## ATOM INDONESIA Referee's Report

## Article No.: # 1233-10343-2-RV

**Title of Paper:** Radiosynthesis of [1311]-xanthine and [1311]- 2hypoxanthine: New Radiolabeled Compound Candidates for Theranostics Purposes

Line #	Referee's Comments
112-134	All chemicals used need to be stated as on the chemical packaging <i>i.e</i> N-chloro-p- toluene sulfonamide 121salt (chloramine-T) as chloramine-T trihydrate
139-142	Mass and mol of starting materials need to be stated as xx mg (xx mmol)
158	See previous comment (above)
190-191	on the base line.
250.200	1. Reactant ratio of chemical reaction has to be mol : mol, mmol : mmol etc.
	# mg means nothing in a equation of chemical reaction
	<i>le</i> . Xanthine (MW, 152.11) $\rightarrow 0.5$ mg = 3.3 $\mu$ mol
	Hypoxanthine (MW, 136.1115) $\rightarrow$ 0.5 mg = 3.6 $\mu$ mol
	Chloramine-T Trihydrate (MW, 281.69) $ ightarrow$ 0.5 mg = 1.77 $\mu$ mol
	It can be seen that ratios of reactants which have been reported dan discussed totally different with their real values.
259-260,	2. There is no direct reaction between Xanthine/ hypoxanthine and chloramine-
274-276	I therefore, optimasing reaction by varying mol ratio of these reactants seem not relevant
306-307	Chloramine-T is oxidant which oxidase I <sup>-</sup> to I* which then attack imidazole functional group of Xanthine/ hypoxanthine to give [1311]-xanthine / [1311]
	(Actually, it already stated in this article, lines 285- 289). Therefore, it would be more relevant to optimise mol ratio of chloramine-T toward I-131 in this chemical reaction
	3. Chloramine-T is oxidant a strong and has been used for quite some time in radiolabeling biomolecules such as antibodies, peptides etc. In many cases these reactions performed at room temperature and short reaction time in avoiding damage to the staring material. So prolonged and heated reaction might not be too suitable for this procedure.
	Note: Mol of free carrier I-131 can be calculated using Avogadro No.
311	See previous comment

**Final comments and recommendations:** The basic idea of this project was excellent but unfortunately not followed by a well methodology which potentially gave misleading results and discussions.

In order to give more comprehensive results and rich discussion for this project it highly recommended to:

- 1. Work on Table 1 and 2 (focus on ratio mol chloramine-T to I-131)
- 2. Do a couple more experiments on ratio mol chloramine-T to I-131 and pH of reaction
- 3. Do experiments with increasing radioactivity of I-131 used (based on the optimased of reaction attained)
- 4. Do a stability test of the purified [ 1311]-xanthine and [ 131 1 I]- 2hypoxanthine

## This paper is recommended to be

- [] Accepted without further revision
- [ ] Accepted with minor revision
- [x] Major Revision is required
- [] Rejected