Reviewer’s report

Title: Pharmacogenetic testing through the direct-to-consumer genetic testing company 23andMe

Version: 0 Date: 07 Feb 2017

Reviewer: Ann Daly

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This is generally an appropriate report. A few suggestions are listed below.

1. Introduction. Paragraph 4. It would be helpful to stress more that all the decisions about what to include in the tests offered by 23 and me are made by the company. It is 23 and me that decides whether a test is "potentially eligible" not a regulator.

2. Oesophageal cancer. Please state that the risk being considered here is for squamous cell carcinoma not adenocarcinoma. In addition, the risk has been demonstrated only in East Asians to date probably because the ALDH SNP being analysed is only common in this ethnic group.

3. Phenytoin. The FDA table lists both CYP2C9 and HLA-B*15:02. The text on p.7 needs to make clear that the table lists both CYP2C9 and HLA-B since currently it seems to be suggesting that the FDA do not mention CYP2C9 at all.

4. p.8 Poor metabolisers. Individuals with the alleles listed may be poor metabolisers-carriage of the alleles is not sufficient to make an individual a poor metaboliser so change "are poor metabolisers" to "may be poor metabolisers".

5. p.9 rs4149056 has a minor allele frequency of 0.19 in Europeans so the 1% mentioned on the last line of this page is not correct. 3% approx. of Europeans are predicted to be homozygous for this variant. The frequency in East Asians is only slightly lower than in Europeans. It is therefore not correct to state that this variant is very rare and it is actually an important risk factor for simvastatin-induced myotoxicity. Please include some relevant references on this point.

6. p.14. Discussion. In the era of genome sequencing, the risk of tests being mentioned here being "out of date" seems low. The main problem with the tests being offered currently appears to be that they are too geared towards white Europeans. I would also disagree that because the FDA does not list a test that it is uninformative-the rs4149056 point mentioned under 5 above is a good example of a test that is of some value but not listed by FDA.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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Yes

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