

IMGT/HLA 3.47.0 Reference File Release Notes

For use with

TruSight® HLA Assign™ Analysis Software

March 2022

Reference changes summary from 3.45.1.0:

1. Updated as per IMGT/HLA 3.47.0.
2. Splice sites added to the core layer.

IMGT/HLA 3.47.0 Reference Update

All alleles were validated for consistency with the IMGT/HLA release database version included in the IMGT/HLA release notes, which can be found with this link www.ebi.ac.uk/ipd/imgt/hla/docs/release.html except for the following alleles:

- DRB4*03:01N—Removed due to lack of exon 2 reference sequence in the IMGT/HLA database
- DQB1*03:276N – the 5' amplification primer site has been deleted in this allele and will not amplify.

Regions Included in the Core Exon Analysis

Core layer includes:

- All sequence in Exons 2,3 and 4 of HLA Class 1, MICA and MICB and exon 2 and 3 of HLA class 2.
- Full sequence of additional exons if these exons include polymorphisms that impact expression.
- Splice sites.

Positions are numbered by position in Assign.

| Locus | Region | Position | Known alleles with impacted expression |
|-------|--------------------------------|-----------|--|
| HLA-A | Exon 2, 3, 4 | all | N/A |
| | 5'UTR | 200 | A*02:01:01:02L |
| | Intron 1, Exon 1 donor site | 374-375 | A*33:03:01:21Q, A*26:01:01:52Q |
| | Intron 1, Exon 2 acceptor site | 502-503 | None |
| | Intron 1 | 478 | A*31:01:02:03N |
| | Intron 2 | 775 | A*02:01:01:134Q, A*24:447Q |
| | Intron 2, Exon 2 donor site | 778-781 | A*01:01:01:02N |
| | Intron 2 | 1008 | A*01:301Q, A*24:450Q, A*24:02:01:02L |
| | Intron 2, Exon 3 acceptor site | 1013-1014 | None |
| | Intron 3, Exon 3 donor site | 1291-1292 | None |
| | Intron 3, Exon 4 acceptor site | 1889-1890 | None |
| | Intron 4, Exon 4 donor site | 2167-2168 | A*03:01:01:02N, A*26:01:01:03N, A*29:01:01:02N |
| | Intron 4, Exon 5 acceptor site | 2267-2268 | None |
| | Intron 5, Exon 5 donor site | 2386-2387 | A*31:01:02:51Q |
| | Intron 5, Exon 6 acceptor site | 2827-2828 | None |
| | Intron 6, Exon 6 donor site | 2861-2862 | None |
| | Intron 6, Exon 7 acceptor site | 3001-3002 | None |
| | Intron 7 | 3218 | A*24:02:01:17Q |
| | Intron 7, Exon 7 donor site | 3051-3052 | A*31:01:02:30Q |
| | Intron 7, Exon 8 acceptor site | | A*24:02:01:17Q |
| HLA-B | Exon 1, 2, 3, 4, 5 | all | N/A |
| | Intron 1, Exon 1 donor site | 358-359 | None |
| | Intron 1 | 461 | B*15:01:01:02N |

| Locus | Region | Position | Known alleles with impacted expression |
|-------|--------------------------------|-------------|--|
| | Intron 1, Exon 2 acceptor site | 486-487 | B*15:01:01:39Q |
| | Intron 2, Exon 2 donor site | 757-758 | B*38:01:01:03Q |
| | Intron 2, Exon 3 acceptor site | 1001-1002 | B*27:05:02:04Q, B*18:01:01:12Q, B*18:01:01:42Q |
| | Intron 3, Exon 3 donor site | 1279-1280 | B*44:02:01:13Q |
| | Intron 3, Exon 4 acceptor site | 1852-1853 | None |
| | Intron 4, Exon 4 donor site | 2130-2131 | B*40:02:01:32Q, B*08:284Q |
| | Intron 4, Exon 5 acceptor site | 2232-2233 | B*56:01:01:05S, B*44:02:01:02S, |
| | Intron 5, Exon 5 donor site | 2351-2352 | B*40:02:01:32Q, B*08:284Q |
| | Intron 5, Exon 6 acceptor site | 2790-2791 | None |
| | Intron 6, Exon 6 donor site | 2825-2826 | None |
| | Intron 6, Exon 7 acceptor site | 2929-2930 | B*51:01:01:97Q |
| | Intron 7, Exon 7 donor site | | None |
| HLA-C | Exon 1, 2, 3, 4, 7 | all | N/A |
| | Intron 1, Exon 1 donor site | 357-358 | C* 15:02:01:30Q |
| | Intron 1, Exon 2 acceptor site | 485-486 | C*07:04:01:16Q, C*07:01:01:14Q, C*05:01:01:53Q, C*03:03:01:52N |
| | Intron 2, Exon 2 donor site | 757-758 | C*15:02:01:35Q, |
| | Intron 2, Exon 3 acceptor site | 1006-1007 | C*07:01:01:100Q, C*15:02:01:08N, C*07:04:01:15Q, C*03:03:01:50N, C*15:02:01:08N, |
| | Intron 3, Exon 3 donor site | 1284-1285 | C*02:02:02:34Q, C*03:04:01:35Q, C*07:02:01:17N, C*07:02:01:125Q |
| | Intron 3, Exon 4 acceptor site | 1869-1870 | None |
| | Intron 4, Exon 4 donor site | 2147-2148 | C*04:01:01:47Q |
| | Intron 4, Exon 5 acceptor site | 2266-2267 | None |
| | Intron 5, Exon 5 donor site | 2388-2389 | None |
| | Intron 5, Exon 6 acceptor site | 2828-2829 | C*04:01:01:84Q, C*07:06:01:05Q |
| | Intron 6, Exon 6 donor site | 2863-2864 | None |
| | Intron 6, Exon 7 acceptor site | 2868-2969 | C*07:02:01:124Q |
| | Intron 7, Exon 7 donor site | 3018-3019 | C*07:02:01:74Q |
| | Intron 7, Exon 8 acceptor site | 3180-3181 | None |
| DPA1 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 624-625 | DPA1*01:03:01:18Q |
| | Intron 1, Exon 2 acceptor site | 4206-4207 | None |
| | Intron 2, Exon 2 donor site | 4454-4455 | None |
| | Intron 2, Exon 3 acceptor site | 4792-4793 | None |
| | Intron 3, Exon 3 donor site | 5076-5077 | None |
| | Intron 3, Exon 4 acceptor site | 5288-5289 | None |
| DPB1 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 467-468 | None |
| | Intron 1, Exon 2 acceptor site | 5001-5002 | None |
| | Intron 2, Exon 2 donor site | 5267-5268 | DPB1*04:01:01:24N |
| | Intron 2, Exon 3 acceptor site | 9279-9280 | None |
| | Intron 3, Exon 3 donor site | 9563-9564 | None |
| | Intron 3, Exon 4 acceptor site | 10108-10109 | None |

| Locus | Region | Position | Known alleles with impacted expression |
|----------------|--------------------------------|-------------|--|
| | Intron 4, Exon 4 donor site | 10221-10222 | DPB1*02:01:02:46Q |
| | Intron 4, Exon 5 acceptor site | 10548-10549 | None |
| DQA1 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 829-830 | None |
| | Intron 1, Exon 2 acceptor site | 4683-4684 | None |
| | Intron 2, Exon 2 donor site | 4934-4935 | None |
| | Intron 2, Exon 3 acceptor site | 5325-5326 | None |
| | Intron 3, Exon 3 donor site | 5609-5610 | None |
| | Intron 3, Exon 4 acceptor site | 5970-5971 | DQA1*03:03:01:16Q |
| | | | |
| DQB1 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 641-642 | None |
| | Intron 1, Exon 2 acceptor site | 2110-2111 | None |
| | Intron 2, Exon 2 donor site | 2382-2383 | None |
| | Intron 2, Exon 3 acceptor site | 5426-5427 | None |
| | Intron 3, Exon 3 donor site | 5710-5711 | DQB1*03:01:01:21Q, DQB1*03:19:01:02Q |
| | Intron 3, Exon 4 acceptor site | 6225-6226 | None |
| | Intron 4, Exon 4 donor site | 6338-6339 | None |
| | Intron 4, Exon 5 acceptor site | 6821-6822 | None |
| | Intron 5, Exon 5 donor site | 6847-6848 | None |
| | Intron 5, Exon 6 acceptor site | 7456-7457 | None |
| DQB1G06 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 636-637 | None |
| | Intron 1, Exon 2 acceptor site | 2080-2081 | None |
| | Intron 2, Exon 2 donor site | 2352-2353 | None |
| | Intron 2, Exon 3 acceptor site | 4936-4937 | None |
| | Intron 3, Exon 3 donor site | 5220-5221 | None |
| | Intron 3, Exon 4 acceptor site | 5729-5730 | None |
| | Intron 4, Exon 4 donor site | 5842-5843 | None |
| | Intron 4, Exon 5 acceptor site | 6323-6324 | None |
| | Intron 5, Exon 5 donor site | 6349-6350 | None |
| | Intron 5, Exon 6 acceptor site | 6958-6959 | None |
| DRB1G01 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 700-701 | None |
| | Intron 1, Exon 2 acceptor site | 5987-5988 | None |
| | Intron 2, Exon 2 donor site | 6259-6260 | None |
| | Intron 2, Exon 3 acceptor site | 8542-8543 | None |
| | Intron 3, Exon 3 donor site | 8826-8827 | None |
| | Intron 3, Exon 4 acceptor site | 9525-9526 | None |
| | Intron 4, Exon 4 donor site | 9368-9639 | None |
| | Intron 4, Exon 5 acceptor site | 10123-10124 | None |
| | Intron 5, Exon 5 donor site | 10149-10150 | None |
| | Intron 5, Exon 6 acceptor site | 11291-11292 | None |

| Locus | Region | Position | Known alleles with impacted expression |
|----------------|--------------------------------|-------------|--|
| DRB1G03 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 708-709 | None |
| | Intron 1, Exon 2 acceptor site | 8711-8712 | None |
| | Intron 2, Exon 2 donor site | 8983-8984 | None |
| | Intron 2, Exon 3 acceptor site | 11240-11241 | None |
| | Intron 3, Exon 3 donor site | 11524-11525 | None |
| | Intron 3, Exon 4 acceptor site | 12223-12224 | None |
| | Intron 4, Exon 4 donor site | 12336-12337 | None |
| | Intron 4, Exon 5 acceptor site | 12806-12807 | None |
| | Intron 5, Exon 5 donor site | 12832-12833 | None |
| | Intron 5, Exon 6 acceptor site | 13619-13620 | None |
| DRB1G04 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 705-706 | None |
| | Intron 1, Exon 2 acceptor site | 8958-8959 | None |
| | Intron 2, Exon 2 donor site | 9230-9231 | None |
| | Intron 2, Exon 3 acceptor site | 12692-12693 | None |
| | Intron 3, Exon 3 donor site | 12976-12977 | None |
| | Intron 3, Exon 4 acceptor site | 13671-13672 | None |
| | Intron 4, Exon 4 donor site | 13784-13785 | None |
| | Intron 4, Exon 5 acceptor site | 14254-14255 | None |
| | Intron 5, Exon 5 donor site | 14280-14281 | None |
| | Intron 5, Exon 6 acceptor site | 14906-14907 | None |
| DRB1G07 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 705-706 | None |
| | Intron 1, Exon 2 acceptor site | 11016-11017 | None |
| | Intron 2, Exon 2 donor site | 11288-11289 | None |
| | Intron 2, Exon 3 acceptor site | 13513-13514 | None |
| | Intron 3, Exon 3 donor site | 13797-13798 | None |
| | Intron 3, Exon 4 acceptor site | 14492-14493 | None |
| | Intron 4, Exon 4 donor site | 14605-14606 | None |
| | Intron 4, Exon 5 acceptor site | 15078-15079 | None |
| | Intron 5, Exon 5 donor site | 15104-15105 | None |
| | Intron 5, Exon 6 acceptor site | 15820-15821 | None |
| DRB3 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 428-429 | None |
| | Intron 1, Exon 2 acceptor site | 8099-8100 | None |
| | Intron 2, Exon 2 donor site | 8371-8372 | None |
| | Intron 2, Exon 3 acceptor site | 10685-10686 | None |
| | Intron 3, Exon 3 donor site | 10969-10970 | None |
| | Intron 3, Exon 4 acceptor site | 11651-11652 | None |
| | Intron 4, Exon 4 donor site | 11764-11765 | None |
| | Intron 4, Exon 5 acceptor site | 11764-11765 | None |

| Locus | Region | Position | Known alleles with impacted expression |
|-------|--------------------------------|-------------|--|
| | Intron 5, Exon 5 donor site | 12261-12262 | None |
| | Intron 5, Exon 6 acceptor site | 13058-13059 | None |
| DRB4 | Exon2, 3 | all | None |
| | Intron 1, Exon 1 donor site | 414-415 | None |
| | Intron 1, Exon 2 acceptor site | 9976-9977 | DRB4*01:03:01:02N, DRB4*01:14N |
| | Intron 2, Exon 2 donor site | 10248-10249 | None |
| | Intron 2, Exon 3 acceptor site | 12989-12990 | None |
| | Intron 3, Exon 3 donor site | 13273-13274 | None |
| | Intron 3, Exon 4 acceptor site | 13975-13976 | None |
| | Intron 4, Exon 4 donor site | 14088-14089 | None |
| | Intron 4, Exon 5 acceptor site | 14560-14561 | None |
| | Intron 5, Exon 5 donor site | 14586-14587 | None |
| | Intron 5, Exon 6 acceptor site | 14886-14887 | None |
| DRB5 | Exon 2, 3 | all | N/A |
| | Intron 1, Exon 1 donor site | 414-415 | None |
| | Intron 1, Exon 2 acceptor site | 8362-8363 | None |
| | Intron 2, Exon 2 donor site | 8634-8635 | None |
| | Intron 2, Exon 3 acceptor site | 10885-10886 | None |
| | Intron 3, Exon 3 donor site | 11169-11170 | None |
| | Intron 3, Exon 4 acceptor site | 11870-11871 | None |
| | Intron 4, Exon 4 donor site | 11983-11984 | None |
| | Intron 4, Exon 5 acceptor site | 12459-12460 | None |
| | Intron 5, Exon 5 donor site | 12485-12486 | None |
| | Intron 5, Exon 6 acceptor site | 12784-12785 | None |

NOTE:

B*39:01:01:02L cannot be ruled out in the core layer as the polymorphism impacting expression is in the 5'UTR primer binding site.

Base Positions Masked for Variant Calling

| Locus | Region |
|----------------|---|
| A | None |
| B | None |
| C | Intron 6, position 2957 |
| DPA1 | None |
| DPB1 | Intron 2, positions 9094-9150, 9154-9156, 9175-9240 |
| DQA1 | 5'UTR, position 378-422 Intron 1, positions 2010-2213, 3943-3946, 4199-4207 Intron 3, position 5722-5729 3'UTR, position 6504-6510 |
| DQB1 | 5'UTR, positions 254-258, 350-352 Intron 1, position 852-888 Intron 2, positions 3190-3227, 3801-3852, 5020-5022 |
| DQB1G06 | Intron 1, position 867-871 Intron 2, positions 4589-4591, 4489-4491, 4629-4631 |
| DRB1G01 | Intron 2, position 6333-6409 |
| DRB1G03 | Intron 1, position 8231-8252 Intron 2, position 9063-9130 |
| DRB1G04 | Intron 2, position 9290-9349 |
| DRB1G07 | Intron 2, position 11341-11388 |
| DRB3 | Intron 2, position 8451-8531 |
| DRB4 | None |
| DRB5 | Intron 2, position 8710-8758 |

3.47.0 CWD List Update

All alleles in the CIWD list supplied by the Immunogenetics Data Analysis Working Group, version 3.0.0, as well as DPA1 and DQA1 from version 2.0.0 are included in the TruSight HLA Assign CIWD list. When CIWD alleles have been split into subgroups after the most recent CIWD list, all alleles in the subgroups are included in the TruSight HLA Assign CIWD list.

Reference Compatibility

The IMGT HLA Reference 3.47.0 is compatible and validated with TruSight HLA Assign v2.1.

Reference Update Instructions

NOTE

In a default installation, the reference library files and the CWD, P, and G group files are installed.

1. In the System group, select **Update**.
2. In the Update window, under Import, select **References**.
3. Browse to the IMGT HLA Reference folder. In the bottom right of the dialogue window, 'Reference Files' is indicated. Select all the files in the folder and select **Open**.
The dialogue window indicates files successfully copied.
4. In the System group, select **Update**.
5. In the Update window, under Import, select **References**.
6. Browse to the IMGT HLA Reference folder. In the bottom right of the dialogue window, select **P&G Group File**. Select all the files in the folder and select **Open**.
The dialogue window indicates files successfully copied.
7. In the System group, select **Update**.
8. In the Update window, under Import, select **CWD Update**.
9. Browse to the IMGT HLA Reference folder. In the bottom right of the dialogue window, 'CWD File' is indicated. Select all the files in the folder and select Open. The dialogue window indicates files successfully copied.
10. Select 'CIWD 2020 v3.47 cat 1' or 'CIWD 2020 v3.47 cat 1-2' as needed from the 'CWD Set' drop down list on the 'Annotation' panel.
11. Click 'Update' on the 'Settings' panel and choose 'Yes' to confirm the changes.

REVISION HISTORY

| Version | Date | Modification | Authorized by |
|---------|-----------|---|---------------|
| 1.0 | 17-Mar-22 | J. Edwards drafted doc. Issued by Hira Meraj 13-May-22 | K. Hunter |