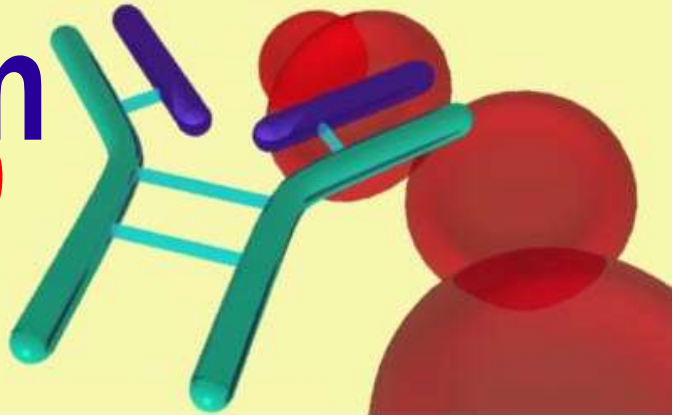


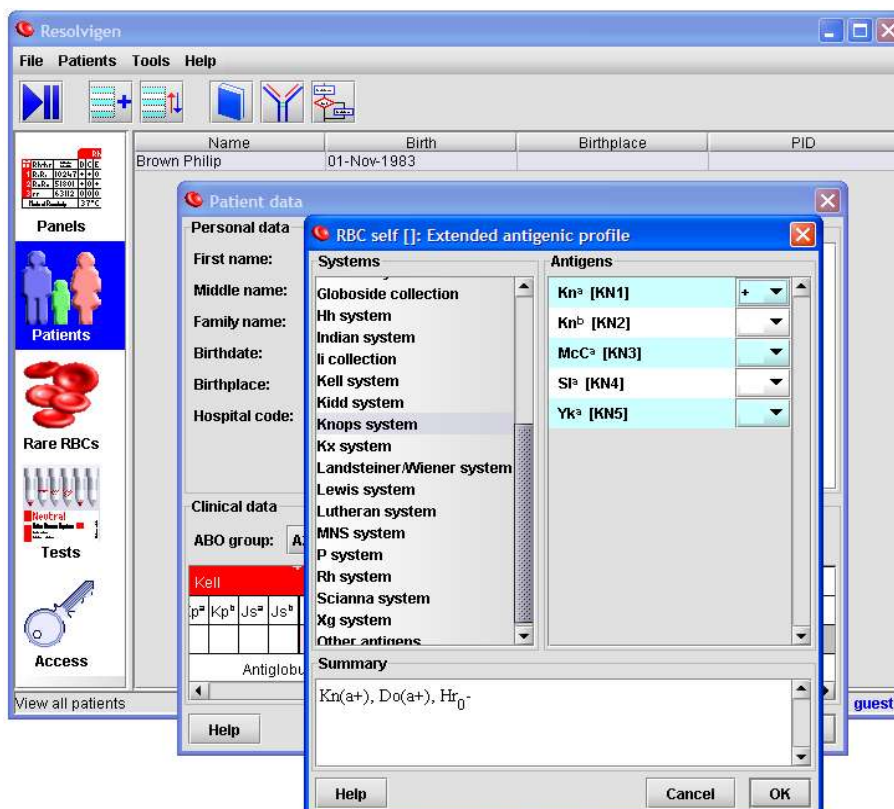
Resolvigen

3



Introducing Resolvigen 3

More than five years after introduction, Resolvigen 2 is still one of the best programs for immunohematological diagnostics available on the market; nevertheless we have decided to develop a new software, Resolvigen 3, that is not simply a revision of Resolvigen 2: it extends the diagnostic capabilities of Resolvigen to take advantage of recent changes like the widespread deployment of automated instruments for immunohematology.



Resolvigen 3 is a completely new software which greatly improves:

- identification of antibody mixes that give a complete covering of diagnostic panels reactions,
- identification of antibodies directed against public antigens,
- automated instrument interfacing,
- data exchange between different users,
- communication with on site data management systems.

Immuno-hematological diagnosis on panels

Using Panels to identify antibodies appears at first as a simple task: check all non reacting RBC sample rows on the Panel, exclude all antibodies marked + on any of those rows; the remaining antibodies are not excluded; in order to identify the antibody or antibodies in serum, check the combinations that cover all reacting RBCs and try to exclude the remaining antibodies using additional RBCs.

Edit antigram results

Antigram description
 Type: Panel A Code: RA326

Antigram data

Cell No.	Rh-hr	Donor Number	Antigen																	Test results																			
			D	C	E	c	e	f	C ^w	V	K	k	Kp ^a	Kp ^b	Js ^a	Js ^b	Fy ^a	Fy ^b	Jk ^a	Jk ^b	Xg ^a	Le ^a	Le ^b	S	s	M	N	P1	Lu ^a	Lu ^b	Special antigen typing	Cell No.	RT	37	C	RT _E	37 _E	C _E	IgG
1	R1wR1	114130	+	+	0	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	+	+	+	0	+			1		2+				
2	R1R1	110269	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	0	0	0	0	0	+	+	+	+	0	+s	0	+			2		1+				
3	R2R2	112848	+	0	+	+	0	0	0	0	0	+	0	+	0	+	+	0	+	0	0	0	+	+	0	+	0	0	0	+			3		1+				
4	Ror	114331	+	0	0	+	+	+	0	+	0	+	0	+	0	+	+	0	+	0	0	0	+	+	0	+	0	0	+			4		2+					
5	r _r	113913	0	+	0	+	+	+	0	0	0	+	0	+	0	+	+	+	+	0	+	0	+	+	+	0	0	+			5		2+						
6	r _r	111775	0	0	+	+	+	+	0	0	0	+	0	+	0	+	+	+	+	0	0	0	+	+	+	+	+	0	+			6		2+					
7	rr	110157	0	0	0	+	+	+	0	0	+	+	0	+	0	+	+	+	+	0	+	0	+	+	+	+s	0	+			7		2+						
8	rr	111413	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	0	0	0	0	+	+	0	0	+					8		1+					
9	rr	112846	0	0	0	+	+	+	0	0	+	+	0	+	0	+	+	+	+	0	+	0	+	0	+	0	0	+			9		2+						
10	rr	112081	0	0	0	+	+	+	0	0	0	+	0	+	+	0	+	+	+	0	+	0	+	0	+	0	0	+			10		1+						
11	R1R1	114327	+	+	0	0	+	0	0	0	+	+	0	+	0	+	+	+	+	0	+	+	+	0	+	+	0	+			11		1+						
	Panel cells		0	0	0	+	+	+	0	0	0	+	0	+	+	0	+	0	0	0	0	0	+	+	0	0	+						0						

Mode of reactivity: 37°C/Antiglobulin, Antiglobulin, Var., Cold, Var.

Unfortunately this is a simplistic approach, that nevertheless remains the basis for antibody identification, but is not enough to cope with more complex cases involving weak antibodies or antibody mixes reacting with most or all RBC samples in panels.

Result interpretation

Possible antibody mixes explaining reactions

- anti-s, M
- anti-s, Rh₄e
- Suspected panreactive antibody

Take necessary steps to confirm suggestions

Description for selected mix

Mix of anti-s, M:

- Anti-s reacting in Coombs (2+), with variable reactivity due to dose effect (1+)
- Anti-M reacting in Coombs (1+), with variable reactivity due to dose effect (+/-); possible complement fix reaction

Perform tests at room temperature to confirm the presence of cold reacting antibodies

Clinically significant antibodies not excluded

With antiglobulin: anti-D, C, E, C^w, V, K, Js^a, Fy^a, Jk^a, Xg^a, s, M

Buttons: Help, Explain, Hints, Cancel, OK

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Resolvigen 3 is able to cope with these more complex cases, for example:

When weak antibodies react only with test RBCs exhibiting the strongest antigenic expressions due to homozygosity (e.g. anti-Jk^a reacting with Jk(a+,b-) RBCs only), dose effect for Rh haplotypes (e.g. anti-D or anti-E reacting with R2R2 RBCs only), or increased antigenic expression (e.g. anti-P1 reacting with P1 strong RBCs only).

When antibodies are so weak that they fail to react with some of the homozygous test RBCs, giving what appears to be spurious reactions; in this case the most likely match is found and the related antibody specificities suggested, hinting at procedures for confirming them.

Varying reaction scores of differently reacting RBCs are analyzed to identify different antibodies in mix, matching the hypothesized titre of each antibody with the variable reactivity of different RBCs for each antibody specificity; this way even antibody specificities whose reaction patterns on the panels being used are completely covered by reactions of other antibodies in the mix can be detected.

When weak or spurious reactions at 37 °C or in Coombs, hint at the presence in mix of a cold reacting antibody specificity, caused by residual reactions due to extended temperature range or for suspected complement fixing reactions, Resolvigen 3 suggests tests be performed at room temperature.

Clinically significant antibodies, which are undetectable because their reactions are covered on panels by strong reactions of detected antibodies, are listed in a special warning section.

Results analysis is able to cope with cases where some test RBC samples fail to react with a suspected antibody specificity due to haplotype effect; for example an anti-k antibody specificity failing to react with Kk, Kp(a+b+) RBCs, due to the CIS inhibiting effect of the Kp^a gene on the only k gene present, with extreme weakening of the k antigen.

This way Resolvigen 3 assists the user when weak positives are detected (which is quite frequent when working with cards or solid phase), and so helping prevent delayed transfusion reactions.

Panel data is also used, when possible, to detect the presence of antibodies indirectly related to panel antigens like anti-Fy³, anti-Fy⁵, anti-Le^x or anti-Jk³ when the related antigen expression can be deduced by the expressions of antigens on panels.

Analysis is extended to antibodies against public and private antigens marked in the 'Special Antigen Typing' section of Panel RBCs, archive RBCs or patient's RBCs used in tests.

Resolvigen 3 uses the patient's RBCs phenotype when a panreactive antibody is suspected to hint at the most likely antibody specificity; the patterns of panel antigens are used as a hint at the antibody specificity; for example:

- an Fy(a-b-) phenotype is a hint for an anti-Fy³ antibody,
- a S-s- phenotype for an anti-U ,
- a D-- for an anti-Hr₀.

but also extremely weak expressions are used as a hint; for example:

- a k+ weak and Kp(a-b+ weak) phenotype is a hint for a McLeod phenotype with an anti-Kn+Kx antibody specificity,
- a Lu(a-b+ weak) hints at an anti-Lu12,
- a D strong, C weak, c negative, E negative, e weak hints at an anti-Sec.

Searching panreactive antibodies beyond panels

Resolvigen 3 is capable of identifying antibodies against public antigens by guiding the operator through a sequence of simple and inexpensive tests; first a list of possible antibody specificities is identified, based on observed reaction profile with panel and patient's RBCs.

Antibodies against public antigens

PRESENCE IN PATIENT'S SERUM OF A WARM, INCOMPLETE, PANREACTIVE ALLOANTIBODY.

Alloantibody specificities considered:

Anti-U, anti-En^aTS, anti-En^aFS, anti-En^aFR, anti-En^aKT, anti-Rh29, anti-Hr₀, anti-Hr, anti-Hr^B, anti-Nou, anti-Sec, anti-Dav, anti-MAR, anti-Lu^b, anti-Lu3, anti-Lu4, anti-Lu5, anti-Lu6, anti-Lu7, anti-Lu8, anti-Lu11, anti-Lu12, anti-Lu13, anti-Lu16, anti-Lu17, anti-Au^a, anti-Lu20, anti-k, anti-Kp^b, anti-Ku, anti-K18, anti-K19, anti-Km, anti-K22, anti-Fy3, anti-Fy5, anti-Jk3, anti-Cy^a, anti-Hy, anti-Jo^a, anti-Co^a, anti-Co3, anti-LW^a, anti-LW^{ab}, anti-Ge2, anti-Ge3, anti-Ge4, anti-Cr^a, anti-Tc^a, anti-Dr^a, anti-Es^a, anti-Sl^a, anti-Er^a, anti-Yk^a, anti-In^b, anti-Cs^a, anti-I, anti-I^T, anti-i, anti-Ok^a, anti-JMH, anti-Emm, anti-AnWj, anti-MER2, anti-Sd^a, anti-I

Antibodies against public antigens

Indicate serum reactivity, compared to reactivity against untreated allogeneic group O RBCs from panels, with:

Ficin pretreated group O RBCs (if the reactivity increases, also enter result for the test 'Autologous ficin pretreated RBCs'):	Does not change noticeably
Allogeneic group O RBCs pretreated with AET or DTT:	Is zeroed or markedly reduced
Untreated group O cord RBCs:	Does not change noticeably
ABO compatible RBCs from patient with paroxysmal nocturnal hemoglobinuria (DAF negative):	Does not change noticeably

Other information:

Autologous ficin pretreated RBCs:	Negative
With fresh serum, can hemolysis be evidenced at room temperature or at 37 °C?	No
Has the patient been transfused in his/her lifetime? Otherwise if	

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Then, the user is asked to perform some tests using reagents and material normally available in any immunohematology laboratory; the user is free to answer all or just some of the questions (obviously, the more data the better).

Based on observed reactions and on known behavior of suspected antibody specificities, Resolvigen 3 is usually capable of reducing the number of antibody specificities to just a few:

Antibodies against public antigens

RESULTS

According to the entered data, the following antibodies are considered possible:

Likely for patient's race:

J_s^b

Unlikely for patient's race:

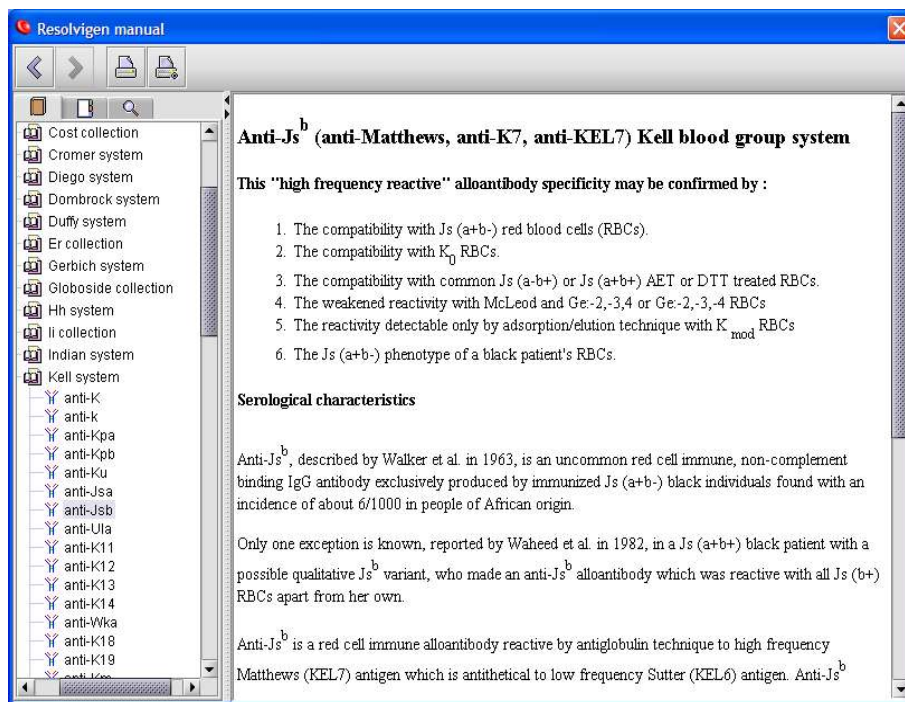
k, Ku/Ku-like, K19, Km, Kn^a

Very unlikely for patient's race:

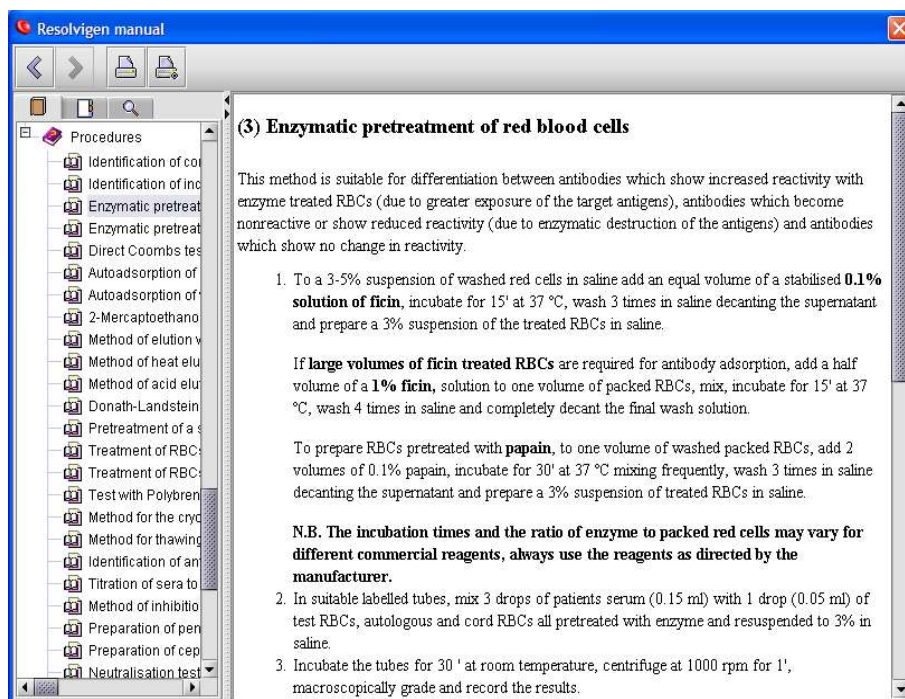
Kp^b, LW^a, LW^{ab}, Sc1, K11, K12, K13, K14, K18, K22, Sc3, MER2

Use of any information or elaboration provided by this software is under user responsibility. take necessary steps to confirm suggestio...

The on line manual provides immunohematological and clinical information related to each antibody specificity,

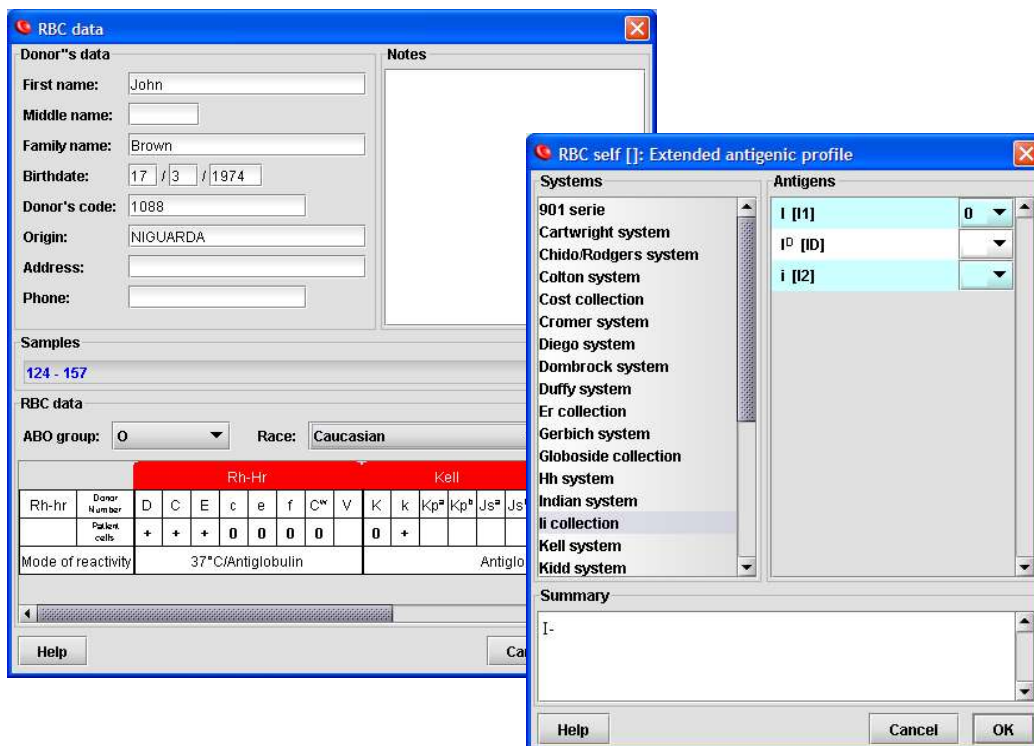


as well as a step by step description of immunohematological methods to be used.

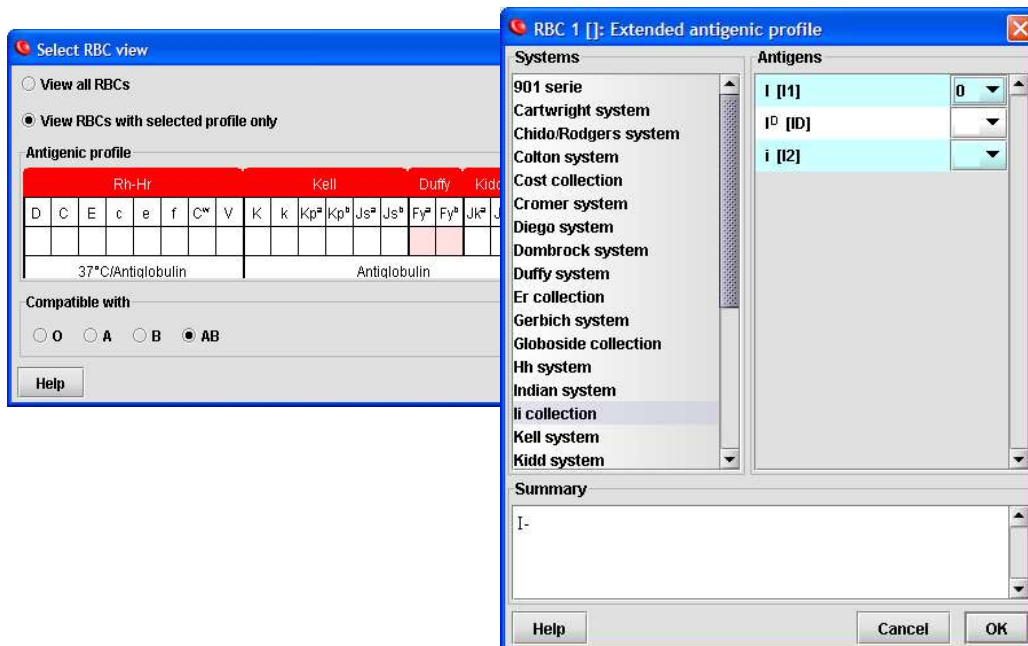


Information storage and exchange

Resolvigen 3 offers facilities for storing, indexing and searching for entered data; information of interest from an immunohematological viewpoint, like blood group or antigenic profile for archived RBCs may be stored:

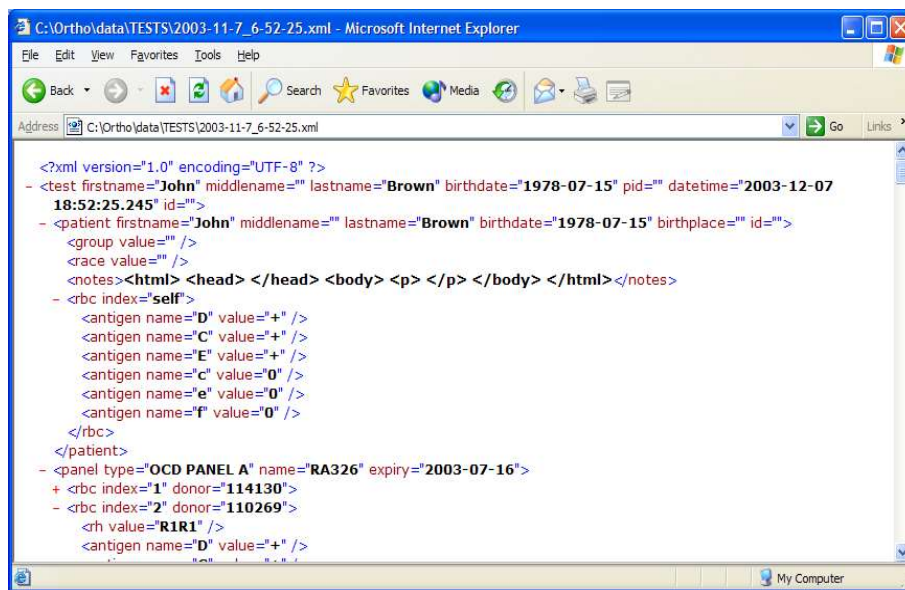


All entered data is indexed and readily available for use, for example for searching among archived RBCs for samples with a given blood group and antigenic profile.



Resolvigen 3 stores each piece of information (Patient, archive RBCs, panel or test) in a different XML file; this is convenient for different reasons:

- XML is a recognized standard for data exchange and is one of the formats for which standards provide digital signature,
- it is very easy to exchange a piece of information with a different user: one user exports the required data to a floppy, or sends it by email and a second user can import data into his own archives,
- XML files by their nature are extensible, thus it will be easy to extend the current format to handle new features,
- XML is an open standard, so it will be easy for anyone to develop applications that browse Resolvigen data: Microsoft Explorer can also be used to read Resolvigen 3 files.

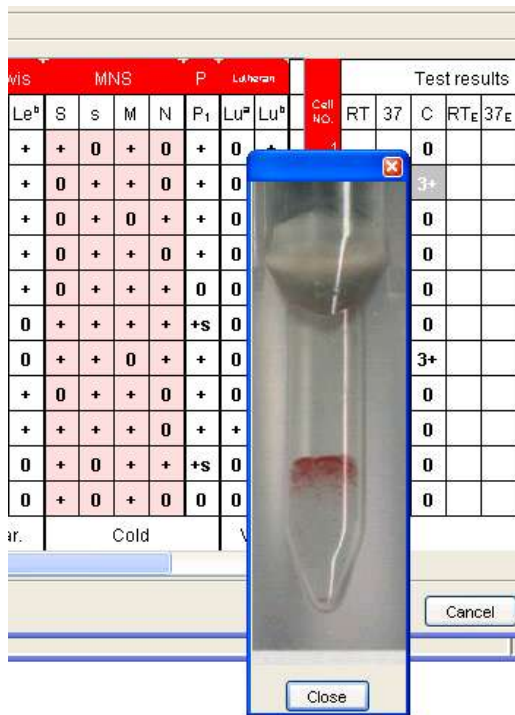


This information is indexed using an embedded JDBC database, but it is very easy to configure Resolvigen 3 to use any JDBC or ODBC database; this way it is possible to use virtually any database, offering yet another possibility for data exchange.

In order to ease the transition for users of Resolvigen 2, Resolvigen 3 is capable of importing Resolvigen 2 databases and Panel distribution diskettes.

Automated instrument interfacing

Resolvigen 3 can import data from automated instruments; besides being a convenient way of reducing both user work load and the possibility of errors, this also gives the added advantage of maximum repeatability in scoring criteria, so making score comparison extremely reliable when used as a mean to identify different antibody specificities in mixes that react with most or all RBCs in panels.



Resolvigen 3 is interfaced to different instruments that read BioVue:

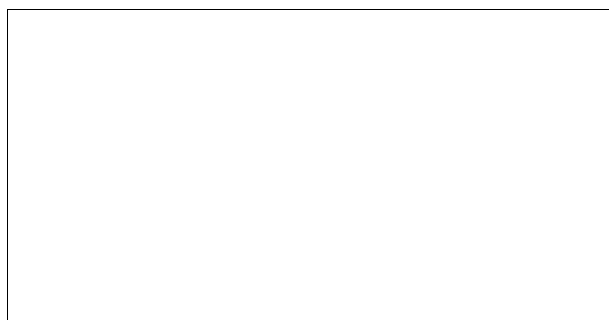
- MiniVue
- OrthoScan
- Innova

When importing scores from an automated instrument, Resolvigen 3 can also read and store images of wells in which tests have been performed.

Images are stored locally and are available for browsing by simply clicking the right mouse button on the related Antigram cell.

Distribution

Resolvigen 3 is distributed by Ortho Clinical Diagnostics; for ordering Resolvigen 3 contact:



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