

Minutes

2025-07-28 HVNC Bi-monthly Regular Meeting

Attendees: Johan den Dunnen, Alex Wagner, Jeroen Laros, Gwendolyn Bennett, Ros Hastings, Hencher Lee, Ivo Fokkema, Matthew Stachowiak, Timothy Hefferon

Regrets: Marina DiStefano,

Agenda

1. Opening and Confirm Agenda
2. Confirm minutes from prior meeting
3. Review action items from previous meeting
4. Announcements
 - a. anonymized minutes from June meeting
 - b. update on Parentheses Task Force
 - c. changes to committee membership: no response from EMQN re: new representative
5. Review the suggested changes to clarify that the restriction that a repeat's sequence length should be divisible by three does not apply to intronic sequences in coding transcripts. See PR #231.
6. Nomenclature of positions upstream and downstream of transcripts.
 - a. Questions before the meeting:
 - i. in reading the changes to existing examples, I am wondering what does this proposal gain us? For example, in describing a promoter variant, we have existing text that says, "when using a genomic reference sequence, this variant can be described as NC_000023.10(NM_004006.1):c.-128354C>T or NC_000023.10(NM_000109.3):c.-401C>T". Which is proposed to be changed to, "when using a genomic reference sequence, this variant can be described as NC_000023.10(NM_004006.2):c.u128110C>T or NC_000023.10(NM_000109.4):c.u278C>T." By this example, the proposal only adds complexity to describing the variant. My previous understanding of this proposal was that it would allow for these variants to be described with just NM, which was not previously allowed.
 - ii. I don't think we all agreed yet on option 4 vs one of the other options; this has not been selected yet; correct? However, if option 4 is selected, we also need to discuss c.u? and c.d? vs simply c.?.
 - b. Would NM-based intergenic positions be allowed, but this is ambiguous, so NC(NM) is required. The original text listed an NM-based example, and Ivo updated this to an NC(NM) example, but we never discussed which syntax to use exactly.
 - c. There haven't been any votes on which option to use yet, so perhaps put out the community consultation page with multiple suggestions? Let's decide on which options to keep. Everybody gets one week to re-read the proposal and to send in their preferences by adding their preferences here: Option 1 - nobody, Option 2 - nobody, Option 3A - 2 votes (+1), Option 3B - 1 vote, Option 4 - 3 votes
 7. Combining variants (revision of SVD-WG010).
 - a. The proposal is summarized. Using deletion-insertions will be optional and allowed

to let tooling process the variants better, when the allele syntax is not supported properly. The distance between the variants is no longer relevant. The nomenclature should not solve problems that tooling has.

b. How should databases handle this? That should be left to the implementation.

c. Should we have recommendations on when allele syntax should be used vs deletion-insertions? It's hard to tell the overlap between two descriptions, but Mutalyzer has a tool that can check whether two descriptions change the sequence the same way.

d. This affects reporting as well, as whether to report variants separately or together also depends on the variants' classification.

e. **Everybody**, review the proposal and submit comments.

f. Note that the website still refers to SVD-WG010 due to the blocking of some PRs (e.g., PR #215).

i. A new PR will be created that just removes the links to SVD-WG010.

8. Split the proposal on repeats to address the following issues separately:

a. There are multiple ways of describing a repeat (see also #114).

i. We'll need to create a community proposal for this. It was already announced on the website quite some time ago. It will be created.

b. Repeats in coding and non-coding sequences are treated differently.

i. a proposal will be created.

c. It is unclear when the repeat syntax is to be used.

i. a proposal will be created.

9. NC(NM) alignment information instability; require NC:g-based description?

a. the annotations aren't stable, so any NC(NM):c description can be unstable.

b. Aren't we already requiring this? This should be clarified.

c. Do we need NC(NM) at all? This may be creating more problems than solutions. It is argued we will always need NC(NM) for interpreting intronic variant descriptions. If we drop NC(NM), we no longer have a reference sequence that can be used to describe intronic variant descriptions. Also, lots of sources have intronic variant descriptions (e.g., the literature) and we need HGVS nomenclature to feed these into tooling.

d. The discussion was shelved for later, so we can continue to the next agenda point.

10. Advancing proposals Proposal Creation and Voting Procedure

a. We discussed how community members bring issues to our attention and in which ways/steps we can handle those.

b. Everybody can add comments to the draft document and we'll discuss this again in the next meeting.

c. (end of meeting)

11. HGVS Validation Test Suite

12. AOB