Current CPRA Calculation

Implemented October 1, 2009

OPTN

UNOS DONATE LIFE

CPRA

- Calculated PRA (CPRA) is the percentage of donors expected to have HLA antigens listed as unacceptable for a candidate on the waiting list
- CPRA is calculated for kidney, kidney-pancreas and pancreas candidates on the waiting list
- If no unacceptable antigens are entered, CPRA value defaults to 0

CPRA (Probability of a positive crossmatch) = $1- (1-\Sigma p_i)^2$

- CPRA is determined using an established algorithm (1, 2)
- It was written by two well-recognized population geneticists and is based upon basic principles of population genetics
- Additionally, the entire proposal for CPRA (algorithm, frequencies, etc.) was reviewed by OPTN/UNOS committees, as well as ASHI, through a panel of three reviewers, that included two population geneticists

---

1. Zachary AA and Braun WE. Calculation of a predictive value for transplantation. Transplantation 1985;39:316-8.
2. Zachary AA and Steinberg AG. Statistical Analysis and Applications of HLA Population Data. In, NR Rose, EC de Marcario, JD Folds, HC Lane, and RM Nakamura, Eds., Manual of Clinical Laboratory Immunology, 5th Edition, Washington, DC, ASM Press, 1997:132-40.

Frequencies

Current CPRA is calculated based on the data:

- HLA frequencies derived from the HLA phenotypes of deceased kidney donors recovered from January 1, 2003 through December 31, 2004
- Ethnic frequencies derived from deceased kidney donors recovered from January 1, 2006 through June 30, 2007

CPRA Frequencies

- Allele group frequencies were derived by gene counting of the broad and split antigens
- Two, three, and four locus haplotype frequencies were estimated by the expectation maximization algorithm using Arlequin computer program (3)

3. Leffell MS, Cherikh WS, Land GA, Zachary AA. Improved definition of HLA frequencies among minorities and applicability to estimates of transplant compatibility. Transplantation 2007; 83:964-972

Ethnic Frequencies (Four Major Groups)

- CPRA is also based on ethnic frequencies for four major groups (White, African American, Hispanic and Asian ethnicities)
- Ethnic frequencies were derived based on deceased kidney donors recovered from January 1, 2006 through June 30, 2007*

	Number	Proportion
White	7,337	0.689
African American	1,558	0.146
Hispanic	1,507	0.142
Asian	242	0.023
Total	10,644	1.000

Donors of other ancestry comprised 1.17% of total number of deceased kidney donors during this period. These groups were not included.

OPTN

* Based on OPTN data as of September 21, 2007

UNOS DONATE LIFE

CPRA Calculation

1. Get a list of all unacceptable antigens including equivalences listed in Appendix 3A*

Example:

- A kidney candidate is listed with antibodies to A1, A3, B35, DR11 and DQ7
- DQ7 is equivalent to DQ7 and DQ3
- A1, A3, B35 and DR11 are only equivalent to themselves
- CPRA calculation will use A1, A3, B35, DR11, DQ3 and DQ7 frequencies

The current version of Appendix 3A can be found on OPTN site at

http://optn.transplant.hrsa.gov/PoliciesandBylaws2/policies/pdfs/policy_14.pdf

CPRA Calculation (cont'd)

2. For each ethnicity separately:

- S1 - Sum all the allele (1 locus) frequencies (A, B, DR, DQ)
- S2 - Sum all the 2 locus haplotype frequencies (AB, ADR, ADQ, BDR, BDQ, DRDQ)
- S3 - Sum all the 3 locus haplotype frequencies (ABDR, ABDQ, ADRDQ, BDRDQ)
- S4 - Sum all 4 locus haplotype frequencies (ABDRDQ)
- CPRA for the ethnicity is:

probability of a positive crossmatch =

1 – probability of a negative crossmatch =

$= 1 – (1 – S1 + S2 – S3 + S4)^2$

CPRA Calculation (cont'd)

- Since all allele groups weren't observed within all ethnic groups, some locus haplotypes do not have frequencies
- DR51, DR52, DR53, Bw4 and Bw6 frequencies are based on the approved equivalences listed in Appendix 3A

Example

CPRA based on A1, A3, B35, DR11, DQ3 and DQ7

S1 - Sum all the allele (1 locus) frequencies (A, B, DR, DQ)

	White	African American	Hispanic	Asian
A1	0.15713	0.05478	0.06246	0.03175
A3	0.13881	0.08041	0.07403	0.02579
B35	0.08472	0.07584	0.16722	0.08929
DR11	0.09416	0.1264	0.07369	0.07143
DQ3	0.12500	0.04959	0.15723	0.17206
DQ7	0.14433	0.15552	0.13165	0.13968
Total (S1)	0.74415	0.54254	0.66628	0.53000

Example (cont'd)

CPRA based on A1, A3, B35, DR11, DQ3 and DQ7

- S2 - Sum all the 2 locus haplotype frequencies (AB, ADR, ADQ, BDR, BDQ, DRDQ)

	White	African American	Hispanic	Asian
A1; B35	0.00632	0.0023	0.00386	0.00397
A3; B35	0.02058	0.01222	0.01255	0.00794
A1; DR11	0.00960	0.0062	0.00709	0.00794
A3; DR11	0.01060	0.0064	0.00529	0.00198
A1; DQ3	0.01448	0.00165	0.00936	0.00904
A1; DQ7	0.01198	0.00383	0.00564	0
A3; DQ3	0.01516	0.00524	0.00646	0
A3; DQ7	0.01312	0.01331	0.00770	0.00338
B35; DR11	0.01227	0.00463	0.01551	0.01025
B35; DQ3	0.01019	0.00296	0.02760	0.01651
B35; DQ7	0.01318	0.00461	0.03002	0.01904
DR11; DQ3	0.02886	0.01457	0.01684	0.03181
DR11; DQ7	0.06491	0.05701	0.04964	0.03500
Total (S2)	0.23125	0.13493	0.19756	0.14686

Example (cont'd)

CPRA based on A1, A3, B35, DR11, DQ3 and DQ7

- S3 - Sum all the 3 locus haplotype frequencies (ABDR, ABDQ, ADRDQ, BDRDQ)

	White	African American	Hispanic	Asian
A1; B35; DR11	0.00195	0	0.00236	0
A3; B35; DR11	0.00198	0.00028	0.00062	0
A1; B35; DQ3	0.00094	0	0	0
A1; B35; DQ7	0.00079	0	0.00039	0
A3; B35; DQ3	0.00123	0	0.00131	0
A3; B35; DQ7	0.00194	0	0	0
A1; DR11; DQ3	0.00232	0.00033	0.00271	0
A1; DR11; DQ7	0.00762	0.00093	0.00281	0
A3; DR11; DQ3	0.00345	0.00127	0.00108	0
A3; DR11; DQ7	0.00768	0.00563	0.00336	0.00202
B35; DR11; DQ3	0.00368	0.00134	0.00298	0.00607
B35; DR11; DQ7	0.00818	0.00276	0.01325	0.01058
Total (S3)	0.04176	0.01254	0.03087	0.01867

Example (cont'd)

CPRA based on A1, A3, B35, DR11, DQ3 and DQ7

- S4 - Sum all 4 locus haplotype frequencies (ABDRDQ)

	White	African American	Hispanic	Asian
A1; B35; DR11; DQ3	0	0	0	0
A1; B35; DR11; DQ7	0.00037	0	0.00112	0
A3; B35; DR11; DQ3	0.00067	0	0	0
A3; B35; DR11; DQ7	0.00312	0.00038	0.00084	0
Total (S4)	0.00416	0.00038	0.00196	0

Example (cont'd)

CPRA based on A1, A3, B35, DR11, DQ3 and DQ7

- CPRA for the ethnicity is: 1 - probability of negative crossmatch = $1 – (1 – S1 + S2 – S3 + S4)^2$

	White	African American	Hispanic	Asian
S1	0.74415	0.54254	0.66628	0.53000
S2	0.23125	0.13493	0.19756	0.14686
S3	0.04176	0.01254	0.03087	0.01867
S4	0.00416	0.00038	0.00196	0
Probability of a negative crossmatch	0.20205	0.33667	0.25238	0.35783
Probability of a positive crossmatch	0.79795	0.66333	0.74762	0.64217

CPRA Calculation

3. Get the final CPRA by applying ethnic weights:

- For each ethnicity multiply CPRA for that ethnicity by ethnic weight
- Sum all the values to get the final CPRA

Example:

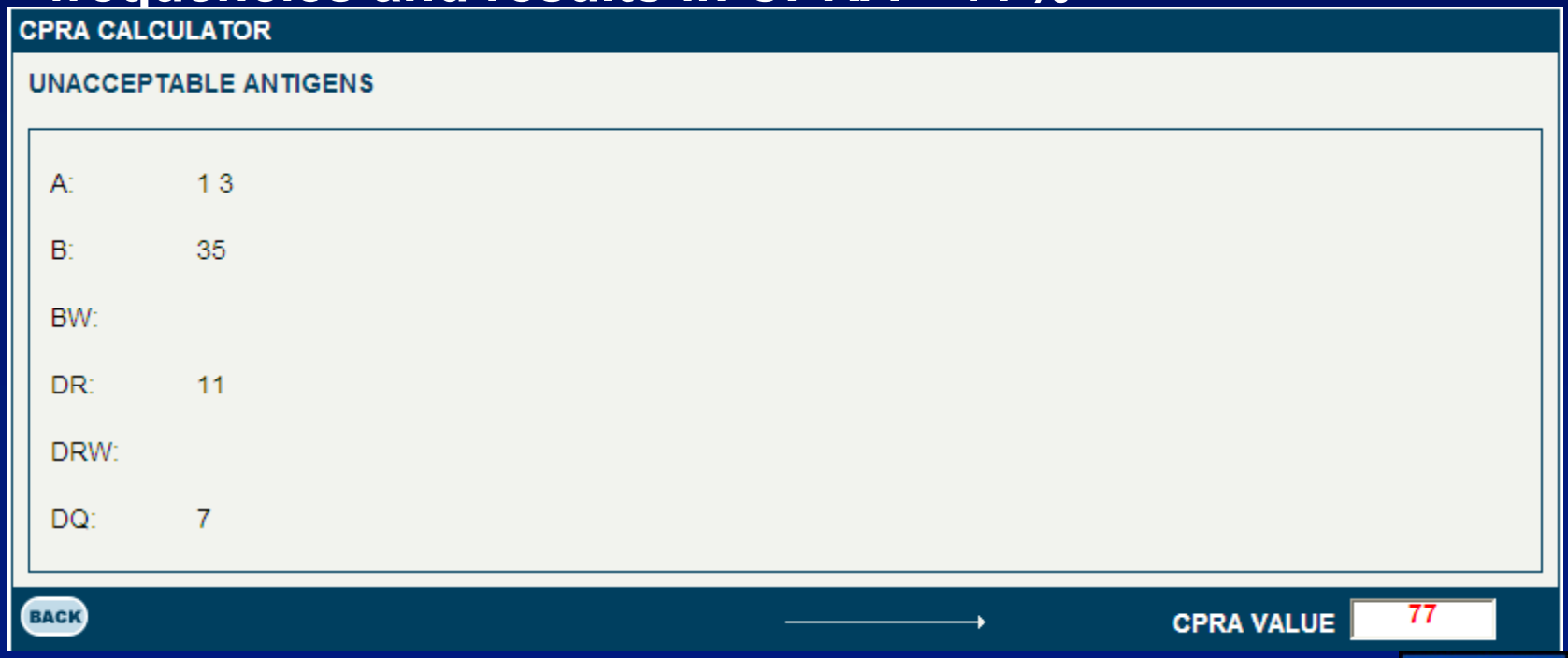
	White	African American	Hispanic	Asian
CPRA for ethnicity	0.79795	0.66333	0.74762	0.64217
Ethnic weight	0.689	0.146	0.142	0.023

CPRA = 0.79795 x 0.689 + 0.66333 x 0.146 + 0.74762 x 0.142 + 0.64217 x 0.023 = 0.76757 or 77%

CPRA Calculation

Example:

- **A kidney candidate is listed with antibodies to A1, A3, B35, DR11 and DQ7**
- **CPRA calculation uses A1, A3, B35, DR11, DQ3 and DQ7 frequencies and results in CPRA = 77%**



See the attached spreadsheet for HLA Frequencies used to calculate CPRA