General suggestions on approach:

Overall objective:

In the event that IARC should classify glyphosate as a possible (2B) carcinogen (or less likely, a probable (2A)) we would like you to be able to say that you have looked at the epidemiology as well as the other data on animal carcinogenicity, gen-tox, and exposure and that the weight of evidence supports the conclusion that glyphosate is not a human or animal carcinogen.

PLEASE NOTE- I am not telling you what you should believe or conclude- that is obviously up to you to decide- I am simply laying out the goal in reviewing this material, which will help to structure the approach.

I have re-organized the literature into a folder structure and will load it to DropBox as soon as I get home- in the meantime you can get to the papers via alphabetical collection. (I will KEEP the alphabetical files as well so you can also reach in and directly find something by author if you wish)

RECOMMENDED APPROACH:

- Background is that if IARC takes action it will probably be on Non-Hodgkin lymphoma and/or multiple myeloma data. This will largely be driven by the Shinasi meta-analysis. This was performed by IARC staff and has been reviewed by Exponent consultants (Elizabeth Delzel is a well known epidemiologist formerly at UAB). This is the place to start your review.
- The Mink cancer review will help get a handle on the underlying studies but does not address the Shinasi paper (it published before the meta-analysis). Germany is the Rapporteur state for
the EU re-evaluation of glyphosate and has also issued a review and a 2015 update—this is largely in tabular form and will also be helpful.

- The multiple myeloma literature clustered together—the key study being the Ag Health Study (NCI) result on MM and glyphosate. We were able to get the data on this to Tom Sorahan in the UK who has now published a re-analysis of this data pointing out the primary problem with this association, i.e. it results from the fact that multiple cases of MM were excluded in the control group due to missing data on smoking and other habits while none were removed from the exposed group. While this is not contrary to study plan, the authors have failed to disclose that there is no association in the raw data and that the association is entirely due to presumably random deficiencies in the database.

- In the MM folder you will also note (lundgren et al) that MGUC (monoclonal gammopathy) is inversely associated with glyphosate—an interesting observation in that MGUS is considered a prodromal state for MM.

- Most of the data on other hematologic malignancy revolves around NHL, especially that of Hardell and Erickson (multiple papers, first author varies so some are “Hardell et al”, some “Erikson et al”—but related. Based on a much smaller data set and less comprehensive exposure assessment, the most telling issue with this data is probably that no association with NHL was found in the much larger NCI Ag Health study.

- Much has been written on epidemiological problems related to glyphosate—especially the issue of exposure. The existence of residues in diet and the limited absorption seen in the field (Farm Family Exposure Study–Acquavella—as well as others) raises a serious question as to whether an “ever” user of glyphosate or even a periodic user who applies, say 3 times a year, actually has a significantly different chronic exposure to glyphosate. (If you have ongoing urinary levels of 1 ug/ml typical of the general population and are exposed 3 times a year and pop your levels up 10-fold above baseline you have gone from a daily average of 1 ug/ml to a daily average of 1 ug/ml to 1.08 ug/ml, and most farmers had non-detectable glyphosate levels before and after exposure)

- There are general critiques and defenses of the Ag Health Study as well as general discussion of epidemiological methods. You may find the former helpful if you get to it, and you pretty much already know the latter (i.e. – Austin Bradford Hill is not new to you!).

- There are reviews provided on the mutagenesis/gene-tox and animal carcinogenicity studies in separate folders.

- The exposure studies are clustered together as well–Acquavella and Curwin (not in original bib) probably being the most important.

- There is an overall review of the Ag Health Study findings—useful for perspective on the AHS but not critical.

- Papers on other cancers—many from the Ag Health Study—are clustered in a folder by cancer type and are highly unlikely to be relevant to the current discussion.

- You should look at the Seralini rat study fiasco only because it created such a ruckus around the globe—this study actually found NOTHING…just the normal (very high) rate of tumors in Sprague-Dawley rats fed ad-libitum (they have a pituitary-endocrine genetic defect that causes
endocrine and mammary tumors). The pictures of rodents with rumors made a big impression. While it is true that most tumors occurred in experimental (as opposed to control) animals—there were 9 experimental groups and 1 control... so this is not terribly surprising. The study is garbage—was retracted—then re-published. IARC will pay no attention to it at all, but media inquiries may come up.

- Other topics—not relevant at the moment.
- General regulatory documents—useful for their general reviews/opinions and to allow you to say that WHO, EPA, and EU as well as AU/NZ and others have reviewed this molecule repeatedly.