Susceptibility Population and Food safety Workshop

Microbial Hazards Workgroup

January 20-21, 2010

Charge to the Breakout Groups –

1. Is the concept of what constitutes a susceptible population clear for this group of hazards? Can you provide a description or definition of the concept that you think should be generally used by risk assessors and risk managers and in multiple public health contexts?

The Workgroup agreed that clarification was needed in the definition of a susceptible population as it pertains to microbial hazards. The Workgroup noted that there was need for a straightforward definition that would provide the framework upon which further complexities could be added or be made case specific. The following definition was chosen: Susceptibility is a capacity characterized by intrinsic factors that modify the impact of a specific exposure upon risks/severity of the outcomes in an individual or population (Parkin and Balbus, 2000).

Vulnerability, sensitivity and Susceptibility need to be better defined. There are other factors that are extrinsic that are not defined here, but should be captured.

The Workgroup stressed the importance of when defining susceptibility conceptually to hold the exposure constant, thereby letting the outcome change based on differences in susceptibility. However the Workgroup noted that this is only for conceptual purposes and exposure would vary and have an impact on outcomes.

The Workgroup discussed the definition of susceptibility for microbial hazards would need to specify what is meant by outcomes. The Workgroup recommended that infection (that is any infection, whether symptomatic or not) is not particularly useful for risk assessment purposes and outcomes should relate to disease manifestations (that is, symptomatic infections). This is necessary given that biomarkers are not available for most susceptible populations.

Discussion followed in regard to whether only adverse outcomes should be part of the definition. However it was decided that a range of outcomes should be considered.

The Workgroup discussed the importance of understanding why certain individuals within susceptible populations have certain outcomes while others within that same population have different outcomes. What is the biological basis for this? Such an understanding could provide biomarkers allowing risk assessment to define and distinguish susceptible individuals and populations. However the Workgroup acknowledged that that current state of the science would not support this.

Regarding intrinsic and extrinsic factors, the Workgroup agreed that an understanding of the former is more critical for risk assessment and likely more available. Following the characterization of intrinsic factors, extrinsic can then be brought in.

Finally, the definition should include to what the susceptible population is being compared. This will be the general normal population and it would also be other susceptible populations.

In summary, the Workgroup suggested that though the above definition does not incorporate the entire picture, it is sufficient for the purposes of risk assessment and risk management. More data are needed on both intrinsic factors and extrinsic factors. For each risk assessment, the definition of susceptible population will need to be considered for each pathogen and each risk assessment should define what is meant by susceptible population, the outcomes being measured, if only adverse outcomes are considered, and what the outcomes are being measured against.

2. Is the definition sufficiently concrete that it can be applied when extracting data from the literature or resource databases? For example, is it possible to actually use the concept of being "immunocompromised" or "elderly" for data mining? If not, are there other more functional terms that should be used?

In general, the Workgroup thought that definitions describing susceptible populations were *not* sufficiently concrete for data mining. In deliberations the Workgroup noted that how one defines a susceptible population may be dependent on the quality of the data that are available. Age was thought to be imperfect, but perhaps the best currently available. Specific age subgroup would need to be defined, such as >85 and l< 30 days; however the Workgroup acknowledged that defining broader groups may be more practical given the lack of data or statistical power. Immunocompromised constitutes a population that is "all over the map" and therefore may not be generally helpful until further defined. The Workgroup thought that the real question was what biologically make them susceptible, but conceded that until biomarkers are available; this is likely to be impractical.

In summary, the Workgroup concluded the need to better define the factors that affect susceptibility and develop more concrete definitions. These could then be compared to databases to determine their practical use in risk assessment. Ideally, the Workgroup desired the underlying reasons for susceptibility. When such knowledge exists, it can be used as criteria for data mining. The Workgroup did not discuss other functional terms that could be used.

3. Does it make sense to consider the probability of an adverse outcome separately from the severity of outcomes when thinking about susceptible populations?

The Workgroup determined yes that it does make sense to consider the two separately for susceptible populations. The Workgroup determined that severity of outcome is related to the susceptibility of the individual and took its lead from the chemical risk assessment given that dose can be related to severity of outcomes.

4. What currently available data resources can be used to characterize susceptible populations in terms of their size, demographics, and exposures?

The Workgroup began deliberations by discussing specific databases that were presented earlier. The Workgroup thought that the Public Health, US databases and NHANES (given participants health status is known), would be useful. Pharmacy databases that include prescriptions may also be useful in determining the size and demographics of certain susceptible population; however it was noted that such information only provides what was prescribed and not what was taken.

Though the Workgroup agreed that some currently available data would be useful in characterizing susceptible populations, the Workgroup thought that characterizing susceptible populations outside of the context of a specific pathogen to be impractical. For example, in considering susceptible populations for *Listeria monocytogenes*, assessors would consider a database that includes pregnancy and still birth rates and not necessarily look for more general resources. The Workgroup acknowledged that such a study that could characterize susceptible populations within the general US population would be useful; however it would likely be costly and require real world conditions to be representative.

5. Is it possible to "mash up" data from multiple resources to provide more detailed descriptions of specific susceptible populations?

In answering this question the Workgroup struggled initially with the definition of "mash up"; however, ultimately settled on combining databases. The Workgroup agreed that yes, is possible, but warned that combining two or more database that may have been developed for different reasons may be technically difficult. The Workgroup also thought this would be pathogen and commodity specific and may not be useful as a general resource.

Following further clarification of the question, it was suggested that web-based tools, such as Google maps, could be combined with other web-based tools or more traditional databases and may not suffer technical difficulties. The Workgroup did not have any experience with this. Though the Workgroup acknowledged that some combining of databases in traditional and non-traditional ways may provide more detailed descriptions of specific susceptible populations, the Workgroup lamented individuals' history data and outcome data are not readily available. The Workgroup suggested that risk assessors need to have input into questionnaires and/or research to provide data on susceptible population and factors and develop standardization to more easily compare studies.

6. Is there significant heterogeneity in the quality and quantity of data available for different susceptible populations or types of susceptibility (e.g. lifestage versus genetic)?

The Workgroup agreed that there is significant heterogeneity that has led to an increased focus on some susceptible populations over others. For example, some age groups may be more susceptible even within the susceptible population, such as the elderly > 85 years and infants < 30 days or subcategories among susceptible groups, such as immunocompromised, certain genetic characteristic, obesity, etc; however, dividing these data into smaller subgroups limits statistical analysis. The Workgroup

recommended that more research is needed to populate the various database, but did not specify or prioritize which different susceptible populations or types of susceptibility were needed.

7. What currently available data resources and tools can be used to characterize the relative susceptibility for different populations?

The Workgroup suggested that surveillance data can be a useful place to start, such as age and pregnancy. Furthermore, outbreak investigations and/or disease surveillance, where attack rate and exposure are known could be used to determine different dose-response curves among different susceptible populations. One of the Workgroup members had experience with susceptibility ranking and therefore the tools are available; however he noted that to determine the relative susceptibilities, exposure was assumed equal for all groups. Another resource could be hospital discharge data; however the Workgroup noted that such data may be more readily available and robust in countries outside of the US. The Workgroup recommended using such data on a case-by-case basis to determine its representativeness.

8. Can the available data sources and tools be used to characterize both the probability of adverse events and the relative severity of the events in susceptible populations?

Cohort studies, particularly prospective studies with clear characterization of exposure, can capture this; however, probably not from surveillance studies. Further, animal studies could be useful. This would need very specific targeted databases on the issues, probably down to the individual.

9. Are data resources available for some populations but not others, or for some hazards and exposure but not others?

Yes, data resources are available for some populations, such as age and pregnancy, but the Workgroup acknowledged that for more specific host issues there is a paucity of available data. The Workgroup also thought this would be pathogen specific.

10. To what extent can data from different populations or about different hazards be used to fill data gaps?

The Workgroup agreed that data from different populations/hazards can be considered for potential use of extrapolation to susceptible populations and where data are unavailable; however the Workgroup stressed that this would be case specific. For example, if the issue was about a putative susceptibility factor and/or outcome one would not expect it to be different across populations/hazards/borders, but for issues, such as the prevalence of disease, one would expect it to be different and not representative.

11. Do we have tools that will allow us to differentiate variability and uncertainty when considering differential susceptibility in risk assessments?

The Workgroup was in agreement that tools are available to differentiate variability and uncertainty when considering differential susceptibility. The tools are statistical methods, 2-dimentional Monte

Carlo analysis, geo-spatial mapping, etc. However the Workgroup stressed that the quality, robustness, representativeness of the data were more critical as it is not always appropriate to use surrogates.

12. Are there untapped data resources and tools that were developed for other purposes that might be used to identify and measure susceptible populations? (For example, medical treatment records or public health records assembled to monitor other issues).

The Workgroup focused on state health labs as an untapped resource of patient history and outcomes and outbreak investigation data. Initially it was suggested that better coordination was needed with states and risk assessors; however the real difficulty was diagnosed as a lack of state funding. For example, states are typically unable to investigate all known outbreaks due to lack of funding. When an outbreak is investigated, a full investigation may not occur, again given funding constraints. The Workgroup suggested that change would need to be done through political means. Improvement in risk assessment needs to begin with data. This Workgroup report could be used to influence fund allocation.

13. What important questions were not included in this charge?

How does one improve the quality of susceptibility and exposure data? How does one influence the collection of susceptibility factors?

How does one derive better animal models and develop better guideline to interpret these models? How do you develop criteria for define which animal models are best as surrogate to humans?

How does one develop an appropriately designed epidemiological study for susceptible populations in the context of foodborne illness?

What other extrinsic factors may be impacting the human immune system of normal healthy individuals and/or susceptible populations. For example, strenuous exercise, eating habits, lack of sleep, stress, immunotoxic chemicals, infections, micro-nutrients, interactions extrinsic and/or intrinsic factors , etc.

How does the proportion of the susceptible population change over time?

What specific missing data are needed for each pathogen so they can be systematically collected in the future. Need to be a collaborative effort during the problem formulation stage of risk assessment and research.

14. Considering the answers to the previous questions, what are the most critical data gaps and needs? Which of these data needs can be addressed in the short term and which require long term solutions?

Need to know the prevalence of the factors in your population and also need to think of this as it crosses over groups, such as gastric acid (young and elderly).

Targeted research at susceptible populations may be very helpful. If you are protecting the susceptible populations then you are likely protecting the normal.

Need better definition of what constitutes appropriate data and/or quality (including assumptions)

Need to have a commitment where some outbreaks are fully investigated with susceptible population in mind (e.g. BMI, immune statues, transplant patients, etc.) Ideally there would be a mechanism to inform outbreak investigators what are the susceptible population data concerns.

Human and microbial genetics, such as genomic and proteomic as tools for getting at some of these issues.

Increased knowledge of acceptable biomarkers in the context of susceptibility.

Improved methods for dealing with large databases and how to target for your particular risk assessment needs.

Develop improved animal model to capture susceptible factors for specific pathogens and across pathogens and specific susceptible populations.

Improved surveillance data to targeted at susceptibility factors

Can NHANES data take whole blood measurements? Can NHANES be mined for data on susceptible population, has anyone looked at this?

Need to understand the biological mechanism that underlies susceptibility factors, such as immune system