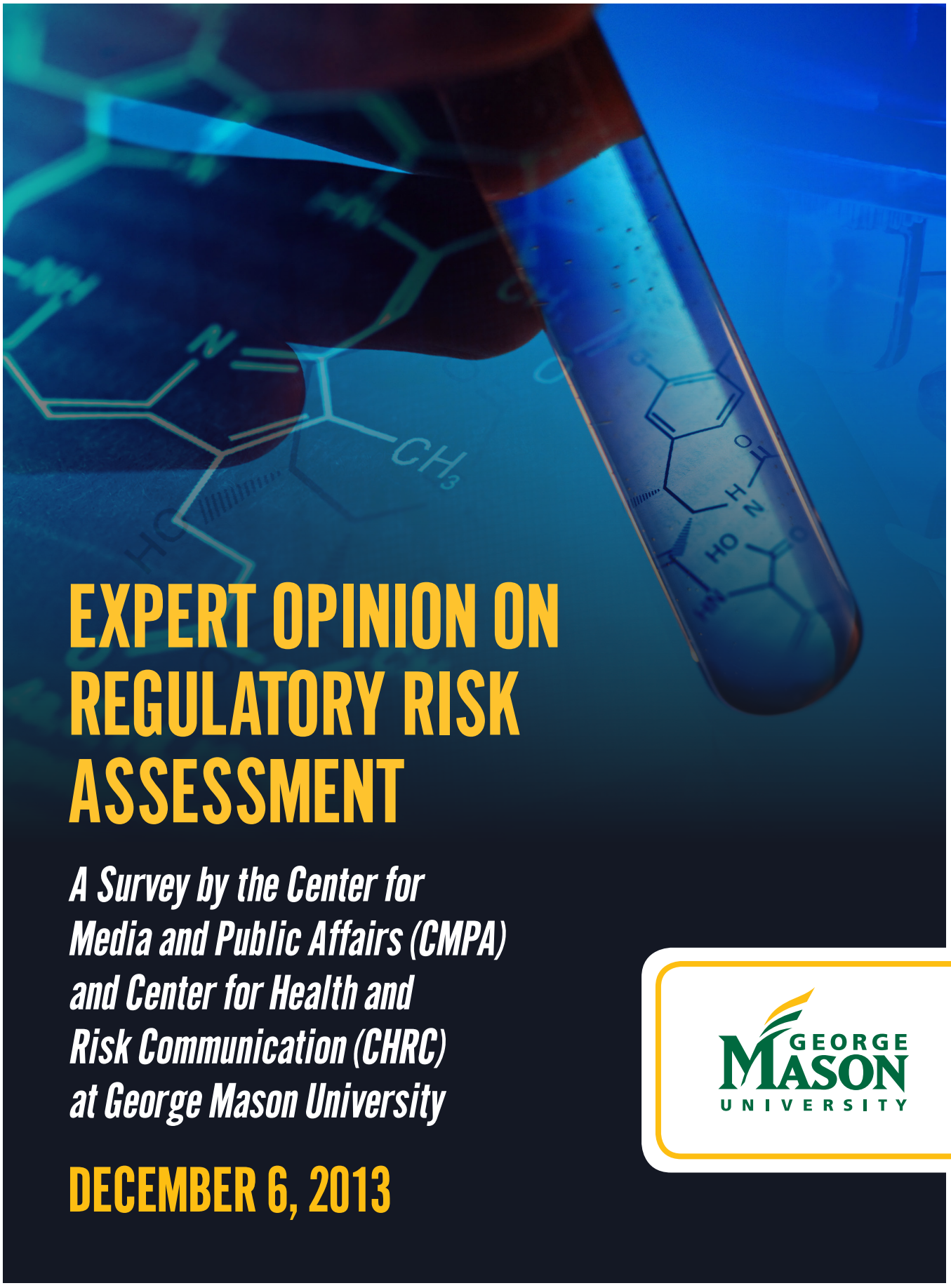

EXPERT OPINION ON REGULATORY RISK ASSESSMENT

A Survey by the Center for Media and Public Affairs (CMPA) and Center for Health and Risk Communication (CHRC) at George Mason University

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GEORGE MASON UNIVERSITY

George Mason University Survey: Expert Opinion on Regulatory Risk Assessment

Introduction

The challenges of assessing and regulating potential health risks to the public and the environment from chemical exposures have drawn much debate and growing interest from the expert community and Congress in recent years. The process and science behind how risk assessments are conducted is opaque to many people, because it involves assessing complex information from toxicology, pharmacokinetics, epidemiology, biostatistics and other areas. In addition, public controversy regarding the utility and quality of assessments increasingly accompanies decisions on the safety of individual chemicals as well as broader health assessment frameworks, such as the EPA's IRIS process.

Public debates on these matters typically involve representatives of industry and environmental groups, public officials, and individual scientists from a variety of institutions whose work bears on these issues. But there is no mechanism to tap into the collective opinion of the experts in these fields to capture their uniquely valuable insight. Moreover, members of the media sometimes focus attention on the loudest or most discordant voices, which may not be representative of informed opinion.

It would be easier for the public and regulators alike to make informed decisions if they had some way of knowing the opinions of the broader expert community. The survey by the Center for Media and Public Affairs (CMPA) and Center for Health and Risk Communication (CHRC) at George Mason University described below was conducted to advance the current discussion over the role of risk assessment in government regulatory decisions by bringing the collective voice of the expert community into the public arena.

To capture the viewpoint of the scientific community, we surveyed members of three professional organizations whose memberships represent repositories of knowledge and experience in regulatory risk assessment. They are the Risk Assessment Specialty Section of the Society of Toxicology (SOT-RASS), the Dose Response Section of the Society for Risk Analysis (SRA-DRS), and the International Society for Regulatory Toxicology and Pharmacology (ISRTP).

Results

The survey results outline the preferences of scientific experts for the conduct of regulatory risk assessments, as well as their valuations of how well current procedures are working. We find general agreement on how elements of regulatory risk assessments should work, coupled with concern over how well they are working in practice.

There is widespread endorsement of commencing assessments with problem formulations and analysis plans that are peer reviewed; data acquisition that includes access to raw data and the use of inclusion/exclusion criteria; applying data evaluation that uses the same criteria for evaluating studies regardless of institutional origin; implementing weight of evidence methodology that incorporates the use of non-linear (threshold) models; and establishing procedures insuring the independence and effectiveness of external peer review.

By contrast, there is widespread concern over the current application of these procedures. Fewer than one in three scientists say that, in their experience, problem formulations are often conducted. Fewer than one in three affirm that raw data from critical studies are often made available to assessors or peer reviewers. Only one in four say that standardized search protocols are often used for collecting data. Fewer than half say that all relevant and reliable studies are often selected for evaluation, and only one in four say consistent and transparent criteria are often used to evaluate studies.

Fewer than half affirm that weight of evidence methodology is often used, or that mode of action information is applied well for characterizing human risk. Only about one in four say that current peer review procedures provide sufficient input from stakeholders.

Finally, respondents criticize the weighting of various factors in risk management. As they perceive current practices, too little attention is being given to scientific factors and economic costs and benefits, and too much attention is given to environmental groups, the precautionary principle, media coverage, and political concerns.

The following is a summary of some of the key findings from the survey that touch on critical areas of developing assessments:

Problem Formulation/Analysis Plans

Over two thirds of the experts (68 percent) believe it is "very important" to complete a problem formulation evaluation and have an analysis plan in place prior to conducting a regulatory risk assessment. However, fewer than half as many (30 percent) say that, in their experience, prior problem formulations were conducted. In addition, almost all respondents believe that analysis plans should be peer reviewed. Most (65 percent) regard an internal review as acceptable, while 34 percent think an external review is necessary. Only five percent say that no peer review of analysis plans is necessary.

Data Acquisition

A major element of risk assessments involves acquiring and evaluating evidence from studies that bear on the assessment. Most respondents (69 percent) regard it as "very important" for assessors to have access to underlying raw data for the most critical studies in order to independently analyze their results.

However, only 31 percent report that, in their experience, such underlying raw data are "often" or "always" made available to assessors, while nearly as many (27 percent) say the data are "rarely" or "never" made available. (The remaining 42 percent say that the data are "sometimes" made available.)

A somewhat smaller majority (59 percent) see it as very important for peer reviewers as well to have access to underlying raw data from critical studies. In this case, only 16 percent report that this is done often or always, compared to 42 percent who say it is done rarely or never.

One area in which there is almost universal agreement among these scientists concerns the use of inclusion/exclusion criteria for selecting the studies to be reviewed. Ninety-four percent support the use of such criteria, compared to only six percent who do not.

However, only 24 percent report that, in their experience, standardized search protocols are often or always used and described for collecting all available study data. This is fewer than the 35 percent who say this was rarely or never done.

Data Evaluation

Respondents are less than sanguine with regard to the existing data evaluation process. While 44 percent say that the goal of using all relevant and reliable studies has often or always been met in risk assessments they are familiar with, 42 percent say this goal is met only sometimes, and 13 percent say it is met rarely or never.

Similarly, fewer than one out of four respondents (24 percent) report that consistent and transparent criteria are often or always used to evaluate the quality and reliability of studies. Only 29 percent reported that such criteria are rarely or never used.

Finally, there is widespread agreement (by 82 to 18 percent) that the same criteria should be used to evaluate the quality and reliability of all studies, regardless of their origin in academia, government, industry, contract labs, etc.

Weight of Evidence

We asked several questions regarding various aspects of the weight of evidence methods used to integrate various types of data in making an overall judgment on risk. Most respondents (89 percent) believe that weight of evidence methodology should be used, described, and documented for all risk assessments.

However, when asked how often, in their experience, weight of evidence methodology was applied in regulatory risk assessments, fewer than half (45 percent) replied that this was often or always used. Thirty-nine percent said it was sometimes done, and 16 percent report that it was rarely or never used.

When this methodology is used, only one out of four (24 percent) describe it as often or always consistent and transparent. About the same number (23 percent) describe it as rarely or never consistent and transparent. A slight majority (53 percent) say that it sometimes meets these criteria.

When asked how well mode of action information is applied in characterizing risk to humans, only 39 percent replied that it is done well, compared to 61 percent who said it is done poorly.

There was far greater agreement on the use of non-linear models and thresholds. When a non-mutagenic mode of action is indicated, 88 percent believe that non-linear (threshold) models should be used to estimate human risk from substances that cause cancer at high doses in lab animal studies. The same proportion would consider non-linear thresholds in mutagenic carcinogenesis as well.

Similarly, when a threshold event is responsible for cancer effects, 82 percent would proceed with a linear low dose extrapolation, and nearly as many (75 percent) would do so in the absence of multiple tumor sites.

Peer Review

As with weight of evidence methodology, there is widespread agreement on the importance of external peer review in regulatory risk assessment. Seventy-three percent see external scientific peer review as very important and 24 percent see it as somewhat important.

In addition, 78 percent believe the peer review process should be conducted independently of the office or program that develops a risk assessment. A smaller but still substantial majority (65 percent) would create an independent entity that insures authors would respond to peer review comments.

In contrast to the agreement on the need for strong external peer review procedures, opinion is split over current practices. Only one out of four (25 percent) believe that current procedures often or always provide sufficient opportunity for input from stakeholders, compared to 31 percent who say this rarely or never happens. Even fewer (21 percent) say current processes assure that stakeholder input is thoroughly considered by peer reviewers, compared to 38 percent who say this happens rarely or never.

Risk Management

Two out of three respondents say they have taken part in formal discussions or reviews of risk management documents, and most are critical of the priorities and practices of risk management. Only 41 percent believe risk management decisions are adequately based on our current knowledge and understanding of biology and toxicology. In addition, they would change the relative weight they see risk managers as giving to various elements embedded in risk management decision-making.

Given a list of eight factors to choose from, respondents believe that risk managers currently give the greatest weight to the legal implications of regulatory decisions, followed closely by political concerns. These are followed by some closely clustered factors—the precautionary principle, environmental group concerns, scientific factors, media coverage, and economic costs and benefits. Industry concerns are perceived as receiving the lowest weight.

By contrast, when respondents are asked how these same factors should be weighted, scientific factors far outpace all others. Economic costs and benefits finish a clear second, and legal implications an equally clear third. Then three factors are closely grouped together—industry concerns, environmental group concerns, and the precautionary principle. Lowest on the list are political concerns and media coverage, in that order.

Methodology

We created an online questionnaire with the assistance of Harris Interactive, a leading survey and market research firm and an industry leader in online polling.

In February 2013, each organization sent a letter to its members inviting them to participate by accessing a link provided by Harris. A total of 186 respondents completed the questionnaire. This group included 167 members of SOT-RASS, 40 members of SRA-DRS, and 27 members of ISRTP. (These numbers reflect membership in more than one organization by some individuals.) Response rates were 23 percent for SOT-RASS, 28 percent for SRA-DRS, and 27 percent for ISRTP.

The questionnaire addressed attitudes toward several important aspects of regulatory risk assessment. These include the use of problem formulation and accompanying analysis plans, the acquisition and evaluation of data, the application of weight of evidence methodology, the role of peer review, and the use of/adherence to guidance documents.

In addition, we asked respondents for their opinions about factors involved in risk management decisions. (Most reported taking part in formal risk management reviews as well as in risk assessments.) Finally, we inquired about various background factors, such as their occupation, discipline, certification, experience, and area of expertise. These sample characteristics are listed as an addendum below.

Addendum: Sample Characteristics

The sample is 58 percent male and 42 percent female and averages 54 years of age. Over 80 percent have a PhD, and 58 percent possess a professional certification, led by 45 percent who are certified by the American Board of Toxicology.

The sample is relatively diverse in occupations and expertise. Respondents' primary area of expertise is spread among 31 percent who are primarily expert in risk characterization, 28 percent in hazard

identification, 24 percent in dose-response assessment, and 10 percent in exposure assessment. Thirty-one percent work in industry, 30 percent are consultants, 25 percent are employed by government entities, and 13 percent are based in academia or non-profit organizations.

Respondents also report considerable and diverse experience in areas of concern. Over 80 percent have worked on industrial chemicals, over 60 percent on pesticides and water contaminants, over 50 percent on consumer products and occupational risks, over 40 percent on air pollution, hazardous waste, and food products, and over 30 percent on pharmaceuticals. In addition, over two-thirds say they have worked in their field for 20 years or more.

This group also has widespread experience with risk assessment. Just under half (49 percent) have developed risk assessments for government agencies, and 77 percent have contributed to or reviewed government risk assessments. In addition, nearly two-thirds (65 percent) have developed risk assessments and 75 percent have contributed to or reviewed risk assessments for non-government entities.

In view of the qualifications and experience reported by respondents, it seems appropriate to regard them as representing an expert community with regard to risk assessment.

For more information on the professional organizations referred to, please see:

The Society of Toxicology: ***www.toxicology.org***

The Society for Risk Analysis: ***www.sra.org***

The International Society of Regulatory Toxicology & Pharmacology: ***www.isrtp.org***

The American Board of Toxicology: ***www.abtox.org/HomePage.aspx***

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Overview: CMPA Regulatory Risk Assessment Survey

Problem Formulation/Analysis Plans	Percent
Problem formulation/analysis plan very important	68
Problem formulation always/often conducted	30
Analysis plan should be peer reviewed	95
External review necessary	34

Data Acquisition	Percent
Access to raw data by assessors very important	69
Raw data made available to assessors often/always	31
Access to data by peer reviewers very important	59
Raw data made available to peer reviewers often/always	16
Inclusion/exclusion criteria should be used	94
Standardized search protocols are used often/always	24

Data Evaluation	Percent
Goal of using all relevant and reliable studies is met always/often	44
Consistent/transparent criteria are used to evaluate studies always/often	24
Same criteria should be used to evaluate studies of all origins	82

Weight of Evidence	Percent
Should use weight of evidence method for all risk assessments	89
Weight of evidence methodology used often/always	45
Weight of evidence approach consistent/transparent often/always	24
Mode of action info applied somewhat/very well	39
Should use non-linear model to estimate human risk from animal studies	88
Non-linear thresholds should be considered	88
When threshold event responsible for cancer, next step is:	
If multiple tumors, use non-linear low dose extrapolation	75
If absence of multiple tumors, use non-linear low dose extrapolation	82

External Input	Percent
External peer review is very important	73
Review should be independent of office/ program that developed the assessment	78
Should create independent entity to ensure authors respond to review	65
Process often/always provides opportunity for stakeholder input	25
Input from experts, public thoroughly considered often/always	21

Guidance Documents	Percent
Served as peer reviewer for regulatory risk assessment	53
If so, very knowledgeable about guidance documents used	63
Government agencies follow own guidance documents often/always	51

Risk Management Factors

- Risk management decisions are based on current knowledge of biology and toxicology very/somewhat well. 41%

How much weight do risk managers *currently* give to:

Risk Management Factors	Great Deal of Weight (%) *	Mean Score (1-5)
Legal implications	72	3.9
Political concerns	66	3.8
Precautionary principle	52	3.4
Environmental groups	49	3.4
Science	47	3.5
Media coverage	43	3.3
Economic costs/benefits	41	3.2
Industry	28	2.9

How much weight *should* risk managers give to:

Risk Management Factors	Great Deal (%)*	Mean Score (1-5)
Science	98	4.8
Economic costs/benefits	67	3.9
Legal implications	48	3.5
Industry	20	3.0
Precautionary principle	19	2.5
Environmental groups	16	2.8
Political concerns	8	2.1
Media coverage	4	1.8

* 4 or 5 on scale from 1=none to 5=great deal Mean score on 1 to 5 scale from 1=none to 5=great deal

Respondent Profile

Background	Percent
Male	58
Average age	54
Ph.D.	82
Years in field 20+	68

Field	Percent
Toxicology/pharmacology	65
Enviro Health	8
Cell/molecular biology	5

Certification	Percent
American Board of Toxicology	45
Academy of Toxicological Sciences	13

Occupation	Percent
Industry	31
Consulting	30
Government	25
Academic/non-profit	13

Primary RA expertise	Percent
Risk characterization	31
Hazard identification	28
Dose-response assessment	24
Exposure assessment	10

Areas worked in	Percent
Industrial chemicals	83
Pesticides	63
Water contaminants	60
Consumer products	53
Occupational	52
Air pollution	47
Hazardous waste	46
Food	42
Pharmaceuticals	31

Risk Assessment Experience	Percent
Developed gov't RA's	49
Developed non-gov't RA's	65
Contributed to/reviewed gov't RA's	77
Contributed to/reviewed non-gov't RA's	75
Took part in formal risk management reviews	66