We thank the Reviewer for the constructive criticisms. Below we provide a point-by-point rebuttal to his/her specific comments. However, his/her remarks about the lack of recognition of past studies do not hold, as many of the papers suggested by the Referee have already been included in the references list of the manuscript, and clearly the Reviewer simply missed them.

These authors have reported associations between their ROS measurement and WSOC in a number of past studies and asserted that the WSOC was secondary (for example, [Daher et al., 2012; Saffari et al., 2013; 2014]). The authors should note this and clearly state what is new about this work, ie, that the processing may be heterogeneous?

REPLY: The statistical association between ROS activity (cellular essay) and WSOC concentrations has already been investigated at a relatively small number of sites (see the review by Saffari et al. [Environ. Sci. Technol. 2014, 48, 7576−7583]). The originality of the present study relies on two aspects:

1. As the Referee pointed out, we investigate here the effect of heterogeneous processes (fog formation) on ROS activity in the particles.
2. Past experiments were based on aerosol samples in which WSOC and other redox-active agents (including metals) were actually physically mixed together, and their contributions to ROS activity could be disentangled only with statistical tools. Here instead, we provide observations of ROS activity of bulk aerosol particles and for interstitial aerosols, with the latter characterized by being naturally depleted of soluble compounds as a consequence of fog scavenging. Conversely, fog water samples largely recover WSOC of the original particle population while the insoluble species are mostly left out in the interstitial aerosol phase. We believe that the exploitation of the natural partitioning effect of fog on aerosol species exhibiting different water solubilities is an original contribution of our study to the research on the nature of the chemical species governing redox activity in the aerosol.

There is a substantial body of published literature on oxidative potential, albeit with different assays, that discusses the effect of oxidation on increased toxicity. Examples include chamber studies and analysis of ambient data (discussed more below). None of these, which are very pertinent to this paper, are cited in this work.

REPLY: The references suggested by the reviewer have already been included in the manuscript. See the detailed comment below.

No evidence or reference is provided establishing that this assay (that is, this specific ROS measurement) is linked to adverse human health effects, although a health connection is implicitly assumed throughout. It would appear the implicit assumption is that because this is a cellular assay it can be directly connected to adverse human health responses, but there are many components to a cellular assay that can lead to various responses, so the connection is not established until empirically proven. This could be done by citing comparisons of their assay responses to other assays that have established links to health outcomes or oxidative stress markers or cite specific associations between this assay and health effects. As the paper stands, there really is no basis for asserting that these results specifically apply to human health, instead the author need to qualify this assertion throughout the paper.

REPLY: The association between ROS activity and adverse health outcomes is certainly a subject of ongoing investigation. Nevertheless, it is not true that cellular ROS assays have not been connected to adverse human

health responses, and it is unfair to state that "*As the paper stands, there really is no basis for asserting that these results specifically apply to human health*", because the link between ROS assays and human health effects has already been established in few epidemiological studies, which have already been explicitly cited in the paper (Page 4, Line 28).

Finally, there is the question of importance on a broader scale and associated assertions by the authors of wide ranging impacts. The authors suggest that populations are commonly exposed to aerosol that has been fog-processed, but is this true, what is the evidence for this? Quantitative support for this assumption should be provided to demonstrate that this mechanism is truly of broad importance, as stated. Overly expansive statements of the importance of this work should also be avoided throughout.

REPLY: Fog and low-level clouds are transient phenomena in the atmosphere but their occurrence can in fact be very high in certain areas of the globe. This is especially true for highly-populated regions in orographic basins in wintertime. Cermak et al. (2009) showed that several pollution hotspots in Europe, including Benelux, the Ruhr district, the basins of Paris and London and the Po Valley, experience low-level clouds and fogs for 35% to 60% of the days in winter months. The fraction of fog days in fall/winter in the Californian Central Valley (6.5 millions inhabitants) is ca. 20% according to Baldocchi and Waller (2014). Fog frequencies of ca. 10% in winter are also characteristic of the Yangtze River corridor (Niu et al., 2010), and even greater values (20% to more than 35%) are typical of the Indo-Gangetic plain (Saraf et al., 2011). All these regions of the globe commonly experience PM pollution peaks in winter months, during the fog season. In this season of the year, the same stable weather conditions favor the accumulation of air pollutants and fog formation. Therefore, fog-processing is potentially a major driver for secondary aerosol formation in wintertime at all these sites. In Gilardoni et al. (2016), we provided a first estimate of SOA produced by aqueous-phase processing of smoke particles in Europe: 0.1 to 0.5 Tg of organic carbon per year, corresponding to 4 – 20% of total primary OA emissions in the region.

Could not find any data on the various sample sizes (N).

REPLY: The information can be found on page 2 Lines 33-35, and Page 3 Lines 1-5:

"Fog samples were collected from 30 November to 30 December 2015 at the meteorological station Giorgio Fea in San Pietro Capofiume (44°39'15" latitude, 11°37'29" longitude), a rural site located 30 km northeast of Bologna (Italy) in the eastern part of the Po Valley (northern Italy). From 30 November to 4 December, an intensive observation period was scheduled, with the concurrent sampling of fog and aerosol samples and the deployment of a HR-ToF-AMS (Aerodyne Research) for online aerosol measurements. During the sampling campaign, a total of 6 aerosol samples and 16 fog samples were collected. Additionally, fog samples collected after the intensive observation period (after 4 December) were pooled in groups of two or three for the analysis of metals and Oxidative Potential. "

We further specify that the full chemical analyses (WSOC, ion chromatography, metals) was performed on 6 aerosol samples and 7 fog samples. ROS activity analysis was carried out on 20 samples (= 6 aerosol + 7 unfiltered fog + 7 filtered fog samples). Finally, sample size information is specified in every table in the present version of the manuscript.

The authors measured and report ROS of collected fog water and claim this is potentially linked to adverse health. How does this happen? Is the exposure route through inhaling fog drops? Likely not. Instead the argument is that the fog serves mainly as a chemical reactor that produces the toxic species. The drops

evaporate and the fine PM is now more toxic. This assumes that all species in the fog contributing to ROS remain during evaporation, but it is stated that much of it is small molecular weight organic acids, which are likely very volatile and lost. If the fog ROS is equivalent to the ambient PM ROS, than these volatile species play no role. There seems to be some inconsistency in the author's arguments. Maybe this can be clarified.

REPLY: The Referee is right in pointing out that the volatility characteristics of redox-active WSOC in fog water eventually affect exposure. If we hypothesize that these are truly absorbed VOCs, such as formic acid, than their partitioning is completely reversible. However, the Referee assumes that fog droplets dry out once inhaled. On the contrary, fog droplets are expected to travel along the respiratory tract, just alike the droplets of nebulized solutions produced by aerosol generators for clinical use. Airways are much warmer with respect to ambient air but also humid close to saturation, and water vapor diffuses quicker than temperature (a physical process which is also at the basis of cloud condensation nuclei counters), therefore evaporation of fog droplets along their travel in the respiratory tract can be much reduced. The size range of Po Valley fog droplets, spanning between 3 and 30 μm (Heintzenberg et al., 1998) indicates that the inhaled fraction can deposit all over the respiratory tract down to the lungs. VOC evaporating from drying droplets can be exhaled but also become adsorbed to the wet tissues of the airways. The issue of the deposited fraction of the volatile fraction of fog solutes is complex and cannot be fully assessed in this paper. It is worthwhile to note, however, that non-volatile SOA are also expected to form from aqueous oxidation of water-soluble VOC and SVOC. For instance, evidence for dimerization of phenolic compounds in Po Valley fog was presented by Gilardoni et al. (2016). Such SOA compounds exhibit a quinoid structure and are potentially redox-active. The correlation found in this study between ROS activity and oxalic acid concentration (a tracer for highly oxidized, low-volatility aqueous SOA) supports the hypothesis of redox-active WSOC components of reduced volatility.

Finally, in respect to the Referee's comment "If the fog ROS is equivalent to the ambient PM ROS, than these volatile species play no role", we would like to specify that, as discussed in the paper, on a per-volume basis, daytime aerosols and fog exhibit comparable ROS, but this is only due to the large mass concentration of daytime aerosols. However, on a per-mass basis, which is the relevant metric here in discussing toxicity, ROS activity of fog is 2.5 times larger than that of both daytime and nighttime aerosols. This is clearly shown in the most important figure of the paper (Figure 1). So there is actually no inconsistency in the results and the statements made in the manuscript.

A number of studies, such as chamber studies, have shown that if you take primary emissions, (say from a combustion source, like an automobile) and oxidize them, the oxidative potential substantially increases [Li et al., 2009] [McWhinney et al., 2011]. Likewise, chamber experiments in which SOA is produced from various VOCs show that some compounds, such as those found in biomass burning emissions, when oxidized have high intrinsic oxidative potentials [McWhinney et al., 2013]. It has even been shown that fresh soot that is subsequently oxidized has substantially increased oxidative potential (eg, [Antinolo et al., 2015; Shiraiwa et al., 2012]). All of these results are extremely pertinent to this work, but never cited nor discussed.

REPLY: On the contrary, several of these studies have already been cited in the manuscript (Page 2, Lines 9-13).

A variety of elemental concentrations of transition metals were measured, which are claimed to be redox active. Take Fe, for example. In the soluble form is redox active, but the insoluble form is not. Most measured elemental Fe is not soluble (many references show this) so no association to the water-soluble form, and hence redox activity, can be assumed a priori. The point here is that the use of elemental metal concentrations to infer toxicity through an oxidative stress response is not correct. This must be rectified in the manuscript.

REPLY: Our observations indicate a specific contribution of metals to ROS activity of PM distinct from that of SOA (Table 3). At the same time, filtration experiments showed that ROS activity is contributed by both soluble and insoluble components of the aerosol (Figure 2). Since several metals showed an enrichment in interstitial particles (like Cr, Mn, Fe, Cd and Pb, Figure S3b) which are depleted of soluble compounds, we explained the ROS activity of the unfiltered extracts of interstitial aerosol samples (Figure 2) with the presence of water-insoluble transition metals. This does not exclude a contribution of metals also to the soluble fraction of redox-active particulate matter (which, for daytime aerosols, can be large). Contrary to the Referee's indications, there is evidence that the soluble fraction of metals such as V, Zn, As and Cd can be > 50% in submicron aerosol samples (PM2.5) (Heal et al.; 2005). Past experiments dealing with fog chemistry in the Po Valley (Mancinelli et al., 2005) highlighted large soluble fractions for several transition metals (e.g., 77% and 81% for Zn and Cu, respectively). The same study showed that, even if Fe is preferentially distributed to the insoluble core of fog droplets, the soluble fraction still accounts for more than 1/3 of total elemental iron. Therefore, a contribution to ROS activity from partially-soluble transition metals such as Fe cannot be ruled out and, on the contrary, is expected.

The authors assert there are policy implications, but is it really a novel finding that aged biomass burning smoke is toxic? There are many publications on the toxicity of smoke to humans (some should have been cited). The main finding here is that cloud process increases the ROS produced by rat macrophage. This specific finding should be stated in the context of overall known toxicity of smoke. (Ie, the authors could state something along the lines of, smoke is known to be toxic, here we show that fog processing of the smoke, increases the toxicity…).

REPLY: Although we agree with the Reviewer that there have been many studies indicating the toxicity of biomass burning particles, the main point of the paper and its novelty is the resulting increased toxicity from fog processing, and not the toxicity of biomass burning aerosol itself. This is clearly a novel finding which has not been reported previously. Nonetheless, we accept the Reviewer's comment and we will cite relevant studies on the toxicity of smoke particles to humans.

Finally, the last line of the main text states: The enhanced toxicity of fog droplets observed in this study suggests that the historical reduction of fog frequency may result in an unintended improvement of air quality in many continental areas, overlapping also with the deliberate reduction of PM emissions put into practice since the early 90's in many developed countries This assumes that fogs are more effective than other atmospheric processes (eg, aqueous reactions in haze or gas phase oxidation followed by partitioning) in converting wood smoke emissions to species toxic to humans. Is there any evidence for this? The point is what proof do the authors have that if the fogs were not present the aerosol would not still chemically evolve over time to a similar toxicity as fog-processed smoke?

REPLY: This Referee's comment is highly speculative. Our conclusion statement in the paper is a direct implication of our own findings. We do not claim that the in-fog processes are the most efficient processes governing ROS activity in the Po Valley aerosol, but, since fog frequency has decreased with time – as it is documented by visibility and liquid water content data –, the resulting specific impact is a parallel decrease in redox-active species concentrations in the particles. We are not aware if in the meantime something has changed also in respect to all other possible processes involving redox-active compound formation in SOA. We simply have no data for this hypothesis, nor Referee has provided data in support of it.

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