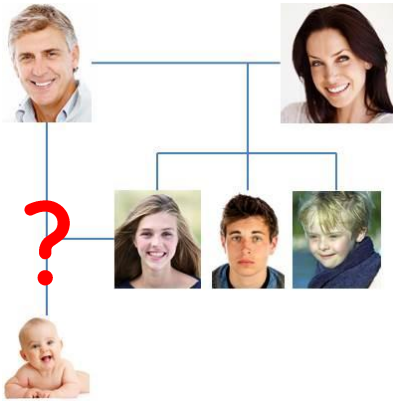
Project Title: FSS-ibd

Project Validation Number:

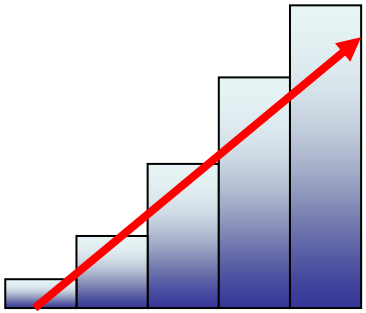
1	Validation Plan	Reference	Comments
1.1	User requirement	\\trident\pco02\My Documents\Hypodue'	A short list of requirements for Hypodue/FSS-ibd
1.2	Detailed specification (of product or service)	\\trident\pco02\My Documents\Hypodue' \\trident\pco02\My Documents\Hypodue'	Functional specification for delivery of FSS-ibd
1.3	Quality standards	C:\Documents and Settings\pco02\Deskt C:\Documents and Settings\pco02\Deskt	GP-154 TS-963
		C:\Documents and Settings\pco02\Deskt C:\Documents and Settings\pco02\Deskt	TS-578 TP-268
		C:\Documents and Settings\pco02\Deskt \\trident\pco02\My Documents\Hypodue'	GP-023 PG-B11
			TS-863

GPS-ibd – What are the benefits?

1. Increase speed of analysis



2. Simplify Analysis of Complex Relationships

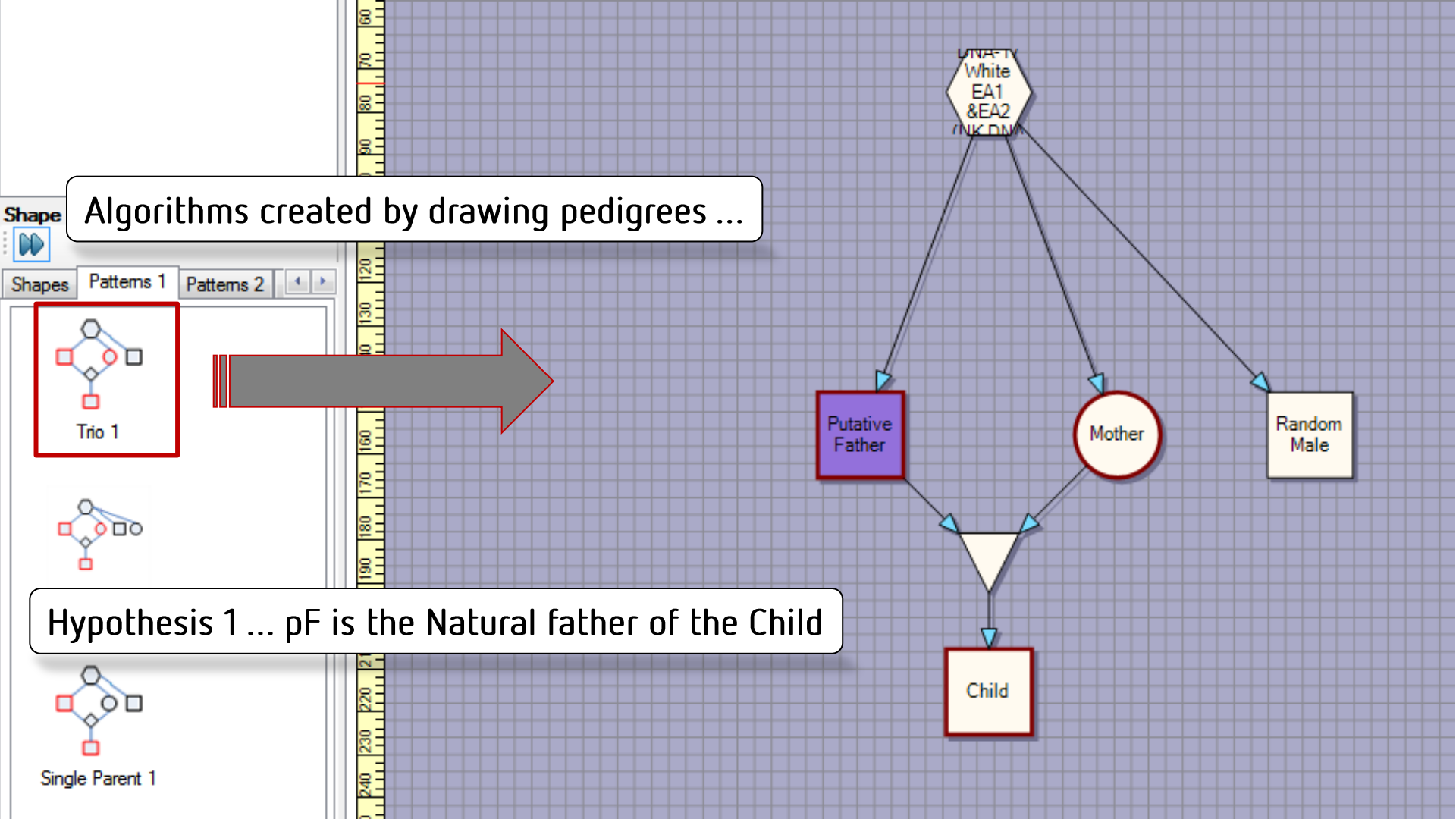


3. Increase Quality & Consistency

4. Reduce Cost

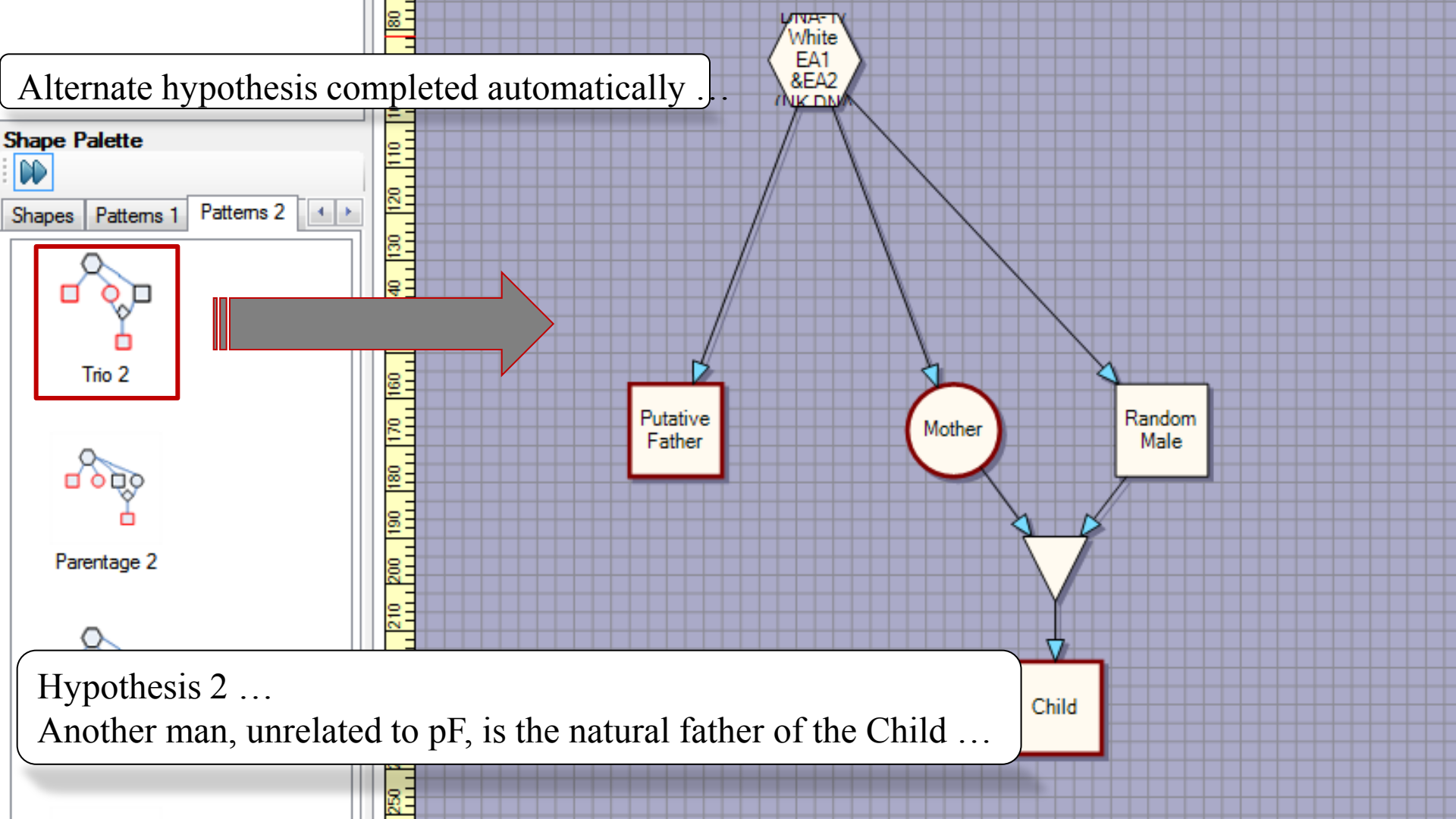
GPS-ibd – How does it work?

Algorithms created by drawing pedigrees ...



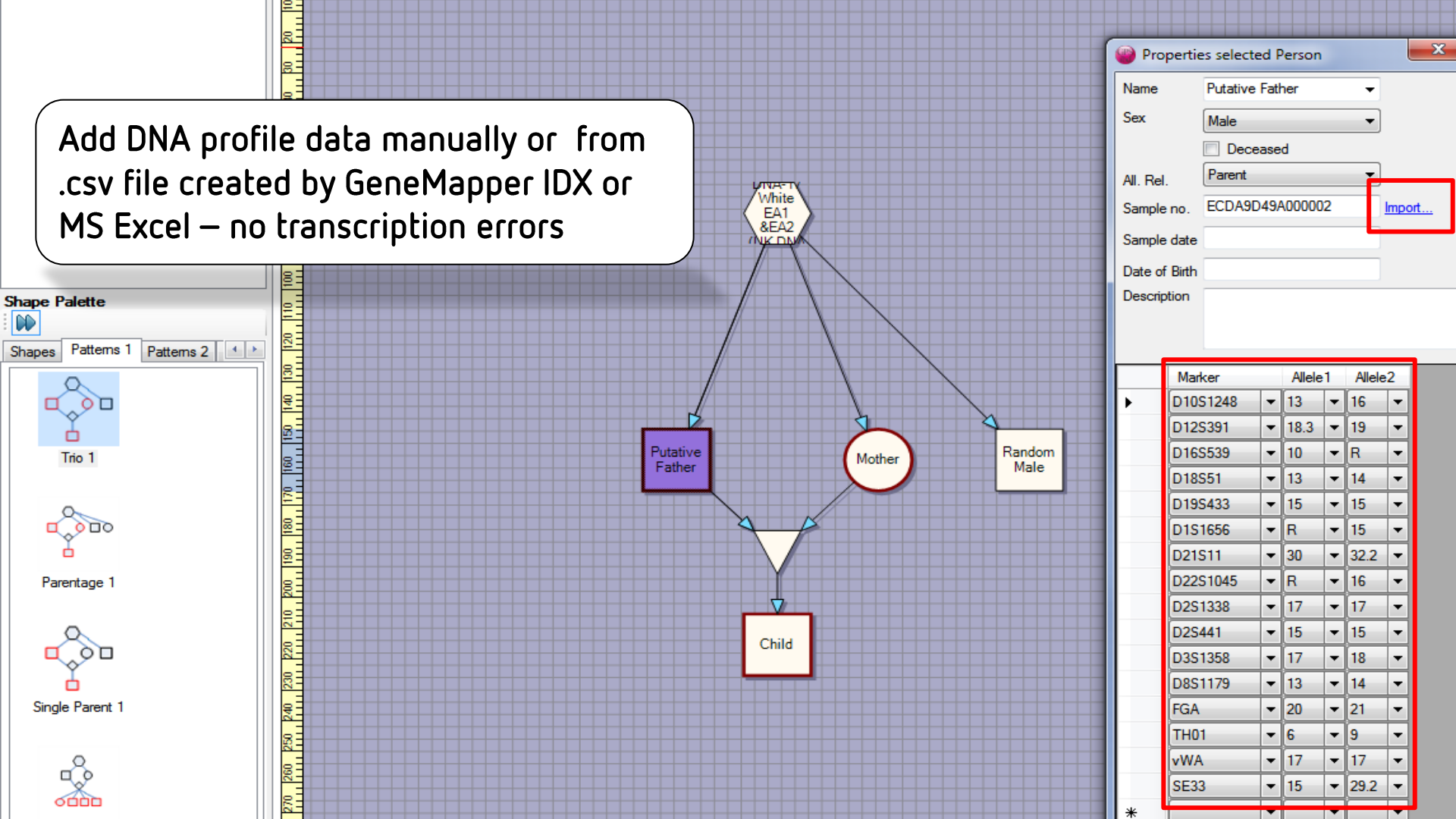
Hypothesis 1 ... pF is the Natural father of the Child

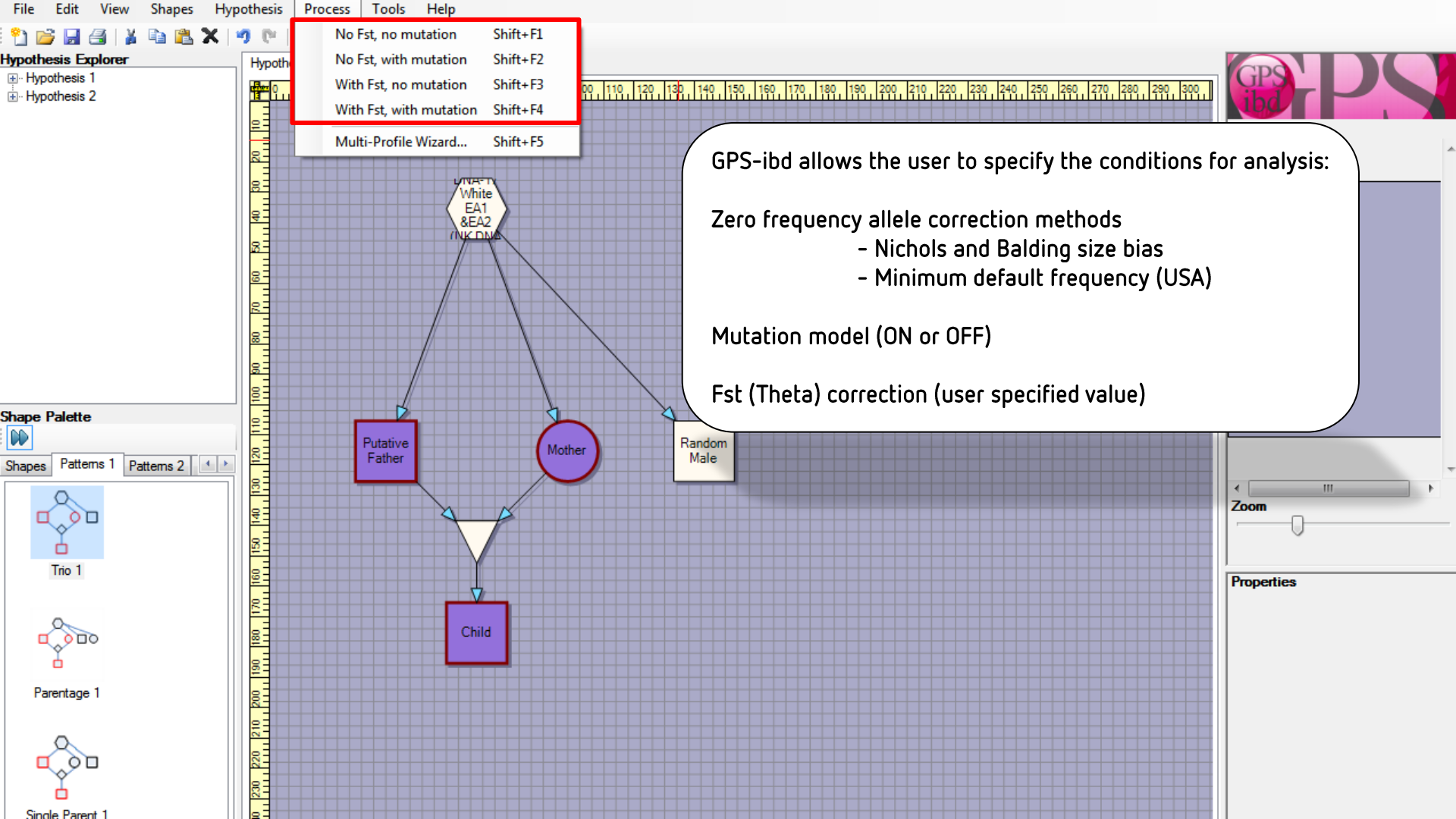
Alternate hypothesis completed automatically …



Hypothesis 2 …
Another man, unrelated to pF, is the natural father of the Child …

Add DNA profile data manually or from .csv file created by GeneMapper IDX or MS Excel – no transcription errors

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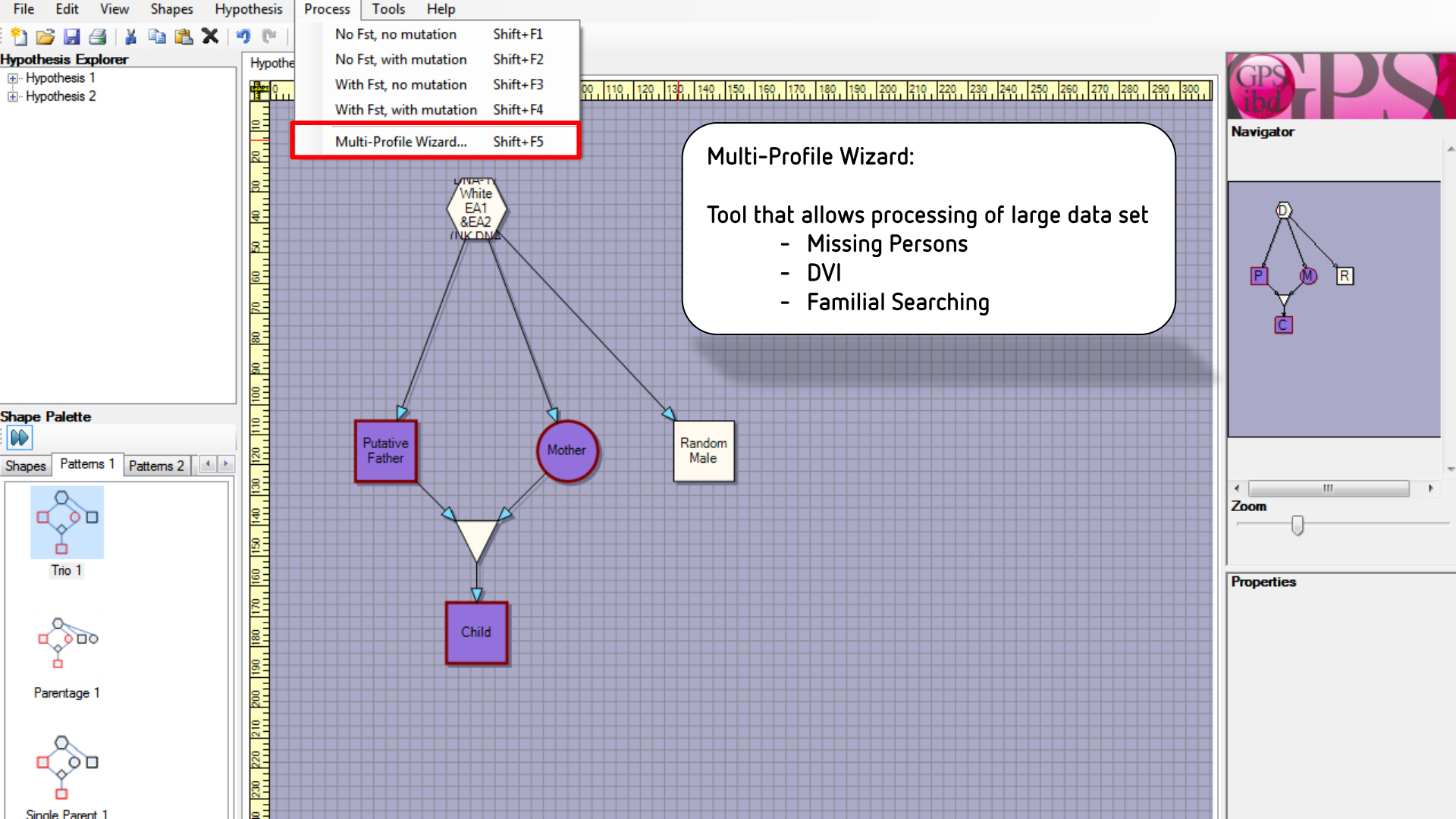
View
Shapes
Hypothesis
Process
Tools
Help
No Fst, no mutation Shift+F1
No Fst, with mutation Shift+F2
With Fst, no mutation Shift+F3
With Fst, with mutation Shift+F4
Multi-Profile Wizard... Shift+F5
Hypothesis Explorer
Hypothesis 1
Hypothesis 2
Shape Palette
Shapes
Patterns 1
Patterns 2
Trio 1
Parentage 1
Single Parent 1
White
EA1
&EA2
Putative Father
Mother
Random Male
Child
GPS-ibd allows the user to specify the conditions for analysis:
Zero frequency allele correction methods
- Nichols and Balding size bias
- Minimum default frequency (USA)
Mutation model (ON or OFF)
Fst (Theta) correction (user specified value)
Zoom
Properties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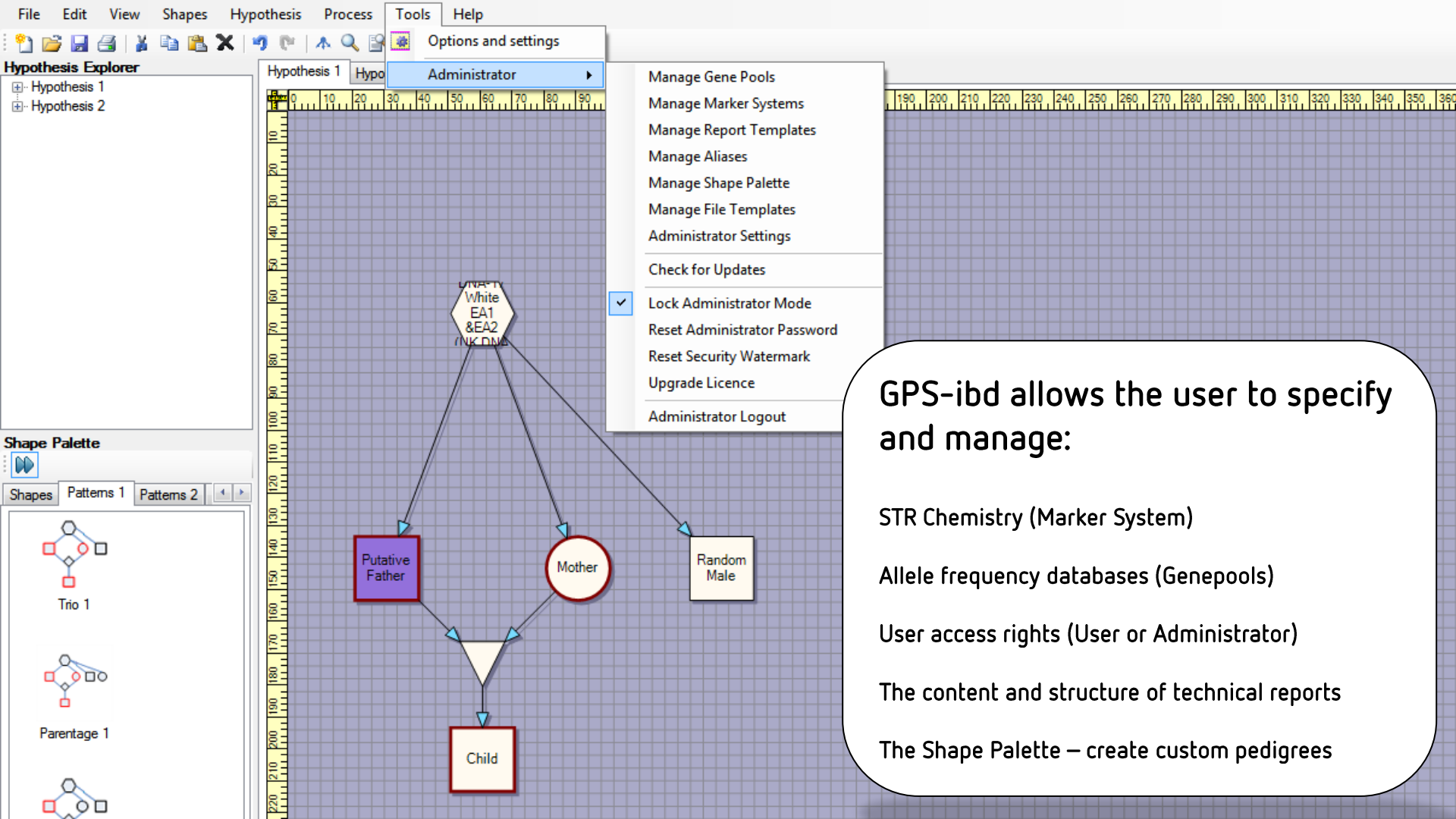
Patterns 2
Trio 1
Parentage 1
Single Parent 1
White
EA1
&EA2
Putative Father
Mother
Random Male
Child
Multi-Profile Wizard:
Tool that allows processing of large data set
- Missing Persons
- DVI
- Familial Searching
Navigator
D
P
M
R
C
Zoom
Properties


File
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Hypothesis
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Manage Gene Pools
Manage Marker Systems
Manage Report Templates
Manage Aliases
Manage Shape Palette
Manage File Templates
Administrator Settings
Check for Updates
Lock Administrator Mode
Reset Administrator Password
Reset Security Watermark
Upgrade Licence
Administrator Logout
Hypothesis Explorer
Hypothesis 1
Hypothesis 2
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Shapes
Patterns 1
Patterns 2
Trio 1
Parentage 1
Hypothesis 1
White
EA1
&EA2
Putative
Father
Mother
Random
Male
Child
GPS-ibd allows the user to specify and manage:
STR Chemistry (Marker System)
Allele frequency databases (Genepools)
User access rights (User or Administrator)
The content and structure of technical reports
The Shape Palette – create custom pedigrees

GPS-ibd Outputs

- USER DEFINED TECHNICAL REPORT

  Case settings;

  - STR Chemistry,
  - Fst correction,
  - Mutation modelling,
  - Zero frequency allele corrections

Sample data

- Sample profiles by locus
- Allele frequencies
- Probabilities H1 and H2 by Locus
- Likelihood Ratio by Locus
- Overall LR

- USER DEFINED CASE REPORT; can be exported as MS WORD (.docx) or ADOBE ACROBAT (.pdf)

GPS-ibd Technical Report - 2016/02/02 GB

Gene Pool Systems

02 February 2016 14:08:58

Operator: Dr Christopher Maguire

Sample No.	Date received	Name	D.o.B	Alleged relationship
ECE3D639E000104	20160201	Female 104		Sibling
ECE3D639E000103	20160201	Female 103		Parent (Mother)
ECE3D6370000004	20160201	pFather 004		Parent (Father)
ECE3D6488000112	20160201	Child 112		Child (Son)

DNA Profiling Data

Multiplex = identifiler (usa), F_{ST} = 0, **Adjustment** = Size Bias, **Mutation** = No

Name	Male 002	Female 001	Female 104	pFather 004	Child 112
Sample No.	ECE3D6370000002	ECE3D6370000001	ECE3D639E000104	ECE3D6370000004	ECE3D648800
D8S1179	12, 14	11, 16	11, 12	15, 16	11, 16
D21S11	30, 31	28, 31.2	31, 31.2	25.2, 30	30, 30
D7S820	10, 12	8, 11	11, 12	10, 11	8, 11
CSF1PO	11, 12	11, 12	12, 12	11, 12	11, 12
D3S1358	16, 18	15, 15	15, 18	17, 18	15, 18
THO1	7, 7	6, 8	6, 7	7, 9.3	7, 7
D13S317	11, 12	8, 11	8, 11	11, 12	11, 12
D16S539	12, 13	8, 12	12, 12	11, 12	12, 12
D2S1338	17, 20	19, 22	20, 22	25, 26	19, 26
D19S433	11, 14	15, 15	11, 15	14, 15	15, 15
VWA	16, 16	18, 18	16, 18	16, 17	16, 18
TPOX	8, 11	8, 8	8, 8	8, 8	8, 11
D18S51	13, 13	12, 13	12, 13	12, 16	12, 13

GPS-ibd – Does it pass the Ronseal test?

GPS-ibd Validation and Verification

- ❑ DOES GPS-ibd MEET THE REQUIRED SPECIFICATIONS

  GPS-ibd has been tested against the 50+ test scripts previously used to test FSS DNA Lineage.
  The functionality remains unchanged and the application performs as required

- ❑ IS THERE ANY DOCUMENTATION OF THIS VALIDATION

  There is full documentation of the testing. This can be made available to ISO 17025 assessors as required

- ❑ CASEWORK VERIFICATION

  Before being introduced into casework the GPS-ibd application has been subject to a series of casework challenges covering all of the scenarios expected in criminal or commercial casework. These include: Single Parent, Trios, Incest cases, Sibling cases

- ❑ MUTATION TESTING

  Extensive testing & validation of functionality against scenarios involving maternal and paternal mutations.

- ❑ REGRESSION TESTING

  Casework scenarios as above run with GPS-ibd, FSS DNA Lineage and FSS-ibd with no discrepancies, showing the mathematical functions of the application remain unchanged throughout the development timeline

GPS-ibd Verification outcomes (1)

ESI-17 (EA1, Fst=0, Size Bias On, Mutation Off)

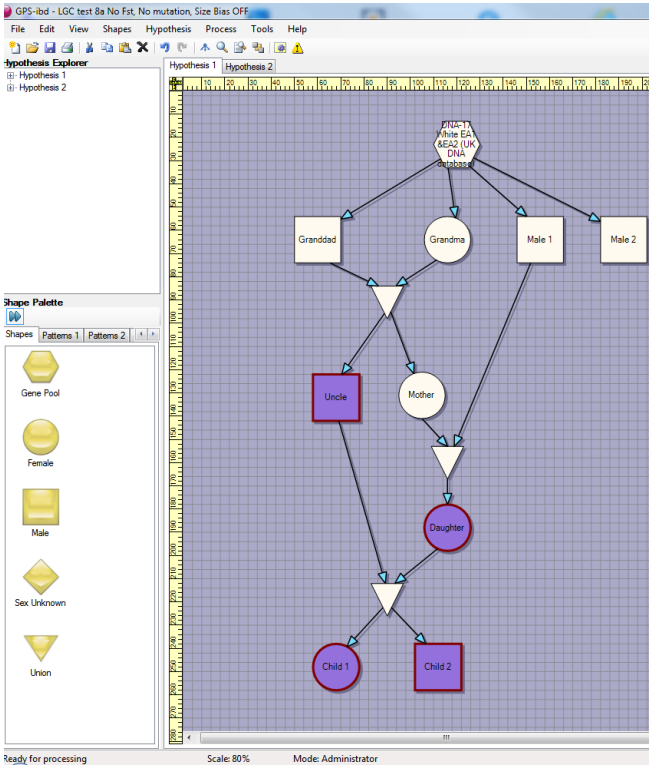
Pedigree Number	Description	LR_GPSibd	LR_R	Difference
1	Single parent	6.22162E+07	6.22162E+07	0.00000.E+00
2	Trio	8.53837E+09	8.53837E+09	0.00000.E+00
3	Incest Trio (Father/Daughter)	1.28507E+09	1.28507E+09	0.00000.E+00
4	Parentage	1.49367E+17	1.49367E+17	0.00000.E+00
5	Two sibs vs unrelated	3.29359E+04	3.29359E+04	0.00000.E+00
6	Three sibs vs one unrelated	9.73332E+08	9.73332E+08	0.00000.E+00
7	Four sibs vs one unrelated	6.8938.E+11	6.8938.E+11	0.00000.E+00
8	Uncle incest - 2 children	1.38441.E+15	1.38441.E+15	0.00000.E+00
9	Brother incest	4.87727.E+08	4.87727.E+08	0.00000.E+00
10	Grandfather/Grandaughter incest	4.70262.E+08	4.70262.E+08	0.00000.E+00

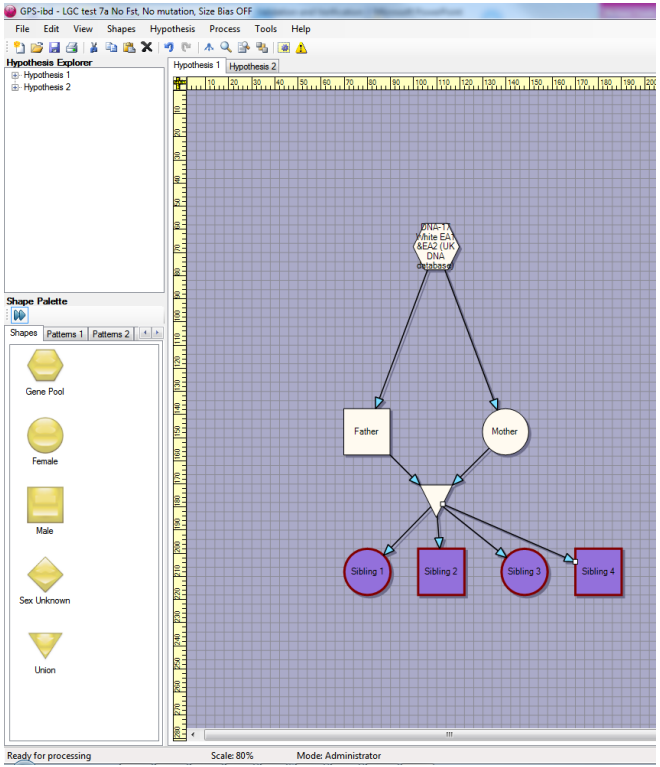
GPS-ibd Verification outcomes (2)

ESI-17 (EA1, Fst=0.03, Size Bias On, Mutation Off))

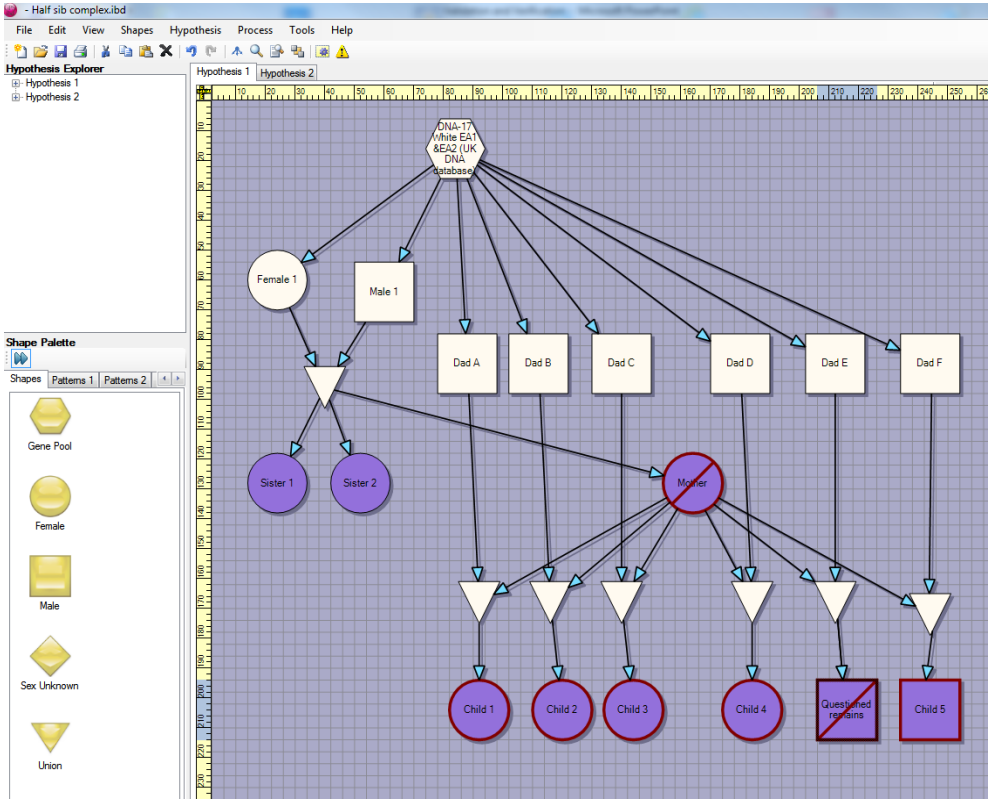
Pedigree Number	Description	LR_GPSibd	LR_R	Difference
1	Single parent	1.41493E+06	1.41493E+06	0.00000.E+00
2	Trio	1.81343E+08	1.81343E+08	0.00000.E+00
3	Incest Trio (Father/Daughter)	6.54688E+07	6.54688E+07	0.00000.E+00
4	Parentage	7.26926E+13	7.26926E+13	0.00000.E+00
5	Two sibs vs unrelated	4.01912E+03	4.01912E+03	0.00000E+00
6	Three sibs vs one unrelated	1.62805E+07	1.62805E+07	0.00000.E+00
7	Four sibs vs one unrelated	7.97840E+09	7.97840E+09	0.00000.E+00
8	Uncle incest - 2 children	1.02842E+13	1.02842E+13	0.00000.E+00
9	Brother incest	4.44221E+07	4.44221E+07	0.00000.E+00
10	Grandfather/Grandaughter incest	3.49650E+07	3.49650E+07	0.00000.E+00

GPS-ibd verification with moderately complex pedigrees





GPS-ibd can be used with very complex pedigrees



GPS-ibd used in ISO 17025 accredited laboratory

LGC achieves ISO 17025 accreditation for Relationship Analysis Services using ground breaking GPS-ibd software.

12 February 2016, London, UK – LGC has been successful in gaining IS0/IEC17025:2005 accreditation through UKAS (the United Kingdom Accreditation Service), under schedule no. 0003 for Relationship Analysis Services using GPS-ibd software.

GPS-ibd, a ground-breaking development in relationship analysis software by VidaVia, can be used for routine civil paternity testing, relationship analysis for immigration casework, human identification in missing person's casework or in mass fatality (DVI) casework. In addition, GPS-ibd can be used for familial searching of DNA databases.