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Abstract (poster session)

Definition of detection limits of quantitative HCV-RNA assay: the influence of standard material

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Objectives: Recent developments in the treatment of Hepatitis C infection using directly active antiviral agents (DAA) have increased the importance of highly sensitive testing for HCV-RNA. Data from the approval studies show that a lower limit of detection (LLOD) of 25 IU/ml should be reached, especially if reduction of treatment duration is an option. To define the LLODs of quantitative nucleic acid testing (NAT) WHO standard material is commonly used. While for many HCV NAT assays the 2nd WHO International standard was used for this purpose, this standard is not publicly available anymore and derived material from commercial companies is used. Even the 3rd WHO international standard is not easily available anymore, as the 4th international standard has recently replaced its predecessor. Methods: To determine the differences between the detectability in the lower range, dilutions of the 3rd and 4th WHO International standards in negative plasma were tested in at least 20 replicates with the HCV QS-RGQ Kit from Qiagen. This assay has a lower limit of detection of 20 IU/ml as tested with standard material from Acrometrix®, which itself was calibrated on the 2nd WHO International standard. Our Results were compared to this approval data, kindly provided by Qiagen R&D. Data was analysed with R enviroment for statistical computing using probit analysis. The different standards were compared at the calculated 50% hit rate, as the 95% confidence values for the hit rate are smallest at this level. Results: 50% hit rate determined by probit analysis using the 3rd international standard showed a value of 8.9 IU/ml, while the 4th international standard showed a value of 6.4 IU/ml. Testing using the Acrometrix® standard showed a 50% detectability for 2.8 IU/ml. Conclusions: Depending on the WHO International standard used for testing and calculation our analysis showed differences in the detection probability. If compared to the data that describe the assessment of the target values for the WHO standards, differences up to 0.5 log IU/ml are not uncommon in different labs using the same assay. Additionally the standards were tested at much higher concentrations as are necessary for determining the LLOD. In our opinion specialized material (e.g. RNA transcripts) should be used to provide long term comparability of determinations for LLOD.