

## Rapporteur notes session 3 afternoon

*Anita Szajek:* A summary of the revision history is given: stage 1 published in June 2008 and stage 2 published in Feb 2009 as an IRA with official date of October 2009. After the stage 2 revision now being implemented a coming stage 3 revision with further updates are expected concerning:

1H NMR spectrum

Chromatographic identity Nucleotide impurities

Protein impurities

Lipid content

Molecular Weight method



## Rapporteur notes session 3 afternoon

*J-M. Spieser*. The short term revision includes  $^1\text{H}$  NMR and CE. Methods are suggested and acceptance criteria at the discretion of the competent authority. A proposal for longer term updates is presented. Including higher specific activity, species verification testing, updating of impurity specification and testing, tightening of N spec, updating of ID test and limit of DS of by SAX HPLC. The anti Ila method is consideration as potency assay. No harmonization so far between EP, JP and USP



## Rapporteur notes session 3 afternoon

*N. Kawasaki:* The proposal for the update on the hep Na and hep Ca pharmacopeias are presented. For hep Na this update includes two new ID tests: WAX HPLC and  $^1\text{H}$  NMR plus two new tests for impurities: a test for galactosamine and an update of the  $^1\text{H}$  NMR test for absence of OSCS. For hep Ca the  $^1\text{H}$  NMR ID test and the galactosamine impurity test is proposed to be introduced at a later stage. It should be noted that both for hep Na and hep Ca the assay is an anti-factor Xa based assay. Purity test for proteins and nucleotides are expected to be further updated



## Rapporteur notes session 3 afternoon

*Edwin Kellenbach* The presentation describes the evolution of the regulatory requirements in heparin field triggered by the crises starting with the implementation of CE and NMR requirements to current stage 2 revision of the USP from a stakeholders view. The active participation from a stakeholder in the various monograph revisions in Europe and in the US is also described.



## Rapporteur notes session 3 afternoon

*Edwin More:* The presentation describes the thorough testing of chromatographic ID, galactosamine impurity and protein impurity methods introduced with the stage 2 revision of the USP. Specific experienced based proposals for optimizing especially the protein impurity method and the heparin chromatographic identification method are given. As we have just learned from Dr. Szajek's presentation a stage 3 revision is being planned also encompassing the methods mentioned. So some of the observations could be considered in coming monograph revisions



## Rapporteur notes session 3 afternoon

*C. Viskov*: A signal at 2.18 ppm in the  $^1\text{H}$  spectrum from a large number of batches of heparin sodium is seen. According USP monograph no signal should be found here. This finding triggered an extensive structural elucidation work which is described: The O-Ac on IdoA2S3Ac was shown to be responsible for the 2.18 ppm peak.

