WELCOME TO TODAY'S WEBINAR.

We will start shortly.

wmda
matching donors • serving patients

Today's webinar

Will be recorded

Will be available on Share

For technical issues/support, please use the Chat function in ZOOM

For questions, use the Q&A function

Questions will be answered after the presentations, but you can submit your questions throughout the webinar

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New Matching Algorithm:
How to interpret search results in the updated Search & Match Service

By *Christine Urban*

DKMS

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Updated Search & Match Service

- Multi-factor Authentication
  - Individual accounts as opposed to group accounts
  - Initial credentials and source of authentication tokens
  - First steps towards future goal – Single sign-on (SSO)

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  - Enter patient information – manual vs API
  - View search results – online vs API

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Add Patient

Patient ID ⓘ   [_____ 🔳]

HLA Details

Class I

HLA-A*   [_____ 🔳] [_____]

HLA-B*   [_____] [_____]

HLA-C   [_____] [_____]

Extra Class II loci ⌄

Medical Details

CMV Status   [_____⌄]   Blood group, Rh   [____⌄] [____⌄]

Ethnicity ⓘ   [_____⌄]   Weight ⓘ   [_____]

Birth Date   [YYYY-MM-DD 📊📅]   Sex   [_____⌄]

Diagnosis   [_____⌄]   Disease Phase   [_____⌄]

Diagnosis Date   [yyyy-mm-dd 📊📅]   Pool Country Code   [_____⌄]

Diagnosis Text   [_____🔳]   Transplant Center ID   [_____]

Search details

Search type   ☑ Run an A, B, DR donor search   Algorithm   ☑ HAP-E

☐ Run a cord search

☑ I declare that the patient has been informed about the transmission of their information to the Search & Match Service.

[Search]

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Probability of Mismatches ⓘ	A	B	C	DRB1	DQB1	DPB1	Registry	Sex	Age	Blood group
				Patient details						
	01:01 02:01:01	08:01:01 39:01:01	07:01:01 12:03:01	03:01:01 03:01:01	02:01:01 02:01:01	04:01:01 04:01:01				

+9/10 (potential) allele matches sorted by sum of probabilities										

673 GRID: **7414DKM000105864812**   Status: **AV**   CMV: No. of donations: **0**   Ethnicity: **UK**

Probability of Mismatches	A	B	C	DRB1	DQB1	DPB1	Registry	Sex	Age	Blood group
0: **0%** 1: **100%** 2: **0%**	A	M	A	A	A	Pe	7414 ✓ PL-DKMS	Male	49	A+ ★
	01:01:01G 02:01:01G	08:01:01G (18:01:01G)	07:01:01G 12:03:01G	03:01:01	02:01:01	(01:01:01) 04:01:01				

674 GRID: **6354000000192406131**   Status: **AV**   CMV: **N 2010-02-24**   No. of donations: Ethnicity: **CAEU**

Probability of Mismatches	A	B	C	DRB1	DQB1	DPB1	Registry	Sex	Age	Blood group
0: **99%** 1: **1%** 2: **0%**	P	P	P	P	P		6354 ✓ GB-ANT	Male	49	☆
	100% 01:YAG 02:ANGR	**100%** 08:AKNJ 39:FGMU	**100%** 07:FPWT 12:AUCW	**73%** 03:WZF 03:APJZ	**27%**					

Updated Search & Match Service

- Multi-factor Authentication
  - Individual accounts as opposed to group accounts
  - Initial credentials and source of authentication tokens
  - First steps towards future goal – Single sign-on (SSO)

- Starting a search and viewing results
  - Enter patient information – manual vs API
  - View search results – online vs API

- Filtering the results
  - Existing & new filters
  - Grouping/sorting options

Filters

✕

Match

Locus mismatch allowed

Locus A	⌄

DPB1 match grade

Select match grade	⌄

Specific allele type on locus

Locus A	⌄

A

29:02:01

Group/sorting

◉ Standard ⓘ

○ Sort by sum of probabilities ⓘ

Donor

Status

☑ Available

☐ Not available

☐ Reserved

CMV

Positive	⌄

Sex

Positive	⌄

Bloodgroup

Select bloodgroup	⌄

Age

17   80

Registry

Accreditation status

☑ Accredited

☐ Qualified

☐ Unknown / Not Accredited

Registry

Select registry	⌄

Cord search filters

TNC

Minimum TNC

CD34+

Minimum CD34+	⌄

Apply filter   **Delete filters**

Filter:

CMV status **1** ∨   Blood group **1** ∨   ⇄ All filters **3**

1 cords   **(Brackets)** = mismatches   **(Bold)** = antigen mismatches   (Underlined) = allele mismatches   *Italics* = uncertainty

Probability of Mismatches ⓘ	A	B	C	DRB1	DQB1	DPB1	Registry	Sex	Age	Blood group	TNC	CD34+
							Patient details					
	01:01	08:01:01	07:01:01	03:01:01	02:01:01	04:01:01						
	02:01:01	39:01:01	12:03:01	03:01:01	02:01:01	04:01:01				A+		
				10/10 (potential) allele matches								
#1 Cord ID: **DUCB20001**			CMV: **G 2011-01-25**	Volume: **24**	Ethnicity:		Viability: **97%**	Attached segments:				
0: **0%**	P	P	P	P	P		4908 ⊘	Female	11	O+	117.0	4.0
1: **0%**							DE-DUS					
2: **42%**												
	01:KSFE	08:GKSB		03:ASVB	02:XX							
	02:GJKB	39:GKSU		15:XX	06:XX							

Feature differences
Hap-E Search vs. Optimatch

Antigen Recognition Domain explained

- The antigen recognition domain (ARD) is the binding groove of the HLA peptide. This is the region interacting with the presented antigen and T-cell receptor.

- All alleles that express the same amino acid sequence in this region are considered an allele match.

- The ARD is encoded on:
  - exon 2 & 3 for HLA class I
  - exon 2 for HLA class II

1. Null allele treatment in Hap-E search

- Null alleles are treated as absent, i.e. the second typing matches as homozygous.

- Null allele matching rules are applied to:
  - All high resolution null alleles.
  - Null alleles as part of multi allele codes if the null allele is part of a haplotype matching the donor's (patient's) HLA typing.

- Null allele matching rules are only applied to one typing of the locus.

02:GFJM ≙ 02:01/02:105/02:125N

Patient typing		Donor typing
A*03:01, A*01:11N	matches	A*03:01, A*03:01
A*03:01, A*01:11N	matches	A*03:01, A*02:125N
If there is a haplotype compatible with the donor typing containing A*02:125N then		
A*03:01, A*01:11N	matches	A*03:01, A*02:GFJM
A*03:01, A*03:01	matches	A*03:01, A*02:XX
A*03:01, A*03:01	does not match	A*03:01, A*01:01:01G
A*01:11N, A*02:125N	does not match	A*03:01, A*03:01

2. Search with two mismatches

Hap-E search

The two mismatches can be on any locus.

Optimatch

Only one of two mismatches is allowed on loci A, B and DRB1. The second mismatch has to be on locus C or DQB1.

3. Donors with DNA and serologic typing

Hap-E search

Only the DNA typing information is used for matching.

Optimatch

Serological information is used as additional constraint in combination with DNA typing information for matching.

4.1 Match grades: Overview

Standard match grades

A Allele match

P Potential match

M Antigen mismatch

L Allele mismatch (antigen match)

DPB1 special grades

A Allele match

Pe Permissive mismatch

G Non-permissive mismatch in GvH direction

H Non-permissive mismatch in HvG direction

X No specification due to ambiguous or missing TCE assignment

4.2 Match grades: Differences

Hap-E search

All alleles in typings are considered.

A Allele match:
- Single allele
  or
- Multiple alleles of the same ARD

P Potential match:
- Multiple alleles of more than one ARD

Optimatch

Only alleles that are part of a haplotype matching the donor's (patient's) HLA typing are considered.

A Allele match:
- Single allele
  or
- Multiple alleles of the same ARD

P Potential match:
- Multiple alleles of more than one ARD

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5. No haplotype based probability available

Algorithm behaviour if the patient / donor typing is ambiguous and has no representation in the haplotype frequency set:

Hap-E Search

No probabilities are calculated.

Optimatch

Probabilities are calculated based on allele frequencies.

6. Cord Blood search options

Hap-E Search

- Allele matched:
  - n/10, n/8 and n/6 search
  - Up to 2 mismatches

- Antigen matched:
  - Not implemented

Optimatch

- Allele matched:
  - n/10, n/8 and n/6 search
  - Up to 4 mismatches

- Antigen matched:
  - n/6 search
    Class I matched at antigen level, Class II matched at allele level

7. Probability display

Hap-E Search

All probabilities are rounded to integer values.

→ 0%:

- Values 0 < p < 0.5
- No shared genotype between donor and patient.

Optimatch

Calculated values 0 < p < 0.5 are displayed as 1%.

→ 0%:

- No shared genotype between donor and patient

8.1 Locus match probabilities in Hap-E search: Definition

- match, i.e. 10/10, 8/8 or 6/6
  - The locus match probability is the **relative probability** that this locus is a match **in the 1 mismatch case.**

- mismatch, i.e. 9/10, 7/8 or 5/6
  - The locus match probability is the **relative probability** that this locus is a match **in the 2 mismatch case**.

This probability provides information on which locus the **next mismatch** will occur.
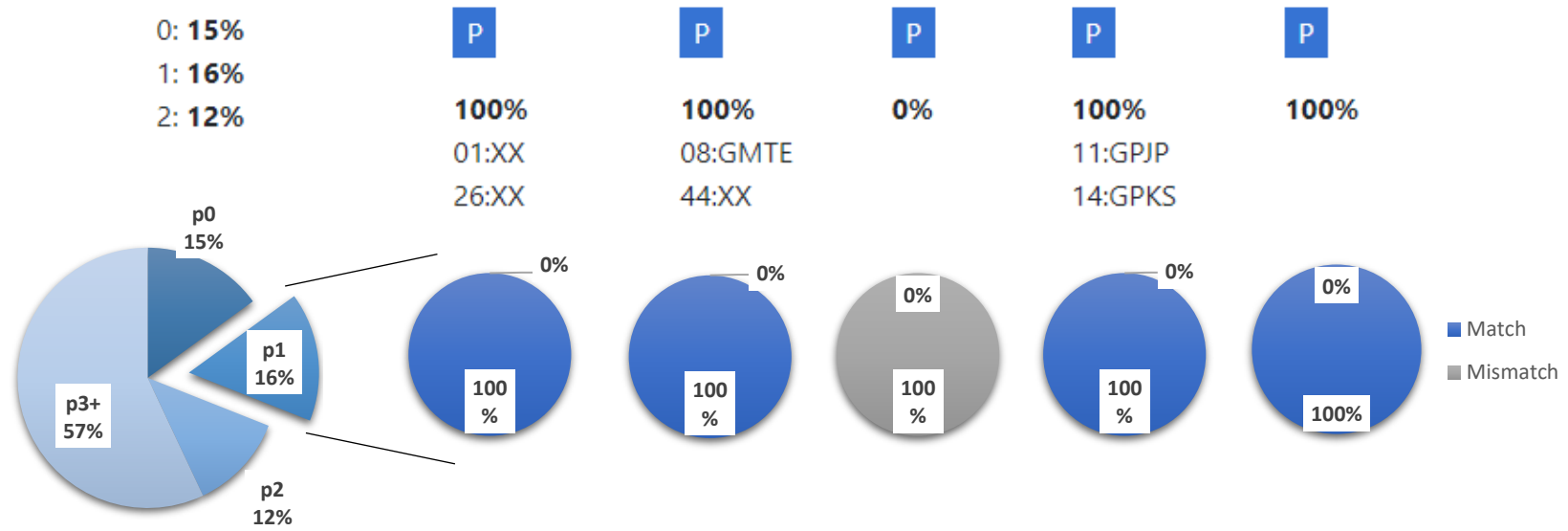
8.2 Locus match probabilities in Hap-E search: Not displayed

In some cases the value is not defined and no locus match probability is displayed:

- match
  - when $p1 = 0$ (division by zero, not defined).
- mismatch
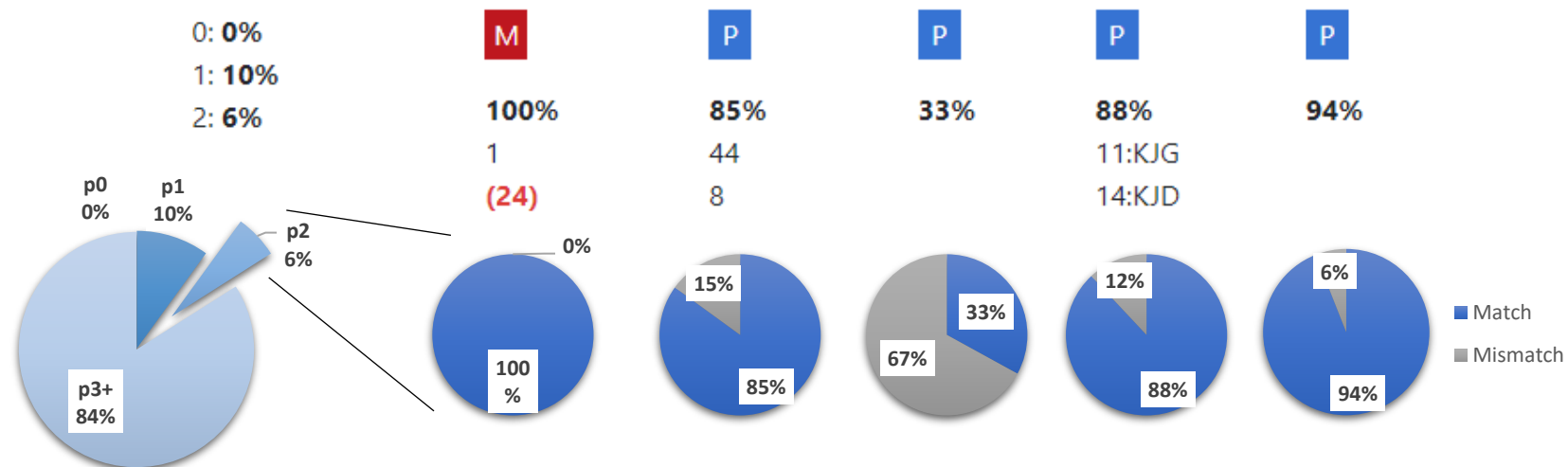 - when $p2 = 0$ (division by zero, not defined).

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8.3 Locus match probabilities: Example 1

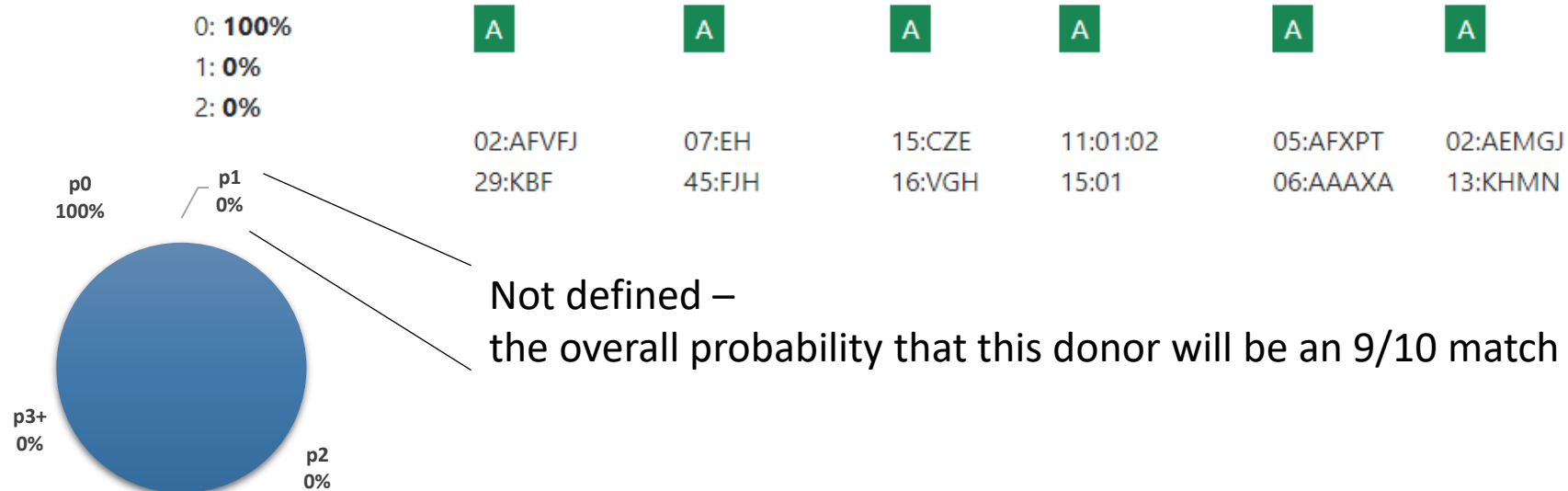# 8.3 Locus match probabilities: Example 2

Have your say in a quick poll!

Knowing that donor ranking and match grade is determined by the p-values, should they be displayed more prominently than the locus probabilities?
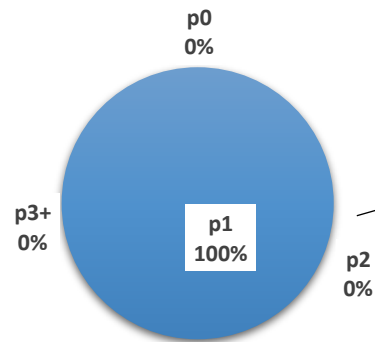
8.3 Locus match probabilities: Example 3

Probability of Mismatches ⓘ

	A	B	C	DRB1	DQB1	DPB1
			Patient details			
	02:01:01	07:05:01	15:05:02	11:01:02	05:02:01	
	29:01:01	45:01:01	16:01:01	15:01:01	06:02:01	

10/10 (potential) allele matches

 # 1 GRID: **57615729D3C1969C4A4** Status: **AV** CMV: No. of donations: **0**

	A	B	C	DRB1	DQB1	DPB1
0: **100%**	A	A	A	A	A	A
1: **0%**						
2: **0%**						
	02:AFVFJ	07:EH	15:CZE	11:01:02	05:AFXPT	02:AEMGJ
	29:KBF	45:FJH	16:VGH	15:01	06:AAAXA	13:KHMN

p0 100%
p1 0%
p2 0%
p3+ 0%

Not defined – the overall probability that this donor will be an 9/10 match is zero.

8.3 Locus match probabilities: Example 4

Probability of Mismatches ⓘ	A	B	C	DRB1	DQB1	DPB1
				Patient details		
	01:KTKP	08:XKT	07:CVAG	11:04:01	03:ENWH	
	26:GAX	44:ENWF	16:04:01	14:BCAD	05:03:01	

9/10 (potential) allele matches

41   GRID: **5761AA51D0B692CF494**   Status: **AV**   CMV: No. of donations:

	A	B	C	DRB1	DQB1
0: **0%**	M	A	A	A	P
1: **100%**					
2: **0%**	01:01	08:01	07:01	11:04	03:XX
	(24:02)	44:02	16:04	14:54	05:XX

p0 0%
p3+ 0%
p1 100%
p2 0%

Not defined –
the overall probability that this donor will be an 8/10 match is zero.

Have your say in a quick poll!

How should the absence of a probability value be displayed?

Helpful resources

- WMDA Share
  - [Feature comparison Matching engines](#)
  - [User Guide Search & Match Service version 2](#)
  - [MFA user guide](#)

- Adding more features
  - [Available and upcoming features](#)
  - Vote

- Patient & Search APIs
  - [API Documentation](#)

VERY IMPORTANT!!!

You have until **31 October 2022** to transition your operations from the old to the new S&M.

Active patient cases will only be transferred to new platform upon written request.

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QUESTIONS?

TODAY'S WEBINAR WAS MADE POSSIBLE THANKS TO THE GENEROUS SUPPORT OF ONTIME COURIER GMBH

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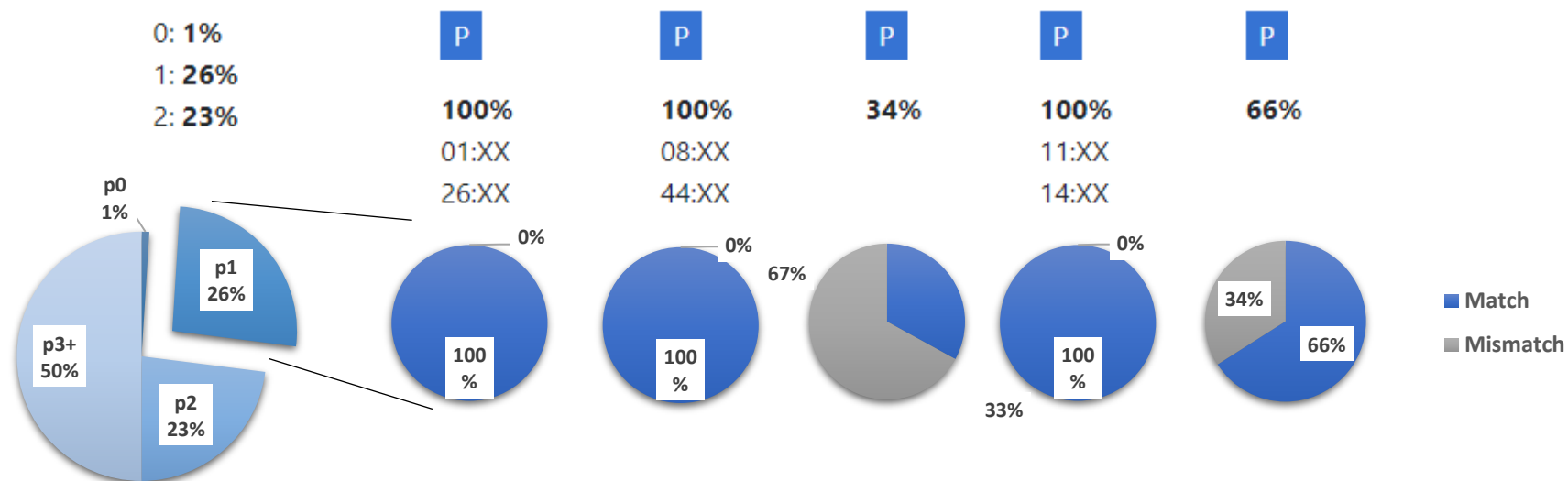Part of LLG

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Thank you for your attention

We look forward to seeing you next time!

More examples locus match probabilities
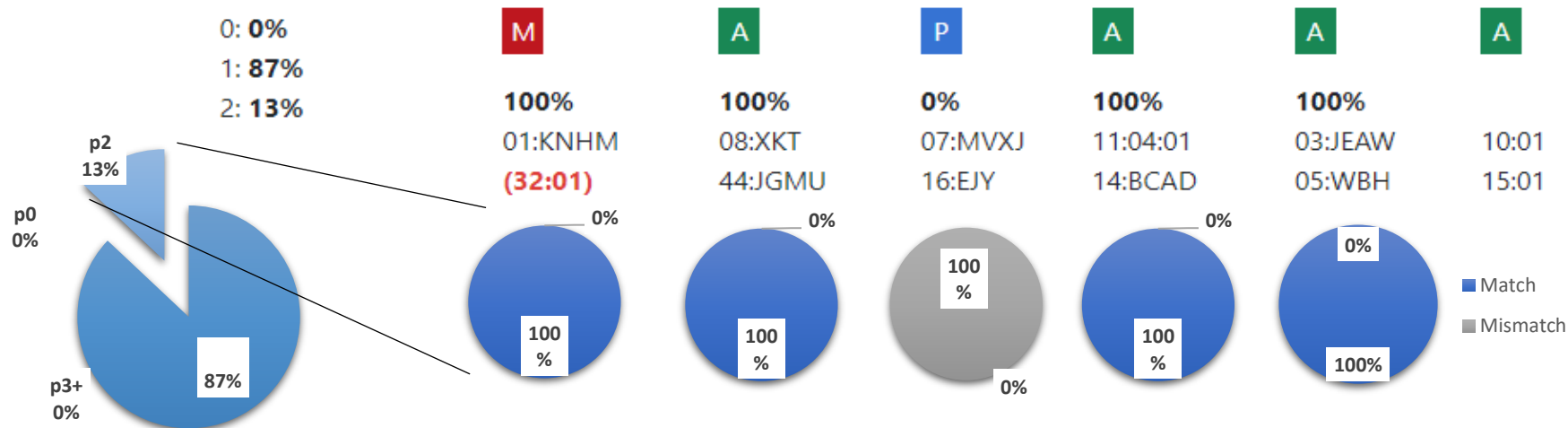
8.3 Locus match probabilities: Examples

Probability of Mismatches (i)

	A	B	C	DRB1	DQB1	DPB1
			Patient details			
	01:KTKP	08:XKT	07:CVAG	11:04:01	03:ENWH	
	26:GAX	44:ENWF	16:04:01	14:BCAD	05:03:01	

10/10 (potential) allele matches

3   GRID: **57617D56408858751DD**   Status: **AV**   CMV: No. of donations: **0**

0: **1%**	P	P	P	P	P
1: **26%**					
2: **23%**	**100%**	**100%**	**34%**	**100%**	**66%**
	01:XX	08:XX		11:XX	
	26:XX	44:XX		14:XX	

p0 1%

p1 26%

p3+ 50%

p2 23%

0%   100%

0%   100%   67%

34%

0%   100%   33%

34%   66%

■ Match
■ Mismatch

8.3 Locus match probabilities: Examples

8.3 Locus match probabilities: Examples

Probability of Mismatches ⓘ	A	B	C	DRB1	DQB1	DPB1
				Patient details		
	01:KTKP	08:XKT	07:CVAG	11:04:01	03:ENWH	
	26:GAX	44:ENWF	16:04:01	14:BCAD	05:03:01	

9/10 (potential) allele matches

# 67	GRID:			Status:	CMV:		No. of donations:

0: **0%**
1: **0%**
2: **0%**

	P	P	P	M	P
	1	44		**(03:ENU)**	
	26	8		14:ECZ	

p0
0%

p1
0%

p2
0%

p3+
100%

Not defined –
the overall probability that this donor will be an 8/10 match is zero.