Abstract 043

Can Half-life Measurements Alone Determine Radionuclidic Purity of F-18 Compounds?

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Current revisions of monographs for F-18 pharmaceuticals in the European Pharmacopoeia call for a radionuclidic purity (RNP) of or better than 99.9%. If (debatably) this requirement is put at end of shelf life, typically 10 hours EOS , the requirement can be very difficult to assure by actual measurements, if all possible radionuclide contaminations should be considered. Clearly, gamma spectroscopy can do much, but only if the contaminant has strong gamma emissions above 511 keV. We have tried to analyse mathematically to what extent that half-life measurements alone can establish RNP for F-18 compounds. The method could in principle be extended to other isotopes. The current method of half-life determination in the Ph.Eur with two measurements at 6h interval is not sufficient nor effective for testing the required RNP level.

We present a theoretical model leading to a practical procedure for testing RNP of F-18 compounds with a confidence of 95%.

We look at a batch of F-18 contaminated with one other isotope with a half-life of $\beta T_{^{18}F}$. The contamination level is α at time 0. The recorded number of counts, $N(t)$, for a sample, that contains one other isotope, is described by

$$N(t) = \frac{N(0)}{(1+\alpha)}\left(\left(\frac{1}{2}\right)^{t/T_{^{18}F}} + \alpha\left(\frac{1}{2}\right)^{t/\beta T_{^{18}F}}\right)$$

with N(0) as the total number of counts at t = 0.

RNP is defined by the expression

$$RNP = \frac{A_{^{18}F}}{A_{\text{tot}}} \Rightarrow RNP(0) = \frac{1}{1+\alpha} \simeq 1-\alpha, \quad \alpha = \frac{A_{^{18}F}(0)}{A_{\text{other}}(0)}$$

If all measured impulses are converted to initial point values (t = 0 min.), the curve should give a straight line with constant value (the initial value of counts) for a pure F-18 sample. Due to the stochastic nature of the F-18 nuclide, the data points will deviate from this line. If the sample is contaminated the curve will increase rapidly. The condition for the pure and unpure curves to be separated is, the difference of the

measurements must be equal to (or larger than) the sum of 1.96 standard deviations for the two curves (confidence of 95%). An approximated expression for the limit of α is

$$\alpha \simeq \frac{3.92\left(\frac{1}{2}\right)^{t/2T_{18_F}}}{\sqrt{N(0)}\left(\left(\frac{1}{2}\right)^{t/\beta T_{18_F}} - \left(\frac{1}{2}\right)^{t/T_{18_F}}\right)}$$

In the figure below a contour plot of RNP(0) ($\simeq 1-\alpha$) is plotted against β and recording time for a total amount of initial counts of 10^6 (the limit of the Liquid Scintillation Counter). We can readily see that after 6 hours, we cannot detect a contamination with $\alpha \leq 0.1\%$ (RNP(0) $\geq 99.9\%$), but after another 6 hours we should be able to detect a RNP(0) of 99,95% or smaller (for $\beta = 20$). However at very low β values there is a strong divergence in the time needed to detect these small RNP's, which in practice sets a lower limit for a detectable β. In the case below this lower β value is ~ 3.

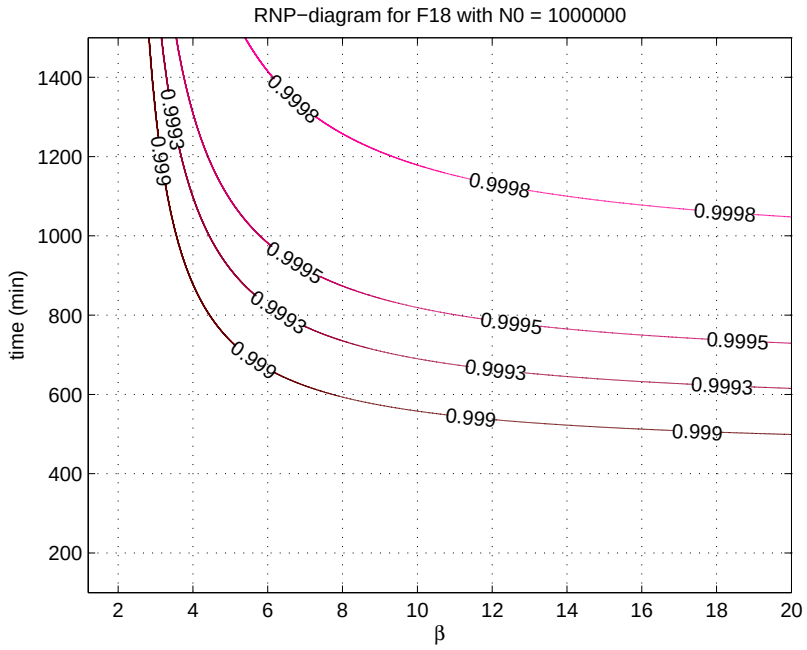

Figure 1: RNP plotted against β and recording time. The confidence is 95%.

In the above method, the lower level of the recording time and β is set by the inherent poisson noise. By using a series of recordings in a method that looks at the mean, rather than just two single points (start and stop), the statistical noise is lowered and consequently the lower limit of β is reduced to approximately 1.5 (recording time of $\sim$ 800 min). In conclusion we cannot find any contaminating isotope with half-lives shorter than 1.5 times 109.77 min. for RNP(0) = 0.9990 and a confidence of 95%.