As of February 5, 2015, this decision is no longer considered by WCAT to be noteworthy.

WCAT Decision Number: WCAT-2003-02212-AD
WCAT Decision Date: **August 26, 2003**
Panel: Randy Lane, Vice Chair
Daphne Dukelow, Vice Chair
Paul Petrie, Vice Chair

Introduction

(1) The worker appeals the August 11, 2000 findings of the Workers' Compensation Review Board (Review Board). The Review Board upheld the July 7, 1998 decision of the Workers' Compensation Board (the Board) denying his claim for colon cancer which he considered was related to his employment as a firefighter.

(2) The appeal was initiated by an August 17, 2000 telephone call which was followed by a September 7, 2000 notice of appeal and an October 12, 2001 submission which was accompanied by a copy of a 2001 article by Baris et al.[1] The worker's employer provided a January 31, 2002 submission to which was attached a copy of a December 20, 2001 report from Dr. Howe prepared in connection with another appeal by a firefighter seeking compensation for colon cancer. The worker then provided an August 7, 2002 submission to which was attached a July 21, 2002 report from Dr. Guidotti. A short August 13, 2001 submission followed.

(3) By letter of November 19, 2002 (revised on November 25, 2002) the worker's employer provided a further submission which was accompanied by an October 16, 2002 letter from Dr. Howe and an October 16, 2002 reply by Dr. Howe to Dr. Guidotti 's July 21, 2002 report.

(4) By letter of December 11, 2002 the worker objected to the employer tendering a further opinion from Dr. Howe. By letter of December 23, 2002 the employer responded to the December 11, 2002 submission. By letter dated December 11, 2002 (but perhaps, more accurately, issued on December 23, 2002) the worker provided a further submission.

(5) Both the worker and the employer are represented by legal counsel.

(6) The notice of appeal seeks an oral hearing. By letter of November 6, 2000 the worker was advised of the decision of the deputy chief appeal commissioner to

[1] Baris, D et al. 2001. Cohort mortality study of Philadelphia firefighters. American Journal of Industrial Medicine 39: 463-476.

deny that request. That decision does not bind us if we consider an oral hearing is necessary. We have reviewed the matter and do not consider an oral hearing is necessary to enable us to make a fair and thorough decision on this appeal.

(7) This panel is deciding two appeals from Review Board findings concerning firefighters and colon cancer. In this case the panel is sitting as a panel of the Workers' Compensation Appeal Tribunal (WCAT) and in the other case it is sitting as a panel of the Appeal Division. The workers are represented by the same counsel and the employers are represented by the same counsel.

Jurisdiction

(8) This appeal was filed with the Appeal Division. On March 3, 2003, the Appeal Division and Review Board were replaced by the WCAT. As this appeal had not been considered by an Appeal Division panel before that date, it has been decided as a WCAT appeal. (See the *Workers Compensation Amendment Act (No. 2), 2002*, section 39).

Issue(s)

(9) At issue is whether sufficient medical or scientific evidence has become available since August 1989 for the Board to recognize the worker's colon cancer as an occupational disease.

Background and Evidence

(10) In his August 16, 1991 application for compensation, the worker, then nearly 66 years of age, who had been employed as a firefighter from October 1951 to September 1985, indicated that his 34 years of exposure to toxic vapours, dusts, gases, chemicals, radiation and carcinogens had resulted in colon cancer. Earlier, on August 26, 1988 the worker had undergone surgery for colon cancer.

(11) By decision of September 27, 1991 the claims adjudicator denied the worker's application for compensation. It was considered that the worker's occupation as a firefighter was not of significance with respect to his cancer of the rectosigmoid colon. The claims adjudicator noted that the application for compensation was approximately two years after the condition was first diagnosed and, owing to the terms of section 55 of the Act, there was no basis to give consideration to the claim.

(12) The worker appealed that decision to the Review Board but the appeal was withdrawn. The worker sought to reactivate the appeal but the Review Board denied that in a September 4, 1997 letter. By letter of June 22, 1998 the Appeal Division agreed with the decision of the Review Board but it referred the file to

the Compensation Services Division of the Board to consider the effects of the revisions to section 55 of the Act.

(13) By decision dated July 7, 1998 the case manager advised that he was unable to conclude that the amendments to section 55 of the Act would allow him to reconsider the earlier decision and pay compensation benefits under the claim. He cited the revised section 55 of the Act and item #32.58 of the *Rehabilitation Services and Claims Manual* (the Manual).

(14) The case manager indicated that the issue was whether subsequent to September 27, 1991 the Board had obtained sufficient medical or scientific evidence to cause it to recognize the disease as an occupational disease for the worker's kind of employment. He referred to a July 3, 1998 opinion of a Board medical advisor and indicated that he was unable to conclude that the Board had obtained, since the time of the original decision, sufficient medical or scientific evidence to cause it to recognize the rectal sigmoid cancer as an occupational disease associated with the nature of the worker's employment. He was unable to conclude that the scientific and epidemiological evidence available would cause the Board to conclude that there was a likely association between employment as a firefighter and the development of colon cancer.

(15) The medical advisor commented that the question of cancer in firefighters had been extensively addressed in recent medical/scientific literature. He commented that epidemiologic studies show relationships but do not show cause and effect. He noted colon cancer was a very common cancer amongst the adult male population in North America; although there had been much speculation regarding its cause, no conclusions had been drawn. He addressed a 1995 review article by Dr Guidotti[2] (which will be reviewed below). He considered the SMR of 150 in that study to be questionable. (SMR stands for standardized mortality ratio, a concept that will be discussed later in the decision). He considered that the review did not include all the studies. He concluded that the SMR for colon cancer in firefighters was, in all probability, somewhat the same as that for the general population and was nowhere near a figure of 200. He considered that there was insufficient scientific and epidemiologic evidence to allow one to conclude that the worker's colon cancer had been caused by his work.

(16) The worker appealed to the Review Board and relied on materials that he had submitted earlier. His employer filed a January 31, 2000 submission.

(17) In its August 11, 2000 findings the Review Board denied the worker's appeal. It noted the worker's materials supplied earlier, some of which were scientific and

[2] Guidotti, TL. 1995. Occupational Mortality among Firefighters: Assessing the Association. Journal of Occupational and Environmental Medicine 37:1348-1356.

some of which were not. The panel noted that the worker had not provided any recent, expert medical opinion which would counteract the opinion of the Board medical advisor. The panel accepted that opinion. It considered there was insufficient new medical or scientific evidence available for the Board to consider recognizing rectosigmoid cancer in the worker's case as an occupational disease pursuant to subsection 55 (3.2) of the Act.

Non-occupational causes of colon cancer

(18) We are aware that lack of physical activity has consistently shown to be an important risk factor for colorectal cancer. High body mass index increases the risk dramatically. Diets high in fiber and vegetables and lower in meat and animal fat are generally thought to protect against colorectal cancer. Smoking and alcohol are thought to be weaker environmental influences.

(19) In his December 20, 2001 report Dr. Howe comments that factors which have been suggested to increase risk include a high-fat/low-fiber diet, high-energy intake, obesity, and low-energy expenditure. He observes that those factors are highly correlated and it has yet to be determined which factor or factors play an etiologic role.

Potential occupational causative agents regarding colon cancer

(20) We note the comments of the Appeal Division panel in *Decision #2002-1282* (on the Board's website) concerning the exposure of firefighters:

> It is generally accepted that firefighters are routinely exposed to extremely hazardous environments including a wide range of chemical compounds and products of combustion in uncontrolled conditions. The literature documents that firefighters are also commonly exposed to a wide variety of potential carcinogens such as benzene which is detectable at nearly all fires; polycyclic aromatic hydrocarbons (PAHs) found in soots, tars and diesel exhaust; arsenic found in wood preservatives; formaldehyde in wood smoke; and asbestos in building insulation. There is also the potential for exposure to uncommon but potent carcinogens such as pesticides, polychlorinated biphenyls and dioxins. (See William N. Rom, *Environmental and Occupational Medicine*, 1998 pages 1455 – 1464; Peter S.J. Lees, "Combustion Products and Other Fire Fighter Exposures", *Occupational Medicine*, Vol. 10, No. 4, 1995; and Vernon N. Dodson, "Exposure to Pyrolysis Products" in Carl Zenz, *Occupational Medicine*, 1994, pp 926-936).

(21) The panel noted the following concerning the 1994 report of the Industrial Disease Standards Panel (the IDSP) prepared for the Ontario Workers' Compensation Board:

> The IDSP Report No. 13 specifically identified asbestos and diesel exhaust as potential causative agents. The report cited one study (Markowitz et al., 1980) that reported "strong evidence" that firefighters are at risk for scarring of the lungs and pleura due to occupational asbestos exposure (p. 142). The report pointed out that exposure to PAHs which are present in diesel exhaust has been linked with colon cancer among coke oven workers. The report also noted acrylonitrile and formaldehyde as probable carcinogens associated with colon cancer both of which have been connected with different types of fires.

Epidemiological concepts

(22) Before discussing the review articles concerning firefighting and colon cancer, it is appropriate to note a few epidemiological concepts. See generally the *Protocol for the Assessment of Medical/Scientific Information - Industrial Diseases Standing Committee, Workers' Compensation Board of British Columbia* at *9 Workers' Compensation Reporter 429* (the Protocol) as well as documents cited in this footnote[3].

(23) Assessments of the contribution of epidemiology to the issue of causation raise the issue of relative risk. Relative risk (RR) is the ratio of the disease incidence or death among people exposed to an agent to the disease incidence or death among the unexposed. A relative risk of 2.0 is often equated with a 50 percent likelihood that an exposed person's disease was caused by the agent, and a relative risk greater than 2.0 would permit an inference that an individual's disease was more likely than not caused by the implicated agent. SMR is defined as a "standardized mortality ratio, equivalent to relative risk (observed cases divided by expected cases)."[4] In cancer incidence studies SMR refers to standardized morbidity ratio; some authors also refer to SIR or standardized incidence ratio. An SMR may be expressed in two ways: 150 or 1.5. When discussing the results of a study we use the form employed by the authors.

[3] See also *Reference Manual on Scientific Evidence, Second Edition* (2000), and, in particular, the *Reference Guide on Epidemiology*, by M.D. Green, M. Freedman, and L. Gordis and the *Reference Guide on Statistics* by D.H. Kaye and D.A. Freedman. The documents are available at http://www.fjc.gov/ which is the website of American Federal Judicial Center, the education and research agency for the United States Federal Courts.
[4] Protocol at page 450.

(24) The principle of relative risk is well explained in the following excerpt from an article by D.A. Freedman and P.G. Stark[5]:

> The basic intuition connecting relative risk and probability of causation can be explained as follows. Suppose that the exposed and unexposed groups in an epidemiologic study are similar except for the exposure of interest, so that confounding is not an issue. For simplicity, suppose also that the two groups are the same size. To have specific numbers, suppose there are 400 injuries in the exposed group and 100 in the control group. In other words, the observed number of injuries is 400, compared to an expected number of 100. The relative risk is 400/100, or 4. Without exposure, there would be only 100 injuries among the exposed, so 300 of the 400 injuries may be attributable to the exposure and 100 to other factors. Apparently, then, each injury in the exposed group has a chance of 3/4 of being caused by exposure. Likewise, a relative risk of 3 corresponds to a chance of 2/3, while a relative risk of 2 corresponds to a chance of 1/2, which may be the minimum level needed to carry the burden of proof in civil litigation.

(25) Freedman and Stark take the position that a relative risk of 2.0 or greater is not equivalent to legal causation, because the relative risk is usually not a reliable factor. Rather, a court must examine the "belief probability," explained as follows:

> The belief probability relates to evidentiary requirements imposed by the law, and the fact probability relates to the facts relevant to legal cases. These two probabilities are directly related to the civil law evidentiary requirement that the proponent of a claim must prove that the other's act is more likely than not a cause of harm. By contrast, the sampling error probability is a characteristic of statistical science. Appreciating the distinctions among these probabilities facilitates an understanding of the relationship between the preponderance of the evidence standard and the probabilities reported by statisticians.

They conclude as follows:

> Courts cannot avoid evaluating the underlying scientific and statistical methodology when evaluating scientific evidence of

[5] The Swine Flu Vaccine and Guillian-Barré Syndrome: A Case Study in Relative Risk and Specific Causation," *64(4) Law & Contemp. Probs. 49.* The panel observes that volume 64(4) of *Law & Contemp. Probs.* contains several articles of note concerning causation in law and science and may be accessed at www.law.duke.ed/journals/cp.

> causation. In particular, they may not rely on the statistical significance of the study, as measured by the sampling error probability, to conclude that the evidence is scientifically reliable or whether the preponderance of the evidence test is met. Nor may they rely on the sampling error probability in combination with the fact probability. It is the belief probability, based only in part on an estimate of the sampling error probability, that determines whether the fact probability is more likely than not true. The belief probability also depends, however, on the other indicia of reliability discussed.

(26) We agree generally with Freedman and Stark's comments concerning "belief probability."

(27) When applying epidemiologic data to a particular worker's case, even a relative risk of less than 2.0 for an occupation may be persuasive if there are individual characteristics particular to the specific worker. A simple example of that would be where the overall risk for a particular occupation is 1.6 but there is a clear dose response which establishes that those with 30 or more years in the occupation have a risk of 2.0 or more and the worker in question has 30 years or more of relevant employment.

(28) An estimate based on a sample is likely to be off the mark, at least by a little, due to random error. The standard error gives the likely magnitude of this random error. Confidence intervals refine this idea.

(29) A confidence interval is a range of values calculated from the results of a study within which the true value is likely to fall. The width of the interval reflects random error. If the limits of the interval do not include 100 (a relative risk of 1.0) the risk is statistically significant. The larger the sample size in a study (all other things being equal), the narrower the confidence boundaries will be (indicating greater statistical stability), thereby reflecting the decreased likelihood that an association found in the study would occur if the true association is 1.0. Confidence intervals are often noted in connection with relative risks. A 95 percent confidence interval means that the range set by the interval will contain the true risk 95 percent of the time.

(30) A p value is the probability of getting a value of the test outcome equal to or greater than that observed in the study when in truth there is no association. (The absence of an association is often called the null hypothesis, that is, the hypothesis that there is no association between an agent and a disease.)

(31) An outcome is statistically significant when the observed p value for the study falls below the pre-selected significance value. The lower the value the less likely that random error would have produced the observed relative risk if the

true relative risk is 1.0. Statistical significance does not address the magnitude of any association found in a study but rather assesses the role of random error. A very common significance level is .05. A .05 value means that the probability is 5 percent of observing an association as large as the one found in the study as association when in truth there is not one. Thus, if one conducted an examination of a large number of associations in which the true relative risk equals 1.0, on average 1 in 20 associations found to be statistically significant at a .05 level would be spurious.

1994 Industrial Disease Standards Panel report[6]

(32) This report reviewed 13 studies of colon cancer in firefighters with varied results. Page 14 of the report summarized its findings as follows:

> Statistically significant increases in colon cancer were identified in three studies. One of those increases occurred among the largest cohort, but the finding was for the broader category of cancer of the intestine.
>
> - Increases did not appear consistently which weakens the strength of the association between firefighting and colon cancer.
>
> Firefighters experience occupational exposure to carcinogens which can cause colon cancer such as asbestos, PAHs, acrylonitrile and formaldehyde.
>
> - Dose response trends were shown in a minority of the studies which conducted that analysis. Since the actual occupational exposures of the firefighters studied is unknown, negative dose response findings are not evidence against an association, but are simply uninformative.
>
> The Panel's conclusions and finding
>
> While there is evidence for and against, the Panel concludes that the weight of the evidence establishes a probable connection between firefighting and colon cancer. The association is strong in three studies, one of which is of the largest cohort, but there is a lack of consistency in the findings. There is some evidence of dose response trends and evidence that firefighters are exposed to recognized colon carcinogens.

[6] Report to the Workers' Compensation Board on Cardiovascular Disease and Cancer Among Firefighters September, 1994 (IDSP Report No. 13, Toronto, Ontario).

Accordingly, the Panel makes the following finding.

A probable connection exists between colon cancer and the occupation of firefighting.

Since there is a lack of consistency in the data, the evidence did not persuade the Panel to recommend inclusion in a Schedule to the Regulations of the *Act* which would invoke a legal presumption that colon cancers in firefighters are due to their occupation, unless the contrary is proved.

The Panel's recommendation

Because a probable connection has been established, guidelines developed and approved by the Panel should be used to assist adjudicators in assessing the merits of each claim for colon cancer from firefighters.

Guidotti, 1995 (see footnote #2)

(33) This paper discusses the concept of the general presumption of risk. A general presumption of risk implies that individual firefighters in general share roughly equally in the elevated risk demonstrated for all firefighters and that the elevated risk is sufficient to make it more likely than not, in the individual case, that the cause of the disorder was related to work as a firefighter. The second part of the argument for presumption, that in the individual case an occupational association is more likely than not, logically requires that the risk be at least doubled compared with expected risk. A general presumption is difficult to defend if the relative risk demonstrated by the population is less than double that expected.

(34) Dr. Guidotti commented that it may seem excessive to insist on an approximate doubling of risk to be demonstrated in relevant population studies before a general presumption of risk is made. He commented that the logic of "more likely than not" applied to every member of the population at risk demanded no less and the criterion is applied only for a general presumption of individual risk, not as a standard for evaluating every individual claim.

(35) Dr. Guidotti outlined the considerations in applying the population risk to the individual case. Characteristics of the individual, such as age, length of service, family history, and lifestyle, may substantially modify the individual risk profile. For an individual with few risk factors for the disorder, the population risk may be an overestimate of total risk but an underestimate of the risk due to occupation. Evaluation of the individual case is needed before population risk estimates can be applied uncritically in compensation cases. He observed that

while actual occupational risks of most diseases recognized on schedules around the world far exceeded the doubled level of elevated risk, "individual presumptions, on the other hand, can and should be made regardless of the magnitude of relative risk compared with the general population if warranted by individual features of the case."

(36) He observed there were a number of unusual characteristics that influence the interpretation of studies in firefighters and their occupational mortality and morbidity. He referred to the healthy worker effect. That effect is a phenomenon that involves an observed decrease in mortality in workers when compared to the general population. The many sources of the effect include the true beneficial effect of the work, the selection processes associated with healthy people being more likely to seek and gain employment, and hiring processes which result in low risk people being more likely to be hired.

(37) Firefighters do not show a strong healthy worker effect in most cohort mortality studies. He observed this might suggest an excess mortality from some cause that is currently concealed by the healthy worker effect. He noted that there were two such effects. The strong healthy worker effect flowing from the strenuous fitness requirement at the time of hire operates much more strongly for cardiovascular disease than for cancer. The second healthy worker effect occurs when workers who become unfit after employment because of illness or the effect of risk factors that later predispose them to premature mortality are removed from the workplace or reassigned to other duties and are lost to follow-up or misclassified. He considered there was good reason to conclude that this effect was strong among firefighters.

(38) He offered some comments of note regarding a preference for data from studies showing strongly positive findings rather than studies that do not show an association. The pooling of data from several studies with varying exposure potential to derive a summary risk estimate cannot effectively compensate for limitations in most studies. Given those considerations and the inherent nature of indicators of outcome in epidemiologic studies, elevated risks detected in a positive study were much more like a "signal" reflecting the true association. Only when study designs are very similar, exposure is clearly documented, and analysis takes exposure into account can the risk estimates from studies be reasonably pooled.

(39) He commented that firefighters have variable exposures although the work is probably more consistent in that regard than it is for most occupations. He observed that thus risk estimates in the positive studies may tend to converge on a most-likely magnitude of risk. More revealing is the overall pattern of risks, whether these risk estimates are consistent, and whether the risk estimates approach or exceed doubling of absolute risk. Whether the risk estimates appear to cross the threshold in more than one well-designed and conducted

study is ultimately more significant than any attempt to devise a true risk. He concluded that in practice, it is more appropriate to infer the approximate magnitude of risk from the well-conducted positive study and to use a relatively wide latitude in estimating the magnitude of risk, surmising that the measure is subject to bias and random error.

(40) Dr. Guidotti determined that available evidence suggested that firefighters as a group have increased risk for colon cancer, a risk shared with cancer of the rectum. He considered the magnitude of the risk in the available *positive* studies was about 150 which suggested that there may be a presumption of risk in the individual case but there was no defensible general presumption of risk (200). He observed the major contributions to the risk of colon cancer remain unknown or in dispute. He considered that in the case of death from colon cancer in a young person who is a firefighter in the absence of a family history suggestive of genetic risk, while the population risk may be well below an SMR of 200, that individual's personal risk may be at or above 2.0 because their personal risk absent exposure is much less than that of the general population.

Golden et al., 1995[7]

(41) The authors conclude that data showed employment as a firefighter increased the risk of developing and dying from certain specific cancers such as leukemia and multiple myeloma and possibly other cancers including those affecting the large intestine. They noted that excess rectal cancer had been found consistently in many studies of firefighters; a similar pattern was evident for colon, colorectal or "intestinal" cancer although the risk ratios tended to be somewhat lower. The 1994 Demers report[8] was considered to indicate that colon cancer incidence, although not significantly elevated, appeared to increase with duration of employment.

Dr. Howe, 2001

(42) Dr. Howe has a Ph.D. in chemistry. He is a professor of epidemiology in the Department of Epidemiology of the Mailman School of Public Health at Columbia University. Immediately prior to that he was chair of the Division of Epidemiology at the school of public health before it was renamed. His curriculum vita on file indicates that he has conducted a number of epidemiologic studies of various designs addressing issues concerning the relationship between lifestyle and environmental factors and risk of a number of cancers. In particular he was co-author of a journal-published review of

[7] Golden AL et al. 1995. The Risk of Cancer in Firefighters. Occupational Medicine: State of the Art Reviews 10(4) 803-820.
[8] Demers, PA. 1994. Cancer incidence among firefighters in Seattle and Tacoma Washington (United States). Cancer causes and control 5(2): 129-35.

fire-fighters and cancer[9]. He has participated in a number of advisory committees addressing various aspects of the epidemiology of cancer. He has prepared reports and given testimony in a number of court cases in Canada, the United States, and the United Kingdom, and has prepared expert reports for workers' compensation boards relating to issues on the epidemiology of cancer.

(43) Dr. Howe's report contains a discussion of the principles and methods of epidemiology. He offers the following notable comments regarding the process of assessment. The first step is to identify all the relevant epidemiologic studies and examine each of them to see if it has a major flaw or potential for bias; he asserts this assessment process and consideration of the strength of the various types of study design is often overlooked in expert assessments.

(44) The next step is addressing whether there is prima facie evidence for an association in that the studies, overall, consistently demonstrate a positive association from which one can exclude the likely contribution of chance. He notes that the assessment process stops if the studies do not provide evidence of an association which is unlikely to be due to chance. His focus is on a positive association unlikely to be due to chance and he does not state that "positive" means a relative risk of 2.0. His concern is more with the role of chance than the magnitude of any association.

(45) If there is a statistical association (that is, the relationship is unlikely to be due to chance), the next step is to consider whether there is evidence to support a hypothesis that the association really represents causality and is not due to some bias. He refers to the identification of potential biases in studies. In addition to this, epidemiologists use a set of criteria for assessing causality - the Hill criteria. He comments that applying the criteria is, inevitably, somewhat subjective; nevertheless, if an association satisfies the criteria, one would generally conclude that causality is supported.

(46) If, after consideration of the issues involved in the assessment of causality between exposure and disease, one concludes there is substantive evidence that exposure can cause the disease under consideration, one has to consider whether, for the individual being assessed, there is substantive evidence that the individual's disease was caused by exposure. To address the question of "more likely than not" the individual concerned would have had to experience a doubling of risk of disease from the exposure, and subsequently, have developed the disease. The overall relative risk for firefighters as a group has to be relied upon to estimate the relative risk for an individual firefighter. If there is clear evidence of a dose response relationship with duration of employment, it

[9] Howe GR and Burch JP. 1990. Fire Fighters and Risk of Cancer: An Assessment and Overview of the Epidemiologic Evidence. American Journal of Epidemiology 132(6):1039-1050.

might be possible to assign a relative risk to an individual based on his years of employment.

(47) Regarding the epidemiologic evidence relating to firefighting and colon cancer risk, Dr. Howe updated the list of relevant studies identified in his 1992 report which accompanied his 2001 report. He listed all the relevant studies, independent of size. He regards the process of identifying a few positive studies, and ignoring a number of others, to be invalid and misleading. He indicated he was unaware of any major potential flaws in the studies and considered they provided a substantive body of epidemiologic evidence to address the relevant issues.

(48) Among the three cohort studies of incidence, there was no evidence of any association. One of the studies showed an SMR of greater than 1.0 with the other two having SMRs less than 1.0. None of the results either for individual studies or for the studies combined are statistically significant. The pooled SMR result was 0.91 with a 95 percent confidence interval of 0.64-1.25. A total of 38 cancers were observed compared to 41.7 expected.

(49) Among the nine mortality studies, there were under 167 observed deaths compared to 143.9 expected, giving an overall SMR of 1.16 (a figure with an associated p value of 0.06 which is almost conventionally statistically significant). There were five individual studies within an SMR of greater than 1.0 and four individual studies with an SMR of less than 1.0. Two of the studies showing a positive association were statistically significant. For Vena and Fiedler[10] the SMR was 1.84 with a 95 percent confidence interval of 1.05-2.99 and for Baris the SMR was 1.51 with a 95 percent confidence interval of 1.16-1.93. The slight suggestion of an overall positive statistical association is primarily driven by those two studies although the 1993 Guidotti study[11] is also positive although not statistically significant at the conventional level (1.61 with a 95 percent confidence interval of 0.88-2.70).

(50) Dr. Howe combined the studies of incidence and mortality and produced a pooled SMR of 1.10 involving six studies having an SMR of less than 1.0 and six studies having an SMR of greater than 1.0. He considered the p value was 0.17, that is, compatible with chance.

(51) Dr. Howe concluded that "there is certainly no strong evidence for any statistical association in these data." His concern was not with the magnitude of any association (that is, whether the relative risk was 2.0 or more) but rather with the

[10] Vena, JE and Fiedler, RC. 1987. Mortality of a Municipal-Worker Cohort: IV. Fire Fighters. American Journal of Industrial Medicine 11:671-684.
[11] Guidotti, TL. 1993. Mortality of urban firefighters in Alberta, 1927-1987. American Journal of industrial medicine 23 (6): 921-40

role of chance. He considered the overall pattern was reasonably consistent with a lack of statistical association but for the sake of completeness he examined the evidence to see whether the data were supportive of a causal hypothesis.

(52) Dr. Howe evaluated whether there were any potential biases, such as confounders, that could be present in the studies under consideration. It has been suggested that firefighters, as a group, should have increased energy expenditure which, if anything, would reduce their risk for colon cancer. He observes that most of the studies of firefighters reported to date have studied firefighters who were employed a number of years ago and it is not clear to what extent the fitness requirements of current firefighters would be reflected in such historical data. He comments that for this reason, and in view of the absence of any data relating to the lifestyle of firefighters as a whole, he did not think one could reasonably make any assumption about the possible existence, direction, and magnitude of any potential confounding factor operating generally among firefighters.

(53) He notes that the individual habits of the particular firefighter are completely irrelevant in pursuing the issue of potential confounders in this context; it is the prevalence of such factors in firefighters, as a whole, which is relevant in this context.

(54) Concerning the Hill criteria he concluded as follows. Strength of association was not satisfied by the studies. The figure of 0.91 for incidence studies showed no positive association. The figures of 1.16 for the mortality studies and 1.10 for the two types of studies combined represented extremely weak associations for epidemiologic studies. Adjusting for a potentially healthy worker effect by a factor of 8 percent (drawn from his 1989 and 1992 reports, which will be discussed later) would produce SMRs of 1.26 for the mortality studies and 1.20 for the studies of incidence and mortality combined. That magnitude of relative risk could very easily be introduced by some unmeasured confounding factor, or by some other bias.

(55) Consistency was not satisfied as the studies, as a group, did not show consistent evidence of a positive association between firefighting and colon cancer. Only three studies provided some meaningful evidence of a positive association.

(56) Dose response relationship was not satisfied. Only one of the six studies which listed results by category of duration of employment (Vena and Fiedler) had a statistically significant test for the existence of a dose response relationship. Notably, he considered the Baris study which found a significant effect in terms of overall association showed "absolutely no evidence of any dose response relationship." He commented that a pooling of the data to create SMRs

revealed "essentially no evidence of any dose response relationship with those employed for 20 years or more having a risk of 1.21 compared to those for less than ten years [1.0]."

(57) Temporality was satisfied in that firefighting preceded the disease. That criterion cannot prove causality; it can only eliminate causation when the disease precedes exposure. Dr. Howe commented that latency was satisfied in that the great majority of cases or deaths occurred a number of years after first employment; however, that was inevitable since firefighters are generally employed initially at ages when colon cancer is rare and reach the age where the majority of cancer occurred after a number of years of service.

(58) Regarding plausibility, Dr. Howe noted firefighters are obviously exposed to a number of chemicals in the workplace, some of which are mutagenic and/or carcinogenic and observed to that extent the hypothesis of causality was plausible. He considered there was a limitation on this interpretation in that there appeared to be no human data to address the question of degree of exposure. One would require that the level of exposure of any specific chemical was sufficiently high to lead to a measurable increasing risk.

(59) Dr. Howe's report of December 20, 2001 on this file addresses the merits of the claim of the other firefighter whose case is also before this panel. His report does not address the merits of the claim dealt with in this decision. The employer has submitted a copy of that report in this appeal presumably for its discussion of the general issue of firefighters and colon cancer.

(60) Dr. Howe considered that there was no meaningful evidence to support the existence of a causal relationship between firefighting and colon cancer. His opinion then proceeded to address the merits of the other firefighter's claim but that portion of his opinion is not relevant to this appeal save for his comments that the worker's individual risk profile for colon cancer was not relevant to the issue of estimating his "probability of causation" if it was assumed that any relative risk from firefighting multiplied risks for other factors, the so-called multiplicative model. He commented that model was widely used in epidemiology for modeling the joint effects of various risk factors and there was substantial empirical evidence that the model was a reasonable assumption in many cases. He observed that in many cases of colon cancer the cause of the particular cancer cannot be established and thus there were many unknown causes of colon cancer.

Dr. Guidotti, 2002

(61) Dr. Guidotti's cirriculum vita indicates he holds an MD and MPH. He has American Board certification in internal medicine, pulmonary medicine, and occupational medicine. He is certified by the Canadian Board of Occupational Medicine and has specialty certification in occupational medicine from the Royal Colleges of Physicians in Canada and England. He is currently a professor in and a chair the Department of Environmental and Occupational Health at the School of Public Medicine and Health Sciences Centre at George Washington University. He has cross appointments as a professor of epidemiology at that same school and as a professor of pulmonary medicine, at the School of Medicine and Health Services. Other positions include that of director of the Division of Occupational Medicine and Toxicology at the School of Medicine and Health Services. He has consulted or assisted in matters related to disease causation for numerous agencies. He has been engaged in studies of health outcomes associated with firefighting for two decades (two of his articles are noted in this decision) and has been consulted on numerous occasions with respect to policy on criteria for adjudicating claims. He has been asked to serve as an expert on evaluating numerous individual claims submitted by firefighters.

(62) Dr. Guidotti offers the following comments regarding the usefulness of epidemiology:

> Epidemiology is a science of generalizations and its analytical framework provides estimates of group risks. It informs, but does not decide, the risk for individuals, which is the basis for tort litigation and for claims adjudication. Law and adjudication require interpretation of these risk estimates in light of individual characteristics and risk factors. Thus, the relevant question is not whether firefighters overall have an increased risk of colon cancer equivalent to a doubling but whether an individual claimant, in this case [the worker], had an elevated risk equivalent to a doubling or greater of his personal risk.

(63) He asserts that the literature "supports the conclusion that there is an increased risk of colon cancer among firefighters in general but not that this increased risk equals or exceeds a doubling, which would correspond to the criterion of 'more likely than not'." He contends recent studies have not refuted that conclusion and have strengthened the evidence for an association both by replication and by demonstrating a dose response relationship (and the Baris study is cited in support).

(64) Dr. Guidotti addresses the opinion of the Board medical advisor. He comments that little of the Board medical advisor's critique is substantive. Concerning the assertion that the literature review in his 1995 paper was incomplete, Dr. Guidotti indicates that the Board medical advisor cites no peer reviewed original studies that Dr. Guidotti missed. He comments that the Board medical advisor's belief that a meta-analysis can be conducted by adding the risk estimates and dividing by the number of studies is a novel idea to which he does not subscribe.

(65) In a discussion that is not found in his other July 21, 2001 report (but which makes up the next four paragraphs of this decision), Dr. Guidotti responds to concerns raised by the Board medical advisor as to the derivation of his estimate in his 1995 paper that the true risk of colon cancer among firefighters is probably on the order of 150 percent:

> I do not consider the summary, overall SMRs of published studies to be determinative, nor do I agree that conventional (let alone "quick and dirty") meta-analysis is very useful. My estimate derived from what I perceived to be the central tendency of those studies that do show an excess risk, because power considerations predictably result in a substantial number of studies showing "negative" results for "rare" (meaning infrequent and unlikely to affect the total, overall risk estimate) diseases. I do not believe that negative studies are as useful as positive studies in estimating the true risk, both because those studies that miss the risk because of power considerations carry no inherently useful information (because, after all, they missed it) and because the biases (classically misclassification bias) and limitations of the epidemiological method generally result in underestimate and a diluted risk estimate rather than an overestimate. I believe that there is no substitute for looking at the data in individual studies, weighing their strengths and weaknesses, and to the maximum extent possible determining the trend of the data within well-designed studies, accounting for possible confounding and dilution.
>
> [Power concerns whether a statistical test will detect an effect when there is an effect to be detected.]

(66) Dr. Guidotti comments that in data from his 1993 study there are trends not visible in the overall risk estimate for colorectal cancer of SMR 161. He comments those trends including consistency by era over the six decades of the study; when there is an excess, it is close to 150 or above. There is evidence for an exposure-response relationship when exposure opportunity (an index

weighing years of service by firefighting duty) is taken into consideration within certain latency groups. He notes this tends to fall off at longer latency periods which is exactly what one might expect from increased mortality at a younger age in a susceptible group. He comments that is one study, others must be considered.

(67) Dr Guidotti indicates that studies that are relatively strong and large have tended to show higher risk estimates and he cites Vena and Fiedler and Wende[12], Baris, and his own 1993 study.

(68) He considers that those studies that show no elevation in risk (Beaumont[13], Tornling[14], Demers[15], Aronson[16]) have tended to be smaller (the latter three), to be aberrant (Beaumont's risk estimates are low almost across the board compared to other studies) or equivocal in other ways (Tornling does show an excess for rectal cancer and Demers showed an excess when compared to police).

(69) He asserts these issues are not readily factored into a meta-analysis formula; they require judgement. He asserts meta-analysis does not address these issues and is, at best, a crude statistical tool. He notes that in epidemiology they are currently experiencing a re-evaluation of meta-analysis because of its conspicuous failure in predicting the result of clinical trials, for which it would seem to be ideally suited.

(70) Dr. Guidotti lists a number of concerns that he has with Dr. Howe's opinion. He considers a fatal flaw in the report that renders the opinion irrelevant is the focus on group data to the exclusion of individual characteristics:

> Apportionment in the individual case requires the weighing of individual risk profiles. Group data are relevant to a presumption or to epidemiological estimates of group risk but are only first-approximation estimates for any individual in the group.

(71) Dr. Howe's emphasis on the Hill criteria, intended to be broad guidelines for the acceptance of the epidemiological evidence, is in error:

[12] Wende K. A study of mortality among City of Buffalo fire fighters (an unpublished 1996 doctoral thesis which updated Vena and Fiedler).
[13] Beaumont, JJ et al. 1991. An epidemiologic study of cancer and other causes of mortality in San Francisco firefighters. American Journal of Industrial Medicine 19: 357-372.
[14] Tornling G et al. 1994. Mortality and Cancer incidence in Stockholm firefighters. American Journal of Industrial Medicine 25: 219-228.
[15] See footnote #8.
[16] Aronson, KJ. 1994. Mortality Among Fire Fighters in Metropolitan Toronto. American Journal of Industrial Medicine 26: 89-101.

> The issue is not whether firefighters as a group have a doubling of risk. It is whether an individual firefighter, in his personal experience, sustained a doubling of personal risk.

(72) Dr. Howe fails to take into consideration evidence for the strength of the known association as demonstrated in the Baris study. Dr. Howe's assertion that there is no clear pattern of a dose response relationship is incorrect as Dr. Howe's reworking of the data shows a 20 percent increase of risk after 20 years of employment.

(73) Dr. Howe uncritically selects studies for analysis. He places emphasis on Bates, a small study[17]. He ignores Burnett[18] which Dr. Guidotti acknowledges does not report colon cancer but reports among the highest relative risks in the literature for rectal cancer. Dr. Howe presents the findings of Tornling only for colon cancer and does not reveal that that study found one of the highest relative risks among the studies for rectal and anal cancer.

(74) Within studies Dr. Howe's evaluation is superficial. For example he includes only the overall risk in Beaumont and fails to note that an elevated rate of colon cancer was seen among San Francisco firefighters who had 10 to 19 years of service, a finding that is relevant to the worker.

(75) Another example of superficial evaluation is Dr. Howe's ignoring of a finding in Dr. Guidotti's 1993 article which suggests that after 20 years firefighters at intermediate levels of cumulative exposure experienced a highly significant elevated risk (3 deaths, 0.26 expected, SMR 1146, $p < .01$). (The risk refers to the category "Intestine and rectum.") Dr. Guidotti adds the comment that several other estimates associated with longer latency and intermediate high exposure opportunity are elevated, making it unlikely that this is a problem of multiple comparisons.

(76) Dr. Howe places undue reliance on studies of limited statistical power that predictably were insufficient to detect reliably a good association (Bates and Tornling are cited as examples). The Beaumont study, a relatively good one, reported a statistical power insufficient to reliably - at an 80 percent probability - detect a relative risk of lung cancer below 1.3. Colon cancer is less often fatal than lung cancer and therefore the power of studies using death certificates is much less.

[17] Bates, MN et al. 2001. Is Testicular Cancer an Occupational Disease of Fire Fighters? American Journal of Industrial Medicine 40:263-270.
[18] Burnett CA et al. 1994. Mortality among firefighters: A 27 State survey. American Journal of Industrial Medicine 26:81-833.

(77) Dr. Howe fails to mention that almost all the death certificate studies are subject to the limitations of epidemiological method, in particular misclassification bias and underreporting, that generally result in underestimates of the true risk. This is particularly a problem with studies of diseases that are not uniformly fatal (such as colon cancer), that do not follow the population beyond retirement or in which substantial numbers are lost to follow-up. (The Beaumont study could not trace 3 percent of subjects. In the United States, with its more comprehensive and centralized death certificate matching capabilities, those subjects lost to follow-up were usually dead. In the Beaumont study in which 39 percent of subjects were dead, this could mean a loss of up to 10 percent of total deaths.) These methodological problems were particularly significant for older studies and were not substantially overcome until more recent studies. Dr. Guidotti considers these issues are "compelling reasons for placing greater emphasis on 'positive' studies over those that do not demonstrate an elevated risk."

(78) Dr. Guidotti asserts that Dr. Howe is virtually silent on these limitations and their profound implications. Dr. Howe commented that the studies are likely of comparable quality but did not note that two were very small, one was based on an older cohort, and all but one lacked any individual exposure metric beyond length of service. Failure to recognize these limitations compromises the rough meta-analysis Dr. Howe conducted.

(79) Dr. Howe did not weight the studies (by inverse variance) which is a standard practice in formal meta-analysis. His analysis falls short of the customary standard of epidemiological practice for pooling. Aside from this, meta-analysis is quite capable of producing misleading results.

(80) In this report Dr. Guidotti adds the comment that Dr. Howe errs in his insistence on using the overall risk estimates in isolation without looking at subgroups within the population. Overall risk estimates are a crude estimate of the individual risk of a person in the population studied. A better estimate is that of the demographic subgroup to which the individual belongs. He cautions that as subgroups are carved out the statistical error around the estimate becomes greater, so that there is a limit to how meaningful risk estimates are for individual cells in the analysis. He comments that even so, in his 1993 study age-adjusted SMRs associated with several cells reflecting longer latencies and intermediate exposures exceed an SMR of 200. He comments that even assuming that the decades in which deaths were not observed represent statistical variation below the mean, rather than a "depletion of susceptible individuals" (a perfectly plausible alternative explanation), this is evidence for a real increase in risk.

(81) Dr. Howe errs in his statement that there are no human data on which to evaluate the supposition that firefighters sustain a degree of exposure consistent with an elevated risk. The exposure of firefighters to potentially

carcinogenic chemical exposures is demonstrable and measurable. His current report confuses the issue of measurement with the issue of exposure by demanding that such measurement be linked to a doubling of risk. There is no example in modern epidemiology of biomonitoring for combustion products that links lifetime cumulative biological measurement of exposure to the products of combustion with any specified level of risk for any outcome. The results of biomonitoring cannot be used in this way because biomonitoring is episodic and risk is cumulative. The requirement that this be demonstrated before an association is accepted sets the bar impossibly high. Because firefighters are not routinely monitored for such exposure the absence of individual measurements of exposure beyond the occupational history cannot be used as an argument against the claim.

(82) Dr. Howe errs in the statement that a multiplicative risk model merely multiplies risk for other factors which he implies are primary. Dr. Guidotti comments that if exposure arising out of occupation acts multiplicatively then, by the criterion of "more likely than not", it is only necessary to demonstrate that the effect of occupation acts on these other risk factors to achieve a doubling of risk compared to that experienced by another individual with the same risk profile, absent the occupational exposure, not a doubling compared to the general population as Dr. Howe argues in his report up to that statement. Dr. Guidotti considers Dr. Howe has vitiated his own argument regarding the assumed (but in fact unnecessary) requirement to demonstrate an absolute doubling of risk compared to the general population.

(83) Dr. Guidotti sums up his analysis of Dr. Howe's report as follows:

> In summary, I find the report by Dr. Howe to be selective, self-contradictory and deeply flawed. Neither his objective of refuting the existence of an association with occupation nor that of demonstrating that the apportionment risk does not apply to [the worker] are convincingly achieved. Dr. Howe dismisses out of hand the requirement to consider individualized risk in the context of an individual claim, which is the entire basis of adjudication.

(84) Dr. Guidotti offers his opinion on the individual claim.

(85) He notes that the worker was 63 at the time of his surgery for colon cancer. This is an age when this cancer often appears. He comments that it should be noted that such comparisons are age-adjusted; in other words, risks are being compared among persons of the worker's age, not of his age to younger firefighters.

(86) He comments that there is empirical evidence from his 1993 study that those who worked in intermediate exposure categories for up to 20 years and for 20 to 29 years do in fact experience a doubling of risk, as measured by SMRs: 231 (not significant) and 1146 ($p < 0.01$), respectively. Other studies have not broken the data down in such a way that this could be determined by latency and exposure opportunity (Table V of the 1993 study). This finding is less consistent in groups with longer latencies and greater exposure opportunity; increased risks are observed beyond this stratum but less often below it. It is not possible to place the worker into the framework of the 1993 study with precision. However the evidence suggests that for firefighters studied there exists a stratum of high risk in which the risk clearly exceeds a doubling for the group and the worker's firefighting experience and exposure exceeded that of that group.

(87) Dr. Guidotti observes the worker had a lower risk, absent his occupation, than would be expected for the average member of the general population. The risk imposed by his occupation, is approximated by the difference in the overall risk of firefighters less that of the general population. This attributable risk should then be compared to the approximated risk of someone like the worker who has less risk than the average member of the general population.

(88) Dr. Guidotti offers the following notable comments concerning causation:

> If the true risk of firefighters for colon cancer is somewhere in the vicinity of 1.2 to 1.5 (which I believe to be the true case because of the tendency for epidemiological studies to underestimate the true risk, the healthy worker effect and because of the guidance of better, larger studies) and his personal risk absent occupation were only half of the general population, his personal a priori risk would be on the order of 2.4 to 3.0, well above the doubling required by the criterion of "more likely than not". In fact, [the worker's] personal risk, absent his occupation, would only have to be 60 percent that of the general population (i.e., reduced by a little over a third by his healthy habits) to achieve this estimated doubling by the minimal [1.2], not the most likely, estimate of the additional risk imposed by his occupation. This is a robust argument, not sensitive to small assumptions in risk or elaborate statistical manipulation.

(89) Dr. Guidotti concludes by indicating it is more likely than not that the worker's colon cancer arose out of work in the course of his occupation as a firefighter.

Dr. Howe, 2002

(90) We note that the 2002 documents prepared by Dr. Howe submitted on this appeal are copies of the 2002 documents prepared by him and submitted on the other firefighter's appeal save the deletion of the other worker's name. That the 2002 reports of Dr. Howe are not particular to this claim creates some problems. It does not appear that Dr. Howe was asked to comment on the July 21, 2001 report of Dr. Guidotti relevant to this claim. Dr. Howe was asked to comment on Dr. Guidotti's other July 21, 2001 report, and as noted above, that other report from the other worker's claim file is not the same.

(91) In his letter Dr. Howe takes exception to Dr. Guidotti's comment that his objective was to refute the worker's claim. He asserts that with all his expert reports he always started with an unbiased position. He refers to two earlier reports prepared by him in which he did not exclude the possibility of a causal association with multiple myeloma and firefighting and in which he commented there was a possibility of a causal association between certain cancers and firefighting.

(92) In his report Dr. Howe responds to the comments of Dr. Guidotti.

(93) Dr. Howe asserts that the first critical step in evaluating the matter is to see whether the scientific epidemiologic evidence provides adequate scientific support that a causal relationship exists between occupation as a firefighter and increased risk of colon cancer. This first critical step is addressed by considering the epidemiologic evidence and not by considering the worker's individual characteristics apart from his occupation. If there is adequate evidence from the epidemiologic studies of an association between firefighting and risk of colon cancer the next step is to estimate the worker's individual relative risk which determines his "probability of causation." If this relative risk from firefighting multiplies the worker's other risks, for example, from diet, then these other risks cannot affect his probability of causation.

(94) Dr. Howe asserts that the assumption that any risk from firefighting multiplies risks from other sources is the usual model applied in epidemiology. Virtually all studies of firefighters, including that conducted by Dr. Guidotti, use the standardized morbidity or mortality ratio to report the results. Thus they are using a simple relative risk model for their own data since the use of the SMR implies that the relative risk is constant across strata of factors such as age, sex, and calendar time which is the exact equivalent of assuming a relative risk model. While individuals may vary in their susceptibility to cancer there is no way of deriving an individual relative risk for the worker from firefighting except from epidemiologic studies of firefighters. The procedure laid out in detail in Dr. Howe's report is the appropriate way of evaluating the worker's claim. It is

based on standard principles in epidemiology whereas Dr. Guidotti's approach appears to contradict the standard principles.

(95) Dr. Howe used the Hill criteria to evaluate the possible causality of any association between firefighting and the risk of colon cancer. This is an essential first step in deciding whether the relative risk has a value of 2.0 or greater if causality is established. Some of the criteria are relevant as to whether the relative risk is 2.0 or greater if causality is established. Dr. Howe maintains he applied the criteria correctly.

(96) Dr. Howe's report demonstrates why the Baris study does not display evidence of a dose response relationship. The suggestion that the study displays such evidence is clearly mistaken.

(97) Dr. Howe fails to understand Dr. Guidotti's reasoning with regard to the assertion that Dr. Howe selectively chooses the studies which he addresses. Dr. Howe addressed all the available epidemiologic studies without exception. The failure of the Beaumont study to include colon cancer was the reason he did not include that study. Cancers of colon and rectum are different diseases and risk factors for one cancer may not be risk factors for the other. He notes Dr. Guidotti is extremely selective in choosing studies to which to refer and Dr. Guidotti gives substantial weight to his 1993 study which, although well-designed and conducted, is only one study amongst many. Dr. Guidotti appears to rely heavily on three cases of cancer of colon and rectum in the 1993 study occurring amongst those working from 20 to 29 years as firefighters without much consideration being given to the far greater number of observed and expected cases of colon cancer which have been seen in many other studies and which do not provide support for the isolated observation.

(98) Concerning the possibility of "exhaustion of susceptibles", Dr. Howe observes that there is a far simpler, far more likely explanation for the pattern of risks seen in the 1993 Guidotti study: the contribution of chance. The p value quoted for the relative risks seen in those who worked 20 to 29 years as firefighters does not take into account the fact that many comparisons are made in the study and thus, the p value quoted is essentially meaningless because of multiple comparisons.

(99) Dr. Howe contends that claiming "exhaustion of susceptibles" after 29 years of firefighting is only speculative. For no other established or suspected carcinogen for colon cancer is such a phenomenon seen. Indeed, colon cancer incidence increases with age essentially for the whole of life. He contends that if one believes Dr. Guidotti's theory there would be a specific carcinogen to which firefighters were exposed for colon cancer and a tiny fraction of the population would be susceptible to this carcinogen and all of this fraction would get colon cancer after completing 29 years of firefighting. For Dr. Howe the

proposition makes no sense and the alternative explanation, chance, is far more reasonable and far more likely.

(100) Concerning the assertion that he relies too much on low-power studies, Dr. Howe indicates he relies on all the studies, not just low-power ones, in arriving at his conclusion. He contends the overall combined results take each study into account with appropriate consideration of the precision or power of the study. The important measure is the overall confidence interval as given in his report.

(101) Concerning the contention that he ignores limitations of the studies and should give greater credence to those with positive results as compared to those with negative or null results, Dr. Howe comments that he sees no evidence of any bias in the studies in general which would result in any association going one way or the other. He indicates the healthy worker effect to which Dr. Guidotti refers could not account for the type of adjustment he is proposing. The healthy worker effect is less important for cancer than for other causes of death as has been shown empirically many times. More importantly, the effect decreases with time since employment, typically exhausting itself ten years after employment. Thus the reduction in the estimated SMR is typically either very small or absent in long-term cohort studies.

(102) Dr. Howe notes Dr. Guidotti provides no evidence for his assumption that those lost to follow-up are probably dead. He notes one may equally speculate that those who died are usually registered in some form, whereas those who were lost to follow-up and are still alive, probably represent those who migrate from the study area without any corresponding registration. He says this is entirely speculative and cannot be treated as providing evidence one way or the other. Even if one assumes the extreme hypothesis of a 10 percent loss in deaths, this would only increase the overall SMRs with respect to colon cancer for the incidence cohort studies to 1.00 and the mortality cohort studies to 1.28. The interpretation of the studies would remain essentially unchanged.

(103) Dr. Howe finds the statement by Dr. Guidotti that one should give greater weight to positive studies than negative and null studies "quite extraordinary":

> To take this position without considering the details of any specific study inevitably produces a strong bias towards finding a positive association without considering the evidence. The essence of assessing evidence is to take an unbiased position and ***not*** start with prior assumptions of the existence of an association **before** considering the evidence.
>
> [emphasis in original]

(104) Concerning the contention that he does not consider the precision of individual study risk estimates when combining the data for overall risk, Dr. Howe asserts Dr. Guidotti is simply and demonstrably wrong. He contends that adding up the total observed and total expected number across studies and dividing these totals to provide an overall SMR gives what is called the maximum likelihood estimate for such a summary. It is exactly equivalent to estimating the SMR for each individual study. He contends that the following example illustrates that this procedure takes into account individual study precision. Consider two studies, the first with an observed incidence of 3 and an expected incidence of .26 and the second with an observed incidence of 3 and an expected incidence of 3. The pooled SMR has a value of 6/3.26, that is, 1.8. If the second study had an observed of 100 and an expected of 100, the pooled SMR would have a value of 103/100.26, that is, 1.0. Thus the second study, which has far greater precision than the first study, essentially wipes out the results of the first study.

(105) Regarding the issue of exposure to chemicals in firefighting, Dr. Howe comments that compounds that are carcinogenic and mutagenic are found at the scene of fires. He sees no evidence that the amount of exposure is sufficient to lead to a measurable increase in risk. Thus, if one found in an epidemiologic study evidence of increased risk the potential exposure to carcinogens would clearly add biological plausibility to such an association. However, given the overall lack of association for colon cancer, the presence of such carcinogens does not help one way or the other in resolving the issue under consideration.

Reasons and Findings

(106) We have considered the helpful submissions from the worker's and employer's counsel. Essentially the submissions argue the strengths and weaknesses of the medical reports advanced to support each position. The worker seeks to have the report of Dr. Guidotti preferred, while the employer relies on the report of Dr. Howe. Since the issue before us turns mainly on reports of the experts, our comments below focus on those documents.

(107) We do not consider that the opinion of the Board medical advisor features prominently in our analysis. We consider that he does not establish his assertion that Dr. Guidotti's 1995 review article failed to include all the relevant studies. We accept that Dr. Guidotti did review the 1992 Demers study[19] (see the footnotes in his 1995 article) and was familiar with the Aronson study, albeit through a document submitted to the IDSP under the married name L'Abbe (see the footnotes to the 1995 article and the August 13, 2001 submission). The Board medical advisor posits a form of meta-analysis not recognized in the

[19] Demers PA et al. 1992. Mortality among firefighters from three Northwestern United States Cities. British Journal of Industrial Medicine 49:664-670.

literature. His review was mainly confined to a critique of Dr. Guidotti's 1995 article rather than a canvassing of the literature.

Admissibility of Dr. Howe's October 2002 documents

(108) Dr. Guidotti's comments concerning Dr. Howe's analysis of the literature were more in the form of a rebuttal submission to which a respondent, in this case the employer, normally is not permitted a response. However Dr. Guidotti's comments concerning the worker's case did introduce new evidence to which a respondent would normally be given an opportunity to respond. We consider that strictly speaking the employer should only have provided a report from Dr. Howe concerning Dr. Guidotti's opinion as to the cause of the worker's cancer.

(109) The WCAT is not bound by the formal rules of evidence and we consider it appropriate to take into account the complete contents of Dr. Howe's October 2002 documents. We consider it would be unduly technical to determine that we will only take into account those parts of Dr. Howe's opinion relevant to Dr. Guidotti's opinion as to the cause of the worker's cancer. The worker has had the opportunity to make submissions in response to the contents of Dr. Howe's materials.

Firefighting

(110) We accept that firefighters are exposed to mutagenic and carcinogenic products in the course of their employment. The International Agency for Research on Cancer (IARC) website (http://www.iarc.fr/) lists all the substances that have been reviewed and contains IARC's reports about them. As noted in the IDSP report, asbestos (found in building materials) is the only Group I carcinogen that is related to colon cancer.

(111) The Board's schedule B also recognizes the association between gastro-intestinal cancer including cancer of the colon and rectum and asbestos. Schedule B provides a presumption in favour of causation regarding gastro-intestinal cancer where there has been 20 years of continuous exposure to asbestos dust and such exposure represents or is a manifestation of the major component of the occupational activity in which it occurred. In this case the worker did not have 20 years of continuous exposure to asbestos dust and, therefore the presumption in favor of accepting the claim does not apply.

(112) There is nevertheless recognition in schedule B for an association between colon cancer and exposure to asbestos dust. This is consistent with pathological evidence that demonstrates that asbestos fibers penetrate the walls of the gastrointestinal tract, reach end points in various abdominal organs, and can be associated with tumors in those organs. We note at this juncture

that the nature of asbestos exposure for firefighters may differ somewhat from more conventional exposure that generally involves airborne friable asbestos dust**.** Because firefighters' exposure would often come during the breakdown phase of the fire when the asbestos insulation has been moistened, it may differ from occupations that have exposure to dry friable asbestos dust. While exposure to asbestos insulation is a common occurrence for firefighters, it does not constitute a major component of the occupational activity.

(113) While the presumption in subsection 6(3) of the Act does not apply in this case it is still necessary to consider whether the evidence of a relationship between asbestos and colon cancer exists on a balance of possibilities under subsection 6(1) of the Act. As well, is the colon cancer due to any other exposure that the worker had in his employment as a firefighter? (See item #26.22 of the *Rehabilitation Services and Claims Manual* - the Manual.)

(114) Diesel exhaust is a probable carcinogen and while there is no direct evidence to link that exhaust to colon cancer in firefighters, exposure to polycyclic aromatic hydrocarbons (PAHs), a constituent of diesel fumes, is related to colon cancer in coke oven workers according to the IDSP report. The IDSP cited a 1971 study in support. The employer's September 24, 1999 submission to the Review Board contended the evidence did not support a finding that occupational exposure to PAHs could lead to colon cancer and it referred to testimony in earlier Review Board appeals that PAHs were associated with lung and skin cancer. IARC's volume 46 (1989) which reviews diesel exhaust and indicates it is a probable carcinogen (Group 2A) contains no reference to colon cancer. Lung and bladder cancers are noted in connection with the human data.

(115) The IDSP report indicates formaldehyde and acrylonitrile are also probable carcinogens and would be present in building materials. In the employer's September 24, 1999 submission to the Review Board the employer noted earlier testimony that formaldehyde was a known animal carcinogen but was not a documented human carcinogen and submitted that the burning of formaldehyde was not known to create carcinogenic products. We note that IARC volume 62 (1995), a revision of the 1987 IARC report available to the IDSP, confirms formaldehyde is a probable carcinogen but makes no reference to colon cancer. It does refer to cancers such as those affecting the nasopharyngeal area. IARC's volume 71 (1999) report which reviewed acrylonitrile (many years after the 1987 report relied on by the IDSP) now classifies it as only a possible carcinogen (group 2B) and makes no reference to colon cancer. In fact, it asserts there is inadequate evidence in humans for the carcinogenicity of acrylonitrile.

(116) We appreciate that the multiplicity and diversity of firefighter exposures and the possible interactive effect of groups of agents present epidemiological difficulties regarding patterns of exposures. We accept that when looking at questions of firefighters and cancers it is appropriate to be guided by the number of years of firefighting a worker was engaged in. While evidence as to a particular worker's exposure to specific chemicals would be desirable we appreciate that in most cases such evidence is not available. We agree with the comments of the panel in Appeal Division *Decision #93-0163* that "it is not possible or reasonable to insist that the worker or his representative identify the precise exposure to a specific chemical in order to show causation." The number of years of employment is the best proxy for exposure risk that we have. In most studies the years of employment are often the only measure of exposure available. The Baris study from 2001 does refer to the number of runs and exposure to diesel trucks but it is in the minority.

Epidemiology

(117) Cancer cases are rarely resolved by opinions that merely canvass the case of a particular worker. In most cases epidemiologic evidence has been gathered and analyzed and that evidence provides a relevant background for any opinion specific to the particular worker. The increasing number of cases involving such evidence appears to have been one of the main impetuses for the issuance of the Board's Protocol noted earlier.

(118) We note the following comments from Appeal Division *Decision #93-0163* which we consider are still applicable to many cancer cases and the associated epidemiological issues:

> In considering the standard of proof to be applied, it is important to recognize the limitations in scientific and medical knowledge relating to cancer and its causes. Cancer is a disease whose causes are incompletely understood. Dr. C stated that although there are a number of known causes of cancer in terms of specific agents which produce cancer, in the majority of cases a specific cause in a specific case cannot be identified. Because of this uncertainty, epidemiology provides the most important *generalized* evidence of whether there is an association between a particular condition existing in the environment, or population, and a particular disease or condition of health.

(119) We concur with the Appeal Division panel in *Decision #93-0163* that epidemiologic evidence informs us but does not determine the matter before us:

> However, epidemiological evidence, like other generalized evidence, deals with categories of occurrences rather than

particular individual occurrences. Epidemiology cannot determine which particular factor caused a particular person's disease, but only what factors are statistically associated with the occurrence of the disease in groups of people. As stated by counsel for the employer:

> It [epidemiology] presents conclusions based on the average person within the particular population. Once this "average" result is obtained, the information can be used to assess the potential risk which an individual within the particular population may face with respect to developing a certain disease.

… Therefore, epidemiology's usefulness to particular claimants relates more directly to issues of risk than of actual occurrence. Epidemiological studies cannot prove or disprove causation in an individual case. Proof of excess incidence of a certain cancer in a certain defined occupational group is not "proof" that the disease of the individual claimant, who belongs to that group, was work caused. Rather, such evidence is supportive of an increased likelihood in an individual case which can be weighed along with other evidence. On the other hand, the fact that there is no general, or a very small, excess does not "prove" that the individual's disease was not work caused. Again, it is relevant evidence to be considered along with all the other available evidence when assessing the possibilities and probability that a particular worker's cancer was caused or contributed to by his work.

Relative risk for firefighters and colon cancer

(120) We consider that there is a difference of opinion between Dr. Guidotti and Dr. Howe. While counsel have made submissions on the issue, we do not consider that Dr. Guidotti's criticisms amount to an uncalled for personal attack or that there is some other basis for his disagreement with Dr. Howe. Further, we do not consider that Dr. Howe's response involves a personal attack.

(121) Dr. Guidotti indicates that the true relative risk for firefighters is between 1.2 and 1.5. That can be compared with the figure of 1.5 assigned in his 1995 review. Clearly, those figures fall below 2.0. Dr. Guidotti's 2002 report and 1995 review also express a preference for positive study results. On the other hand Dr. Howe has tendered a lower pooled figure for all studies regardless of their outcome.

(122) We do not consider that the evidence establishes that the biases toward the null association are necessarily stronger than biases away from the null such that we should *automatically* attach greater weight to studies whose positive results may have overcome the biases toward the null. However, we do appreciate that the best designed studies with sufficient size to have statistical power merit particular attention. There are distinctions to be made among (1) studies that find a statistically significant association of a positive relationship, (2) studies that show a positive association that is not statistically significant, (3) studies that show a negative association that is not statistically significant, and (4) studies that show a negative association that is statistically significant. None of the reported studies show a negative association that is statistically significant (i.e. with a confidence interval that does not include 1.0). However there are two studies (Vena and Fiedler, Baris) that show a statistically significant positive relationship between the occupation of firefighting and colon cancer. These two studies support the proposition that there is an association between the occupation of firefighting and colon cancer that is beyond a chance association. As pointed out in Dr. Howe's analysis there are three mortality studies (Howe, Guidotti, and Bates) that have a positive association with a confidence interval that includes 1.0 which are suggestive of an association but do not exclude a chance association. One incidence study (Demers) also falls into this positive association group that is not statistically significant. There are four negative mortality studies (Beaumont, Demers, Aronson and Tornling) and two incidence studies (Tornling and Bates) that suggest no association but are not statistically significant and do not exclude the possibility of a positive association. Again, there are no studies that demonstrate no association at a statistically significant level (with a confidence interval that does not include 1.0)

(123) As an example of one of the concerns that might support the extra weighing of studies with positive results, it is true that as asserted by Dr. Guidotti that follow-up may not capture all the firefighters of interest and if they have died because of cancer the incidence of cancer may be underestimated. However we consider the possibility that subjects merely moved from the jurisdiction to be equally plausible. We do not consider that we can assume that the subjects died and the death was due to cancer and their deaths are not ascertainable through a registry system. As for biases away from the null association there is the question of publication bias which suggests that there is a bias toward publication of studies that establish a relationship between a condition and an exposure. If there is such a bias then the large number of studies that have failed to establish relative risks well above 1.0 with 95 percent confidence intervals that do not include 1.0 might provide some weight against being persuaded by the studies which point to a statistically significant positive relationship.

(124) We consider in the absence of a demonstrable concern with a study and its resulting relative risk that the results of all studies should be given some weight. There may be cases where, owing to concerns with design, a study is not the equal of a larger better conducted study but that concern would apply to any study, regardless of whether it produced positive results or inconclusive or negative results. Thus the focus perhaps should be on design although magnitude may also be of significance. In that regard we note that the Baris study is considered one of the larger studies with statistical power that is well designed and allows for subgroup analysis.

(125) Regarding concerns that may tend to skew results, we accept that there may be a healthy worker effect that pushes results toward the null. Th Protocol notes that the healthy worker effect often creates an approximately 10 percent to 20 percent difference in the ratio of observed to expected deaths. Yet we do not consider that the evidence cited establishes that it is especially compelling regarding cancer generally. The 1995 Guidotti review noted that the healthy worker effect did not operate as strongly for cancer as it did for cardiovascular disease. There is the question of whether there is an extra healthy worker effect with respect to colon cancer based on the fact that physical activity level is considered one of the most important factors associated with colon cancer. The available data do not address that question in a definitive way, but the recognition that high physical activity level is considered to lower the risk of colon cancer merits consideration, given the relative fitness and activity level of firefighters.

(126) The healthy worker effect has been a consistent finding in virtually all mortality studies of firefighters (e.g. see Bates). How big is the healthy worker effect? Bates notes that relative risk estimates for all cause mortality have generally been in the region of 0.80-0.95. In the Bates study the mortality rate estimates ranged below 0.70 (which the authors attributed to the stringent health and fitness entry criteria for firefighters in New Zealand), while the Baris study for Philadelphia had a 0.96 rate for all causes of death.

(127) Dr. Howe, based on his 1989 and 1992 reviews, considered that the effect was on the order of 8 percent as his literature summary at that time had established an overall relative risk of 0.92 in firefighters for all cancers combined and posited that the effect had prevented the risk from equaling 1.0. He applies that same 8 percent figure in his 2001 and 2002 reports. We note that he did not expressly advise in those reports whether he assessed if the magnitude of the effect should be revised in light of intervening studies. However, we consider that his earlier reports at least provided a stronger evidential basis for the magnitude of the effect as opposed to the report Dr. Guidotti who does not identify a specific healthy worker effect but includes it as part of his range of 1.2 to 1.5.

(128) We note that the 1993 Guidotti study posited that one interpretation of the observation that the overall firefighter SMR came close to that of the general population is that the absence of a healthy worker effect suggested a hidden elevation in risk and was an indication of excess risk compared to other employed groups. Dr. Guidotti did not determine that that was the only interpretation. We note that another explanation could simply be that there is no significant healthy worker effect regarding cancers generally and firefighters. That might not exclude the existence of a healthy worker effect associated with activity and colon cancers.

Meta-analysis

(129) Reference to Dr. Howe's pooling of the studies to obtain a figure for the healthy worker effect raises the question of the propriety of his pooling the studies to obtain a relative risk. The 1995 Guidotti review comments that attempts to pool cannot effectively compensate for the limitations in most studies. We note that at page 453 of the Protocol meta-analysis involving a pooling of the results from various studies was considered appropriate.

(130) That there are concerns with the use of meta-analysis in connection with observational studies in epidemiology is obvious from recent publications canvassing the issue[20]. Stroup et. al. caution that when combining observational studies heterogeneity (variation) in populations, designs, and outcomes is expected and when heterogeneity of outcomes is problematic "…a single summary measure may well be inappropriate" (p. 2010). The authors also point out that "the extreme diversity of study designs and populations in epidemiology makes the interpretation of simple summaries problematic, at best."

(131) A meta-analysis of asbestos exposure and gastrointestinal cancer by Frumkin and Berlin[21] identified six major problem areas in pooling various study results: exposure levels, choice of comparison group, latency, specification of end points, ascertainment of diagnosis, and age distribution of the test population. Frumkin and Berlin used a sophisticated 'random–effects model' which allowed for a separate SMR for each cohort. They observed that because of variation in population age structures, fiber type, industry, analytic strategy, etc. each population would be expected to yield a different SMR.

(132) While we do not consider that concerns over the reliability of individual studies should be ignored, we consider that pooling may be appropriate as a first step in the analysis to provide a broad overview of the available data.

[20] See Stroup DF et al. 2000. Meta-Analysis of Observational Studies: A Proposal for Reporting. Journal of the American Medical Association (283) 2008-2012. See also Egger, M et al. 1998. Spurious precision? Meta-analysis of observational studies. British Medical Journal (316) 140-144.
[21] Frumkin, H and Berlin J. 1988. Asbestos Exposure and Gastrointestinal Malignancy Review and Meta-analysis. American Journal of Industrial Medicine 14: 79-95

(133) Dr. Guidotti indicates that if pooling is done weighting of the studies by inverse variance is the "customary standard" of epidemiological practice for pooling. The worker contends that Dr. Howe was non-responsive to that criticism. We note that Dr. Howe does not directly assert that his technique of adding up observed and expected cancers from all studies and calculating the overall SMR is the customary standard. He does indicate that the calculation does give the maximum likelihood estimate and that is an affirmation of the initial calculation.

(134) We note Dr. Howe's assertion in his May 15, 1992 report in which he defends the pooling of data. He comments that pooling SMRs for all the studies of adequate quality represents the "single best procedure" that can be used to assess the likelihood of a causal association. He observes that the cohort studies of firefighters are similar in design and execution and it seemed to him that the types of exposure received by firefighters is likely to be similar in the North American situation where the bulk of the studies were conducted. He asserted there was really no sensible alternative to such pooling. He commented that it was important to consider the variability in SMRs of individual studies as compared to the average as a test of consistency.

(135) As noted by the worker, in his 2001 and 2002 reports Dr. Howe did not name any of the textbooks which he indicated would clarify the matter. Thus his response is somewhat lacking. However aside from any shortcoming in Dr. Howe's response is the significant fact that Dr. Guidotti does not provide a figure for pooling using inverse variance. We do not know whether meta-analysis with inverse variance would produce a figure significantly different from the one produced by Dr. Howe. Dr. Guidotti's criticism, in the absence of such a calculation, is not persuasive.

(136) The pooled result obtained by Dr. Howe is not especially compelling. Regardless of whether the pooled result concerns incidence or mortality or the two combined, the figure finishes below 1.2. As noted in the Protocol at page 445, a relative risk of 1.4 or 1.5 is, by itself, not very impressive because there are so many confounding variables. The Protocol goes on however to note two qualifications regarding the overall relative risk. An intermediate relative risk can become more 'convincing' when a dose response relationship is indicated, and where a relative risk is below 2.0 the "attributable risk technique" can be used to provide a measure of the probability that an individual case is work-related.

(137) We note that Dr. Howe's pooled results are very close to the SMR figure of 1.2 found in Appeal Division *Decision #2000-1409,* a case involving colon cancer and a forest firefighter. The panel cited a report of Dr. D who reviewed seven mortality studies of urban firefighters (there are no studies for forest firefighters) and obtained that figure. He also determined the pooled risk for three cancer incidence studies was 1.1. (The panel noted that Dr. D was the lead author of a

1994 incidence study dealing with Seattle and Tacoma firefighters (noted at footnote #8) and a 1992 mortality study dealing with Seattle/Portland/Tacoma firefighters[22].)

(138) Dr. Guidotti considers that the pooled figure calculated by Dr. Howe does not take into account findings concerning cancer of the rectum such as those found in Tornling and Burnett. Yet this is a case of colon cancer.

(139) Dr. Howe comments that the two cancers are different and the risk factors for one cancer may not be the same for the other cancer. In Appeal Division *Decision #00-1409* the panel noted Dr. D's observation that the risk factors can be different for colon and rectal cancer. We note that, as established earlier, Schedule B's presumption regarding gastro-intestinal cancer and asbestos exposure includes colon and rectum cancer in the same presumption. That suggests it is considered that colon and rectal cancer share a similar disease process, at least with regard to asbestos exposure. We note that presumption does not say anything about colon and rectum cancer and any process concerning other exposures such as those involving PAHs.

(140) We also note the comment in the IDSP report that while there was a probable connection between colon cancer and firefighting there was not a probable connection between rectal cancer and the occupation of firefighter. We also note different rates for colon and rectal cancer in the Golden article discussed earlier. In the Beaumont study we note that the rates for colon cancer and rectal cancer measured in relation to length of employment do not parallel each other closely. If the cancers at the two sites are part of the same process why would there be different rates?

(141) That the overwhelming number of studies provide separate figures for colon and rectal cancer (even as recent as the Baris and Bates studies of 2001) strongly suggests that the data were gathered on the assumption that the two cancers may not be part of one overall cancer process. Even aside from whatever belief may have fueled the separation of the data is the fact that the data are separate, and we do not consider it would be appropriate to combine the two.

(142) Regarding Dr. Guidotti's assertion that Dr. Howe's evaluation within studies was superficial, we note Dr. Howe does not respond directly to Dr. Guidotti's comment regarding the Beaumont study but he does address Dr. Guidotti's discussion of the 1993 Guidotti study and the exhaustion of susceptibles which will be discussed below.

[22] Demers, P. et al. 1992. Mortality among firefighters from three northwestern United States cities. British Journal of Industrial Medicine. 49(9):664-70

(143) Dr. Guidotti's assertion that the Bates study is emphasized is confusing. Dr. Howe included the results of the study in his pooling of the data. There is no suggestion that Dr. Howe placed any extra weight on that study. It may be that owing to its small size Dr. Guidotti considers that its inclusion in the collection of studies to be pooled with other larger studies means that it will be featured as prominently as those larger studies. Yet we do not consider that is the case. The precision associated with any of the larger studies is not undervalued via the pooling process as illustrated by the example in Dr. Howe's October 2002 report noted above.

(144) We are cognizant that any meta-analysis should not overlook any significant concerns associated with individual studies. However, Dr. Guidotti's observations that Dr. Howe did not take into account that two of the studies were very small, one was based on an older cohort, and all but one lack any individual exposure metric beyond length of service, are not compelling. Those limitations are obvious to any reviewer of individual studies. Dr. Guidotti does not outline any significant design flaw that would tend to support a significant discounting of the results of various studies. We are aware from his comments noted above that he considers the results of some of the studies problematic. We question whether Dr. Howe erred when he confirmed that he did not see real limitations in the studies.

(145) We are aware that studies of firefighters are not uniform in the sense that they may differ in the nationality of the firefighters, the period during which they were exposed, the types of exposure involved, and the type and usage of protective equipment like self contained breathing apparatus, to name a few. Thus pooled data cannot be accepted uncritically, since they are based on the assumption that all firefighters have a relatively common exposure. This assumption likely holds for common, routine fires, but is open to question where there are unusual or atypical fires.

(146) Demers in his 1994 article, for example notes that most fires involve exposure to PAHs, but exposure to vinyl chloride and acrylonitrile may happen only under certain conditions. Interestingly, Demers used "duration of fire combat employment" as an exposure measure, rather than the more common "years of employment," but found that even that more specific measure may not be adequate for measuring exposures to substances not present at all fires. He reasoned that exposure may vary substantially between and within fires due to the composition of the material being burned, the temperature of the fire, and the availability of oxygen. He concluded: "Thus the lack of association seen between duration or fire combat employment and various outcomes in this study may in part be due to the use of a poor surrogate for exposure." Aronson points out that very different exposures can occur for two firefighters at the same fire even if they are side by side. The uniform exposure assumption inevitably dilutes the variability in risk associated atypical exposures.

(147) We further note Dr. Guidotti's comment in his 1995 review that the work of firefighters is more consistent regarding exposure than most occupations. As noted earlier, we consider that there may be considerable variation in the exposures of firefighters in different study groups. Dr. Guidotti, like many other researchers, notes the need for an exposure index that better reflects personal exposure, but indicates that "exposure opportunities" in a given job should become similar over time.

(148) While Dr. Howe indicates that the assessment process stops once one is not satisfied that the studies consistently demonstrate a positive association from which one can exclude the likely contribution of chance, we consider it appropriate to proceed further and assess the data using the Hill criteria.

(149) *The Reference Guide on Epidemiology* noted earlier (see footnote #3) contains comments on the role of statistical significance testing in judicial consideration of epidemiologic studies, which are of assistance in interpreting and applying the large number of epidemiologic studies in this case. The *Guide* states, at p. 359:

> There is some controversy among epidemiologists and biostatisticians about the appropriate role of significance testing. To the strictest significance testers, any study whose *p*-value is not less than the level chosen for statistical significance should be rejected as inadequate to disprove the null hypothesis. Others are critical of using strict significance testing, which rejects all studies with an observed *p*-value below that specified level. Epidemiologic studies have become increasingly sophisticated in addressing the issue of random error and examining the data from studies to ascertain what information they may provide about the relationship between an agent and a disease, without the rejection of all studies that are not statistically significant.
>
> [footnotes omitted]

(150) In a footnote to the first sentence in the above quote, the authors note that similar controversy exists among the courts that have confronted the issue of whether statistically significant studies are required to satisfy the burden of production (whether it will be admissible in court). A number of courts in the United States have required that a study be statistically significant before it can be relied on by an expert, while others appear more cautious about using significance testing as a necessary condition, instead recognizing that the likelihood of random errors is important in determining the probative value of a study. We consider the latter approach to be a reasonable one.

Applying the Hill criteria

(151) A critical analysis of epidemiologic studies includes an analysis of causation based on criteria generally accepted by epidemiologists as factors useful in making judgments about causation. These criteria were initially developed by the U.S. Surgeon General in 1964, to be used to assess the relationship between smoking and lung cancer, and they were expanded upon by A. Bradford Hill in 1965[23]. They are listed by Hill as follows:

> Strength of the association
> Consistency
> Specificity of the association
> Temporal relationship
> Dose response relationship
> Biological plausibility
> Coherence
> Experiment
> Analogy

(152) Similar criteria are set out in the Board's Protocol.

(153) The original presentation at which Hill posited these factors indicated that they were applied when there was a clear-cut association between two variables that was not due to chance and one wanted to consider aspects of the association before deciding that the most likely interpretation of the association was causation. We do not consider that Dr. Howe tortured the method; he did not apply it to the specific question of whether the association was of a given magnitude. He certainly kept the size of the relative risk in mind throughout his opinions (and some of the factors are relevant to whether the relative risk is 2.0 or greater) but he reviewed the Hill criteria to assess the broader question of whether a relative risk of above 1.0 denoted causation.

(154) It is true, as pointed out by Dr. Guidotti, that the ultimate question is whether an individual firefighter in his personal experience has a doubling of risk. We do not consider that Dr. Guidotti "put the cart before the horse" as asserted by the employer. When Dr. Guidotti asserted that the issue was not whether firefighters as a group have a doubling of risk, we do not consider that he was contending that evidence concerning firefighters as a group was irrelevant to the case before us or that he was essentially assuming a link between the occupation and colon cancer. His report did evaluate the literature. The case before us

[23] A Bradford Hill, The Environment and Disease: Association or Causation? 58 Proceedings of the Royal Society of Medicine. 295. Hill acknowledged that his factors could only serve to assist in the inferential process: "None of my nine viewpoints can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a *sine qua non*."

does concern a particular firefighter and we must decide his entitlement. However, assessing the individual risk cannot be divorced from an assessment of the risk attached to firefighters as a group.

(155) We consider that, in the case before us, the critical factors are strength of association, consistency, and dose response relationship and that those factors are not satisfied when applied to the firefighter population in general.

(156) As indicated above, pooling of the data reveals a strength of association well below 2.0. We appreciate that there are two studies that show a statistically significant positive association between firefighting and colon cancer. The Baris study involved one of the most comprehensive study designs that included sufficient numbers to achieve statistical significance at both the cohort level and also with some subgroup analysis. There are also four other positive studies that do not achieve statistical significance. There are also six studies that indicate a negative association, but none of these achieve statistical significance with confidence intervals that do not include 1.0. These data provide some support for a positive association for firefighters as a whole, but fall significantly short of a doubling of risk for all firefighters.

(157) As for consistency, we accept Dr. Howe's observations that the studies overall are not consistent with a common relative risk. As noted in the meta-analysis literature heterogeneity of outcomes may result from variation in exposure between different populations. We note that the studies vary widely by location with four from different parts of the US; three from different parts of Canada, and one from New Zealand and one from Sweden. We consider it significant that Dr. Guidotti does not contend there is consistency.

(158) As for a dose response relationship, we consider it significant that according to Dr. Howe only one of the six studies (Vena and Fiedler) has a statistically-significant test for the existence of the dose response relationship. The issue of dose response relies to a large extent on the precision of the exposure measure. An exposure that quantifies the dose for individual workers is more likely to demonstrate a dose response relationship where one exists, than a proxy measure of exposure that is non-specific.

(159) Dr. Guidotti comments that his 1993 study showed a doubling of risk for firefighters who worked in intermediate exposure categories for up to 20 years (SMR 231 not significant) and for 20 to 29 years (SMR 1146 with $p < 0.01$). He comments other published studies have not broken the data down in such a way that this could be determined by latency and exposure opportunity. Dr. Howe observes that there is a far simpler explanation of the pattern of risks seen in the 1993 study: chance. He notes that the p value quoted for the relative risks seen in those who worked 20 to 29 years does not take into account the fact that many comparisons are made in the study and that the p value is essentially meaningless because of multiple comparisons. Even aside

from that comment we note that one study cannot be determinative of the issue before us especially when the SMR arose out of three observed cancers with only 0.26 expected. Those figures play a very small role in the pooled data. As well the figures concern cancer of the colon and rectum; they are not figures solely related to colon cancer. We note that there is no information as to the breakdown of the cancers within that category. It may be that there were three rectal cancers or even three colon cancers.

(160) The results of the Baris study contain some suggestion of a dose response relationship but a review of the study shows that the evidence is somewhat problematic. The overall SMR in that study of 1.51 for firefighters and colon cancer rises to 1.68 with a 95 percent confidence interval of 1.17-2.40 for more than 20 years employment. Yet the SMR for firefighters with *less* than nine years is 1.78 with a 95 percent confidence interval of 1.12-2.82. A higher ratio associated with shorter employment raises concerns. The higher ratio may be due to some susceptibility factor or chance. The SMR for 10 to 19 years was 1.11 with a 95 percent confidence interval of 0.68-1.18. The figures in the Baris study do not show a steadily increasing statistically significant SMR associated with duration of employment. There was an increase in relative risk from the 10-20 year category to the 20 year plus category, and that is some evidence of a dose response, albeit it is not determinative of the issue.

(161) Another aspect of the Baris study which is relevant to a dose response relationship is the information concerning any relationship between the number of runs undertaken by firefighters and colon cancer. The Baris study points out that the number of runs does not directly capture attendances at fires because a run might be a trip to a non-fire event. However, we consider that, even aside from that caveat, a larger number of runs would likely include a larger number of attendances at fires. The SMR for the low number of runs category was 1.93 and it increased to 2.22 for the medium category. Both confidence intervals for the two SMRs did not include 1.0, and thus were statistically significant. The SMR of 1.22 for the high category of runs had a 95 percent confidence interval of 0.64-2.35.

(162) The Baris study found that the *type of run* produced statistically significant association for several types of cancer including colon cancer. Firefighters who worked only in engine companies (first-in units involved with the most frequent and acute types of exposure) had a statistically significant SMR of 1.94 (confidence interval of 1.38 – 2.73) for colon cancer. This finding may illustrate the issue of the adequacy of an exposure measure discussed in the literature. Example seven in the Protocol (p. 461) illustrates the difficulty in identifying the effect of unusual or atypical exposures that are experienced by a minority of the study population. In that example a large study of asbestos workers revealed no particular elevated risk for respiratory cancer (SMR of 1.08) over a 40 year

period. However, when the researchers controlled for exposure to crocidolite (a form of asbestos that has a strong tendency to cause mesothelioma), that was used for only a brief period in the production process, the workers with exposure to crocidolite had an estimated relative risk of 49.0 – a very high figure. It is necessary, therefore to consider the question of whether the exposure measure of years of employment is sufficiently sensitive to pick up unusual or atypical exposures that may be related to unusual outcomes such as relatively rare forms of cancer. In this respect studies with sufficient statistical power that identify positive findings may merit special consideration to determine whether they have identified a significant association that is otherwise diluted by inclusion of study subjects without the atypical exposure.

(163) We accept that there may be some individuals who are especially susceptible to occupational carcinogens, yet the exhaustion of susceptibles seems inconsistent in the Beaumont study in that the SMR drops when comparing the category of 10 to 19 years with 20 to 29 years and then rises again for the category of over 30 years. If the susceptibles succumbed in years 20 to 29 what explains the increase in the longer category of 30 years plus? We note in passing that Dr. Guidotti's comment that the Beaumont study showed a risk for rectal cancer that remained elevated over time for firefighters with ten or more years of service appears to be inconsistent with the idea that rectal cancer and colon cancer are part of the same cancer process. As noted earlier, one would think that if they are part of the same disease process they would have a similar profile in the data.

(164) We accept that when the study results are pooled there is some suggestion of a dose response relationship. Dr. Howe's assertion that there is essentially no evidence of any relationship with those employed for 20 years compared with those employed for less than ten years seems not to acknowledge that the pooled relative risk is 1.21 for those in the 20 year or more category. His comments at pages 13 and 19 suggest that he was seeking a clear pattern before he would acknowledge any dose response relationship. There may be some evidence but it is not especially persuasive given that the pooled relative risk of 1.21 has a p value of 0.17 which would indicate that the result being due to chance cannot be significantly discounted.

(165) Another point to keep in mind concerning causation is the marker theory noted by Appeal Division panels in *Decisions #93-0163*, *#00-1409*, and *#2002-1282*. Lung cancer and mesothelioma are markers for exposure to asbestos and one would expect to see excesses of those diseases in studies if firefighters were exposed to sufficient amounts of asbestos to increase their risk of colon cancer from asbestos exposure. Yet those excesses were not seen in firefighter studies in contrast to studies of insulation workers which showed excess colon cancers and a clear risk of lung cancer and mesothelioma. The Vena and Fiedler study

which showed an excess in colorectal cancer in firefighters and showed a pattern of increasing risk of that cancer with increasing years of service had the opposite finding with respect to lung cancer. As well, the Baris study notes that the SMR for lung cancer was not elevated. However, as noted earlier, firefighters' exposure to asbestos may not involve exposure to friable fibers so much as moistened fibers. It is possible that the latter are ingested rather than inhaled with the result that there may be differing effects on the lungs and colon depending on the route of entry into a worker's body.

(166) This marker theory does raise the question of whether asbestos which is linked to colon cancer is encountered in sufficient quantities by firefighters to cause colon cancer. Asbestos is currently the only definite carcinogen known in the literature to cause colon cancer. If firefighters are not in general sufficiently exposed to this definite colon cancer and lung cancer carcinogen to have increased incidence of lung cancer, why would colon cancer be regarded as occupational in origin for urban firefighters?

Risk Assessment

(167) We consider that there are four broad questions to be addressed in determining a particular worker's risk for colon cancer due to occupational exposure:

1. What is the risk of colon cancer for firefighters in general assuming that except for occupational exposures all other risk factors are the same as the general population?

2. To what extent does the healthy worker effect impact the general occupational risk for firefighters?

3. Are the particular worker's non-occupational risk factors the same as the general population; if not, to what extent do the non-occupational risk factors impact the worker's individual risk?

4. Are the particular worker's occupational exposures similar to the average exposures for firefighters as a group; if not, to what extent do the worker's occupational exposures impact the worker's individual risk?

(168) Evaluation of these four questions on the basis of available evidence provides a basis to estimate the worker's individual risk of colon cancer due to his occupation. We will examine each in turn.

What is the risk of colon cancer for firefighters in general assuming that except for occupational exposures all other risk factors are the same as the general population?

(169) We find that the relative risk of firefighters generally and colon cancer is not as high as 1.5. After reviewing the studies and the commentaries on their results, we consider that the relative risk is in a range between 1.1 and 1.3 and we find it to be 1.2. We consider that the evidence does not support a finding that the risk tends to be at one end of the range or the other and we find it to be at the midpoint. We accept that use of the midpoint may be viewed as somewhat arbitrary. A relative risk of 1.2 is above Dr. Howe's pooled SMR of 1.10 for mortality and incidence studies and the pooled SMR of 1.16 for just mortality studies and the pooled SMR of 0.91 for incidence studies. It is not as high as Dr. Guidotti's upper figure of 1.5 but does reach the lower end of his range of 1.2 to 1.5. We are aware of the higher risk found in the Baris study but we do not consider that one study can determine our assessment of the relative risk. The Baris study is, of course, notable given its size and the number of years of exposure captured by the study. As noted above, it did have somewhat problematic data regarding differing risks associated with different measures of exposure.

(170) In our discussion earlier we noted that there were differences amongst studies depending on such key variables as whether the study showed a positive result or a negative result and whether the confidence intervals included 1.0. We are cognizant that there are no statistically significant studies showing a negative association. There are studies that are not statistically significant which have relative risks above 1.0. We do not consider that the presence of two studies (Vena and Fiedler and Baris) with positive results (1.83 and 1.5 respectively) which do not include 1.0 in the confidence intervals must mean that we must weight those studies so heavily that the relative risk must be seen to be 1.5 or closer to that figure than a range of 1.1 to 1.3. It must be kept in mind that even in those studies the confidence intervals were fairly wide (1.05-2.97 and 1.19-2.71).

(171) We consider it is appropriate to have regard to the results of all studies regardless of whether they establish the existence of a positive association. Certainly study design is relevant but in the absence of a significant flaw we consider a study's results should be factored into the assessment of a relative risk. There are power considerations attached to large studies but we question the extent to which such considerations should lead to the discounting of smaller studies.

To what extent does the healthy worker effect impact the general occupational risk for firefighters?

(172) In our review we have noted comments that the healthy worker effect may not be as large for cancer as it is for other diseases, say cardiovascular disease. That might suggest that an effect with a range of 10 to 20 percent posited in the Protocol is too high. Yet we accept that activity is very relevant when it comes to

colon cancer and activity may be more relevant to that cancer than to many other cancers. We further accept that at the date of hiring firefighters are more active than the general population and continue to be more active. We question whether the healthy worker effect concerning colon cancer and firefighters is as small as 8 percent posited by Dr. Howe as his figure is derived from looking at all cancers combined. His calculation did not appear to make allowances for any effect that activity may have regarding colon cancer. We consider the healthy worker effect in the context of firefighters vis a vis colon cancer exceeds 10 percent and may be as much 20 percent. As noted by the dissenting panel member it is likely that several factors of the healthy worker effect are relevant to colon cancer and firefighting. We consider that 15 percent is a reasonable figure to allocate to the effect given those factors and the global range noted in the Protocol.

(173) We find that the healthy worker effect for firefighters and colon cancer is 15 percent. That figure would bring the occupational risk for firefighting and colon cancer to 1.35. We note that the figure of 1.35 falls in the middle of the 1.2 to 1.5 range which Dr. Guidotti indicated contained the true risk. As indicated in the quotation at page 22 of this decision, Dr Guidotti included the healthy worker effect in arriving at the true risk of 1.2 to 1.5 for firefighters and colon cancer. We interpret his opinion to be that the true risk inclusive of the healthy worker effect would not exceed 1.5.

(174) Initially we considered that the healthy worker effect should be regarded as part of the worker's non-occupational risk profile. Thus it would be a reduction in the worker's personal risk in a manner similar to whatever reduction is occasioned by individual characteristics such as his diet, physical activities, and family history. The reduction would involve the worker starting with a relative risk of 0.85 as a result of the healthy worker effect.

(175) However, on reflection, we consider that the healthy worker effect should be added to the relative risk imposed by the worker's occupation.

(176) The literature speaks of a diminution of the healthy worker effect over the years.[24] A component of the healthy worker effect arises from the selection criteria imposed by employers when workers are hired at the outset, and that effect is believed to be increasingly less operative over time.

[24] See generally the IDSP's Report to the Workers' Compensation Board On the Healthy Worker Effect at http://www.canoshweb.org/odp/default.htm and such recent articles as Baillargeon, J et al. 1998. Characteristics of the Healthy Worker Effect: A Comparison of Male and Female Occupational Cohorts. Journal of Occupational and Environmental Medicine 40: 368-373 and Baillargeon, J and Wilkinson, G. 1999. Characteristics of the Healthy Survivor Effect Among Male and Female Hanford Workers. American Journal of Industrial Medicine 35:343-347.

(177) There is a persisting component of the healthy effect that we consider is relevant to firefighting and colon cancer. That is the effect that is associated with continued employment and the activities associated with that employment (the healthy worker survivor effect). We consider that the benefit that may flow from work as a firefighter is so closely tied up with the risk associated with the occupation that the healthy worker effect should be added to the SMR associated with the occupation generally to ascertain the true risk.

(178) In that regard, we observe that as noted earlier in this decision both Dr. Guidotti and Dr. Howe added a consideration of the healthy worker effect to the SMR associated with firefighting and colon cancer when commenting on the risk associated with that employment. In his 1992 report Dr. Guidotti also indicated that the pooled SMRs and their confidence intervals should be adjusted by a correction factor to take into account the healthy worker effect. It is true that they do not articulate why they took into account that consideration as part of the occupational risk (rather than as part of the non-occupational risk) but we consider that the above analysis offers a rationale for such consideration by them of the effect.

(179) We are aware of concerns within studies as to how the healthy worker effect can be controlled for.[25] The methods of control proposed such as restriction of the cohort to survivors of a fixed number of years of follow-up or lagging the exposure to exclude recent exposure incurred by those who remained on the job are not available to us in assessing the literature generally. As well, we are concerned with matters of compensation and we consider that we must make a reasonable, albeit possibly rough, attempt to take the healthy worker effect into account in assessing causation.

(180) We are aware that the simple method of adding a percentage may not be sufficient to assess the impact of the healthy worker effect. We note two recent articles by Choi[26] in which he posits that an adjustment for the healthy worker effect can be achieved by dividing the SMR of interest by a comparable SMR that is less affected by the occupational exposure such as the SMR for all causes of death in the study. Using an all causes of death figure of 0.96 in Baris or the similar figure of .962 from the 1993 Guidotti study, the healthy worker effect acting on an SMR of 1.2 for firefighting and colon cancer would

[25] See Arrighi, HM and Hertz-Picciotto, I. 1994. The evolving concept of the healthy worker survivor effect. Epidemiology 5:189-196.

[26] Choi, BC. 2000 A technique to re-assess epidemiologic evidence in light of the healthy worker effect: the case of firefighting and heart disease. Journal of Occupational and Environmental Medicine 42:1021-34

Choi, BC. 2001. Mathematical procedure to adjust for the healthy worker effect: the case of firefighting, diabetes, and heart disease. Journal of Occupational and Environmental Medicine 43:1057-63.

produce an adjusted SMR of approximately 1.25. (We note that this may be the method used by Dr. Howe to adjust the SMRs rather than simple addition. He applied a healthy worker effect of 8 percent to the pooled SMR of 1.16 for mortality studies to obtain a figure of 1.26 (1.16 divided by 0.92 equals 1.26).

(181) We note that the adjusted SMR is slightly larger than the result of simply adding the difference between 1.0 and 0.96 to the SMR of 1.2 for firefighting and colon cancer to take into account the healthy worker effect. Use of this method of factoring in the healthy worker effect would not change the outcome if we used 0.96 or 0.92 or 0.85 as a measure of the healthy worker effect.

(182) We are aware that Choi considered that a number of factors would have to be met before this method could be used. One factor was that the studies involve chronic non-malignant disease. He did not consider that cancer was likely to be affected by the healthy worker effect, a sentiment shared by numerous commentators. However we have considered a healthy worker adjustment given that colon cancer may be affected by the healthy worker effect as a result of the physical activity associated with firefighting.

(183) We have two further observations regarding these calculations. In the Choi articles the impact of the healthy worker effect is used to modify the SMR for firefighters generally. That fits with our determination above to add a factor for the healthy worker effect to the SMR for firefighters generally. We have concerns that using the figure for all causes of death may underestimate the impact of the healthy worker effect regarding colon cancer. Hence the use of an additional 0.15 above to modify the SMR generally.

Are the particular worker's non-occupational risk factors the same as the general population; if not, to what extent do the non-occupational risk factors impact the worker's individual risk?

(184) We have considered what regard should be given to the worker's non-occupational risk factors.

(185) We note that the Appeal Division panel in *Decision #93-0163* appeared to be open to the idea that a firefighter's personal risk might be different from that of firefighters generally. It determined that there was no evidence to establish in that case that there was a substantial difference. Dr. Howe contends that if the relative risk from fire fighting multiplies other risks, for example, from diet, those risks do not affect a probability of causation. As illustrated by his 1992 report, he considers that risks (or protective factors) are not additive. He adds that there is no direct evidence as to whether, if there were cancers associated with firefighting, such firefighting risks would multiply or add to risks from lifestyle factors such as smoking or diet. He notes that one has to therefore rely on more

circumstantial evidence. In his experience, risks tend to be more often multiplicative than additive, and in particular risks from dietary factors appear to multiply each other rather than add to each other. Thus the probability of causation for any particular individual would be unrelated to his risk of cancer due to non-occupational lifestyle risk factors.

(186) Dr. Guidotti considers that the relative risk applicable to the worker may be modified by taking into account his individual characteristics regarding such matters as his exercise regimen, family history and abstention from smoking and alcohol abuse. He notes that age, occupation and exposure to work – related carcinogenic hazards are the only strong risk factors. Other factors suggest a low risk: absence of family history, lean body mass, physical activity level, vegetarian diet, and abstention from smoking as an adult.

(187) Dr. Guidotti does not directly assert that the worker's risk was as low 50 percent or 60 percent of the general population but does comment that the worker's risk would only have to be 60 percent of the general population (owing to his healthy habits) and indicates that if it was that low then a true risk of firefighters of 1.2 to 1.5 would mean the worker would achieve a doubling of the additional risk imposed by his occupation.

(188) Dr. Guidotti's observations about a personal risk of 60 percent of the risk of the general population are not a direct opinion on the worker's circumstances. It is clear he was hypothesizing about how low a risk the worker would have to have to experience at doubling of his risk and that is very different from actually asserting it was in fact that low. Had he wished to offer a direct opinion on the matter we consider that given his experience as an expert witness that he would know the language required to give an express opinion and would have provided such an opinion. Even if his report is interpreted as offering such an opinion we are not persuaded by it.

(189) We consider it significant that Dr. Guidotti does not refer to any literature to establish a reduction of 40 to 50 percent risk arising out of the worker's healthy habits.

(190) It may be that the worker's personal habits differed from those of the population as a whole. A comparison between the worker and the general population appears apt as we understand that the applicable theory is that other than occupational exposure epidemiology assumes that the study population and the general population are generally the same. (Steps are taken in studies to ensure similarity via matching for age and gender). Thus the effect of occupational exposure can be measured. The healthy worker effect is a difference between the populations. If there are other differences they may be factored in. However an appropriate evidential basis is required to be able to factor them in and assign reductions in personal risk in the individual case.

(191) In the absence of persuasive evidence on the point we have concerns about finding the presence of a noticeable reduction on top of the 15 percent reduction in risk associated with the healthy worker effect. What evidence is present to support a finding that the worker's dietary habits and his behaviour toward alcohol and tobacco can be quantified in the manner apparently asserted by Dr. Guidotti? The evidence before us does not provide persuasive analysis of what figures can be reliably formulated. We acknowledge diet and alcohol and tobacco use have some effect but we consider that positing a further reduction of risk of more than 15 percent owing to the worker's healthy habits would be problematic. To continue to add percentage points in acknowledgement of particular traits or behaviours suggests that there is much more precision in the calculations than we consider the evidence supports. We do not consider a reduction of risk of 30 percent is established.

(192) We find there is little scope to determine that the worker's non-occupational factors are such that his starting personal risk, absent his occupation, starts at 0.5 or 0.6 with the result that his personal risk was 2.4 to 3.0 assuming a true risk of firefighters of 1.2 to 1.5 asserted by Dr. Guidotti. We do not consider that Dr. Guidotti offers a robust argument in this regard that is not sensitive to small assumptions. With respect, his argument is contingent on the very significant assumption, for which there is little or no persuasive evidence, that the worker's initial risk absent his occupation is in the order of 0.5 or 0.6.

(193) We find that even after taking into account the question of the worker's personal circumstances that any reduction in personal risk did not exceed 15 percent.

Are the particular worker's occupational exposures similar to the average exposures for firefighters as a group; if not, to what extent do the worker's occupational exposures impact the worker's individual risk?

(194) The worker reports that he was involved in a particular fire which exposed him to cellulose nitrate film which produces nitrogen dioxide, and he was also exposed to solvent fumes. He was also an inspector involved in examining sites with hazardous commodities.

(195) There are significant concerns with using such exposures to find that the worker's occupational exposure as a firefighter was significantly different from other firefighters. We question whether we can allocate a factor to take into account such exposure which may or may not have involved exposure to carcinogens relevant to colon cancer. Exposure to materials at a theatre fire may have exposed the worker to carcinogens but there is no indication that they were associated with colon cancer. Similarly, hazardous materials can involve solvents, corrosives, poisons, gasoline, diesel, and other materials whose names may be known or unknown. We question whether we can allocate a factor to take into account such exposure which may or may not have involved

exposure to carcinogens relevant to colon cancer. Would attendances as an inspector have involved exposures to substances considered more likely to have been carcinogenic than exposures at fires generally? It should be kept in mind that according to IARC the only probable carcinogen for colon cancer is asbestos.

(196) We consider it is likely that firefighters in the cohort studies noted in our decision would have attended fires at which hazardous materials were present. Thus it seems likely that the relative risks established by those studies contain such exposure as a component of the risk. We strongly question whether the worker's attendance at a theatre fire is sufficient to say that his occupational risk must be modified. We do not liken that to a distinct added occupational exposure factor like that of service on an engine company (as observed in the Baris study). The apparent added risk associated with such service is established by a study and does not depend on a hypothesis in the absence of data. As well, we do not liken it to the discussion in the Protocol of the experience of asbestos workers with a brief exposure to crocidolite who had a very high risk of respiratory cancer as that was a case of a discrete exposure associated with a known carcinogen supported by data establishing the high risk.

(197) We consider that the length of the worker's employment is a relevant factor to take into consideration. The figures found in Dr. Howe's report suggest a dose response relationship (a relative risk of 1.2 after 20 years), albeit one from which chance could not be excluded. The Vena and Fiedler study is recognized to have a statistically significant result for dose response. The 1993 Guidotti study did have a remarkable relative risk associated with 20 years or more of exposure but the disease category included both colon and rectum cancer and we do not know whether the relative risk was driven by colon or rectal cancers or both. As noted above, the Baris study contained suggestions of a dose response in relation to a number of runs. In that study there was an increase in the overall relative risk for firefighters from 1.5 to 1.68 for firefighters with more than 20 years employment. That suggests that any acknowledgment of the fact the worker had 22 years of active firefighting and 12 years as an inspector and investigator might mean that his occupational risk was greater than the 1.2 figure noted above for firefighters generally and be as high as 1.4. We note that the Baris study does not provide a figure for more that 30 years of employment and we are not persuaded we can justify adding as much as 0.3 to the worker's occupational risk to raise it up to a range from 1.4 to 1.7.

(198) The worker's age is of note. The Appeal Division panel in *Decision #2000-1409* noted Dr. D's observation that the rate of colon cancer among men in B.C. age 60 to 79 is 160 per 100,000, more than a seven fold increase from the rate of 22 per 100,000 for men age 40 to 59. The point might be made that colon cancer is more predominant in older men and the occurrence in this worker may be a function of the increased risk for men of his age.

(199) We note that an Appeal Division panel in *Decision #2002-1282* found that the colon cancer of a firefighter who died at age 52 was related to his more than 17 years of fighting fires. That panel took into account the 1994 IDSP report, various medical opinions, information concerning substances firefighters are exposed to, the 1995 Guidotti review, the 2001 Baris report, Appeal Division *Decisions #93-0163* and *#2000-1409*, and a report from Dr. B when it found in favour of the worker's estate. We have considered that decision. The material before us is more extensive and we consider it provides a different basis for analyzing the epidemiologic evidence concerning fire fighting and colon cancer.

(200) We are aware that opinions of Dr. Guidotti have been accepted in a number of Appeal Division cases. However that does not mean that his report before us should be accepted uncritically and found to be determinative of the matter before us. That a physician considers the worker's relative risk was at least equal to 2.0 does not determine the matter. We consider that an opinion needs to contain a reasoned and persuasive discussion of the epidemiology.

(201) We find that the worker's personal relative risk was not 2.0 taking into account the epidemiological evidence and his personal circumstances. Even making allowances for a more robust healthy work effect than that acknowledged by Dr. Howe and noting the worker’s number of years of employment, does not significantly advance the worker's case.

(202) His personal risk would have been in the range of 1.8 assuming a personal risk absent occupational exposure of 0.85 and an occupational risk of 1.55. We do not consider that it was more likely than not that his cancer was due to the nature of his employment. Further, we do not consider that the possibility that it was due to the nature of his employment was equally balanced with the possibility that it was not such that section 99 of the Act would be applicable.

(203) We note that the area of firefighters and cancer has been the subject of recent amendments to at least four Canadian workers' compensation acts. In Alberta, as part of amendments in 2003, among other matters, there is a presumption of causation when there is a primary cancer site at the colon and there has been a minimum period of 20 years of "regular exposure to the hazards." The 2002 amendments to the Manitoba act concern three cancers, leukemia and non-Hodgkin's lymphoma but colon cancer is not listed in the diseases to which a

presumption attaches in the case of firefighters. The 2003 Saskatchewan amendments also do not include colon cancer. The Nova Scotia amendments of 2003 which permit the Governor in Council to list diseases and relevant periods of employment in connection with a presumption applicable to firefighters were proclaimed on July 30, 2003. Regulation 140/2003 establishes that Nova Scotia has a presumption applicable to firefighters and colon cancer. We are aware of these developments but note that we are making a decision in the context of the applicable provisions of the British Columbia statute and the evidence we have before us.

Section 55

(204) Generally section 55 of the Act provides that a claim for compensation for disablement from occupational disease must be made within one year from disablement. If special circumstances precluded the filing of an application within one year after disablement from an occupational disease compensation may be paid if the application is filed within three years of that date. Compensation from the date of application only is payable if the application is more than three years after the date of disablement and there were special circumstances which precluded an application within one year of the date of disablement.

(205) In 1994 the Act was amended to bring into force subsection 55 (3.2) which permits the Board to pay compensation provided by Part 1 of the Act if sufficient medical or scientific evidence was not available on the date of disablement for the Board to recognize the disease as an occupational disease, and this evidence became available on a later date, and the application was filed within three years after the date sufficient medical or scientific evidence as determined by the Board became available to the Board. Subsection 55(3.3) provides that the Board may apply subsection (3.2) to an application in respect of a death or disablement from an occupational disease that the Board previously considered since July 1, 1974 under the equivalent to this section. Thus the Board was permitted to re-examine certain earlier decisions to deny claims under section 55.

(206) In the case before us the issue is not whether evidence has become available since 1991 as indicated by the case manager and the worker in his August 7, 2001 submission. The point of reference is the one-year anniversary of the date of disablement rather than the date of adjudication. The worker's surgery was August 1988 and thus the point of reference is August 1989. We consider that a significant amount of new evidence has been produced since August 1989 but it is not sufficient to enable us to find that the worker's cancer was an occupational disease. We do not consider it was due to the nature of his employment. We agree with the case manager that the amendments to section 55 of the Act do not allow the Board to reconsider the claim and pay

compensation benefits. Subsection 55(3.2) does not advance the worker's claim.

Expenses

(207) We consider that given its contents and further to section 7 of the *Workers Compensation Act Appeal Regulation* the worker should be reimbursed for the cost of the report from Dr. Guidotti. In this appeal the employer has not requested reimbursement of the cost of Dr. Howe's reports; reimbursement was requested in connection with the other appeal.

DISSENT

(208) I agree with the panel majority that a significant amount of new scientific evidence has been produced since August 1989. However, I differ with respect to the weight to be given to that evidence. I find that the evidence is sufficient to recognize the worker's rectosigmoid cancer as an occupational disease in this case, and thereby satisfies the requirements of section 55 (3.2). The following details my reasons for reaching a different conclusion than the panel majority.

(209) I am in agreement with the panel majority that the issue in this appeal turns mainly on the reports of the two experts who have provided opinions in this case. Dr. Guidotti supports a work relationship between the worker's exposures as a firefighter and the colon cancer. Dr. Howe did not provide an opinion specific to this case. However, in his report from another colon cancer case he concludes there is no basis to establish a work relationship between colon cancer and the occupation of firefighting in general and, therefore no basis to consider a work relationship for an individual worker.

(210) Dr. Howe concludes that the pooled epidemiological evidence does not support a causal association of 2.0 to give a probability of causation of 50 percent for firefighters in general. He states that, given the lack of a causal association of 2.0 for firefighters as a group, it would be inappropriate to estimate the probability of causation for an individual worker. He relies on an assumption that any relative risk from firefighting "multiplies risks for other factors." He indicates a worker with 20-plus years of exposure as a firefighter would have a risk for colon cancer from firefighting of about 1.2, far less than the 2.0 required to give a probability of causation of 50 percent.

(211) Dr. Guidotti was asked to comment on the opinion of Dr. Howe, and to offer a considered medical opinion on the facts. Dr. Guidotti concludes from the literature that there is an increased risk of colon cancer among firefighters in general, but the association falls below a doubling for firefighters as a group. He concludes that a review of the literature that takes into account the relative

strengths of some studies indicates to him that the true risk of colon cancer among firefighters "is of the approximate magnitude of 150."

(212) The relevant question, according to Dr. Guidotti, is whether the worker had an elevated risk of colon cancer from firefighting equivalent to a doubling, or greater, over the non-occupational risk; not simply whether firefighters overall have a doubling of risk.

(213) Dr. Guidotti comments at some length on Dr. Howe's analysis, and concludes that his report is an explanation of epidemiological methodology, not an application of the findings of epidemiological science to the specific features of this worker's claim. Dr. Guidotti contends that Dr. Howe's failure to take into account the evidence of risk factors in the individual case "renders his opinion irrelevant." Dr. Guidotti is also critical of Dr. Howe's failure to take into account the epidemiological evidence that shows "a 20 percent increase of risk after 20 years of service."

(214) Dr. Guidotti prefers an analysis of the epidemiological evidence, taking into account the relative strength of studies and emphasizing the contribution of the studies that have the greatest statistical power, rather than averaging all studies through pooling, which he argues places undue reliance on studies of limited statistical power that are unable to reliably detect a true association. Dr. Guidotti places greater emphasis on "positive" studies that demonstrate an elevated risk.

(215) Dr. Guidotti does not accept Dr. Howe's assumption that non-occupational risk factors act "multiplicatively." If that were the case, he asserts that "…it is only necessary to demonstrate that the effect of occupation acts on these other risk factors to achieve a doubling of risk compared to that experienced by another individual with the same risk profile absent the occupational exposure…."

(216) Dr. Guidotti notes that the worker in this case had 22 years of active firefighting and 12 years of service as an fire inspector and investigator. In 1956 he experienced an episode of toxic inhalation related to burning cellulose nitrate film which produces potentially lethal nitrogen dioxide. There was no family history of colon cancer. His lean body mass, level of physical activity, vegetarian diet and abstention from smoking as an adult all indicate a lower than average individual risk. The worker's exposure to carcinogenic hazards as a firefighter is a strong risk factor in this particular case.

(217) Dr. Guidotti concludes that when taking into account the risk factors in this case, the worker belongs to a subgroup of firefighters "…in which the risk clearly exceeds a doubling for the group." He bases his opinion on the following factors:

- The true risk of colon cancer for firefighters as an occupational grouping is between 1.2 and 1.5.

- The worker has a significantly lower risk from non-occupational factors, than the general population (possibly a little over one-third less by virtue of his healthy habits).

- The worker's 20 plus years of exposure as a firefighter significantly increases his risk above that of the average risk-level for firefighters in general.

(218) Dr. Guidotti concludes from the evidence that it is more likely than not that the worker's colon cancer was due to the nature of his employment as a firefighter.

(219) The fact that an expert in the field concludes that it is likely that the worker's colon cancer was due to his exposures as a firefighter does not necessarily determine the matter. That opinion must be weighed against the available scientific facts, and the evidence in this particular case, to determine how much weight is to be given to the opinion in deciding the issue. In the final analysis, if the evidence shows that it is at least as likely, as not, that the worker's colon cancer was due to his exposure as a firefighter, then the claim is acceptable. If the evidence falls short of that standard, then the claim must be denied.

(220) I agree with my colleagues with respect to the four questions to assist in weighing the evidence in this case. The second and third questions determine the level of non-occupational risk. The first and fourth questions identify the occupational risk level. If the occupational risk is at least double the non-occupational risk, then the attributable risk to employment as a firefighter would be 2.0 or greater, and would indicate that it is at least as likely as not that the colon cancer was due to the nature of the worker's employment as a firefighter.

What is the risk of colon cancer for firefighters in general, assuming that except for occupational exposures, all other risk factors are the same as the general population?

(221) The majority conclude that the relative risk for colon cancer for firefighters is between 1.1 and 1.3, based primarily on the pooled results of all the studies advanced by Dr. Howe. For the most part, these studies rely on years of employment as a firefighter, since more specific exposure data is not available for this profession. As the epidemiological literature indicates, the variability in relative risk found in epidemiological studies may be due, in part, to different types and levels of exposure between study populations.

(222) I find Dr. Guidotti's expert opinion, that the true risk likely falls between 1.2 and 1.5 for all firefighters as a group, more persuasive. His analysis takes into account the greater degree of reliability of larger studies that are well designed and have increased statistical power.

(223) Based on the superior design of the Baris study which found a relative risk of 1.51 percent before any healthy worker effect is taken into account and the expert opinion of Dr. Guidotti, I am persuaded that the relative risk for firefighters is at least 1.30, and rely on this level of general risk for firefighters for purposes of this decision. This relative risk is close to the lower level of the range identified by Dr. Guidotti and is at the upper range identified by the panel majority.

To what extent does the healthy worker effect impact the general occupational risk for firefighters?

(224) I agree with the majority that Dr. Howe's healthy worker effect estimate of 8 percent does not reflect the fact in the medical literature that activity level is a significant factor for colon cancer. The healthy worker effect generally refers to the impact of two factors on relative risk. First, the strenuous fitness requirements at the time of hire (selection bias) indicates a lower risk than the general population as a whole, which includes those individuals who are unable to work for health reasons. The healthy worker effect also takes into account the fact that workers, who become unfit after employment, leave the workforce and are often lost to follow-up or may be misclassified. Added to these two factors is the physical activity level of firefighters on an ongoing basis, and its specific impact on reduction of risk for colon cancer.

(225) Taking into account these three dimensions of the healthy worker effect for firefighters generally, I am in agreement with the majority that the healthy worker effect exceeds 10 percent, and may be as much as 20 percent. The literature on the healthy worker effect also indicates that there may be a slight decrease in the magnitude of the healthy worker effect with increasing age. Based on the available evidence in this case, the literature regarding increased physical activity levels associated with lower risk and the approach in the Board's Protocol I find that the healthy worker effect for colon cancer and firefighters is between 15 and 20 percent. For purposes of this decision, I find that a reasonable estimate of the healthy worker effect for firefighters, in general, is 15 percent.

(226) Initially, I considered it appropriate to add the healthy worker effect to the risk of colon cancer for firefighters, since this risk modification is common to all firefighters, and the healthy worker effect masks some of the true risk for firefighters as a population. However the healthy worker effect for firefighters as

a group relates to the non-occupational risk level for firefighters and, therefore, must be taken into account by reducing the starting SMR for firefighters by the magnitude of the healthy worker effect. This is consistent with the approach in the Board's Protocol, which indicates that the healthy worker effect reduces the SMR below 1.0. This is also the approach used generally in epidemiology as illustrated in the discussion of the healthy worker effect on page 32 of this decision. If the non-occupational healthy worker effect is added to the occupational risk, it does not provide an accurate reflection of the true non-occupational risk and reduces the impact of the healthy worker effect by 50 percent. The general healthy worker effect, therefore, reduces the non-occupational risk for firefighters below the 1.0 risk for the general population by 15 percent resulting in a base non-occupational risk of .85.

(227) Epidemiology assumes that, aside from the bias of the healthy worker effect, all personal risk factors for firefighters are the same as the general population. The healthy worker effect for firefighters as a group is a separate issue from the personal non-occupational risk level for an individual firefighter which takes into account diet, family history, smoking history, alcohol use, and activity level outside of work. Where there is evidence that the individual firefighter's personal non-occupational risk differs from the general population risk, the personal risk must also be taken into account in addition to the healthy worker effect for firefighters generally to arrive at the true non-occupational risk.

Are the particular worker's non-occupational risk factors the same as the general population; if not, to what extent do the non-occupational risk factors impact the worker's attributable risk?

(228) Dr. Howe is of the view that non-occupational risk factors do not play a role in determining whether the worker's colon cancer was due to occupational exposure. In my view, this position is inconsistent with the requirement in section 99 of the Act, that the decision be made in accordance with the merits and justice of the case.

(229) I consider that the non-occupational risk factors are a relevant consideration in this case. This is consistent with the "attributable risk" approach outlined in the Board's Protocol that considers the probability of a work relationship in an individual case. If the worker's non-occupational risk factors are lower than those in the general population, then the attributable risk for the occupational exposure is increased accordingly. The corollary of this also applies: If the worker's non-occupational risk factors are higher than the risk for the general population, then the impact of the occupational risk factors are reduced accordingly. A firefighter, who has a high-fat, low-fibre diet, who is inactive, who smokes, and who consumes alcohol to excess, would have a higher non-occupational risk than a firefighter who has a low-fat, high-fibre diet, who is very active, who is a non-smoker, and who does not consume alcohol to excess.

Expressed in statistical terms a firefighter who has a personal risk that is 20 percent higher than the general population because of unhealthy habits would have a non-occupational risk of 1.05 (taking into account the starting SMR of .85 due to the healthy worker effect). A firefighter who has a personal risk that is 20 percent lower than the general population would have a total non-occupational risk of .65, since the personal risk would further reduce the non-occupational risk from the healthy worker effect. As can be seen, the starting point for measuring the effect of the employment exposure is the composite non-occupational risk to determine whether the occupational exposure doubles that risk.

(230) Dr. Guidotti states: "In fact, [the worker's] personal risk, absent his occupation, would only have to be 60 percent that of the general population (i.e., reduced by a little over a third by his healthy habits) to achieve this estimated doubling by the minimal [1.2], not the most likely, estimate of the additional risk imposed by his occupation."

(231) The panel majority interprets this as not offering a direct opinion, since it is not couched in "the language required to give an express opinion." I do not consider Dr. Guidotti's opinion as indirect as the panel majority. It is inherent in Dr. Guidotti's opinion that the worker's occupational risk exceeds a doubling of his non-occupational risk. Dr. Guidotti indicates that the worker's healthy habits reduce his risk, compared to the general population, by at least a third to achieve a doubling of risk. Dr. Guidotti bases this opinion on the fact that "the general population contains many individuals who are institutionalized, who smoke and drink, who are sedentary, and whose diet is more in keeping with the fat rich, low fibre North American norm." I understand Dr. Guidotti's opinion to be based on the worker's non-occupational risk of approximately one-third below the general population.

(232) The literature contains extensive research into non-occupational factors related colon cancer. The research shows that a significantly lower risk of colon cancer exists for populations whose diet avoids meat and consists mainly of vegetables, fruits and whole grains.[27] A recent study in the American Journal of Epidemiology[28] found that subjects with a high red meat intake, a low legume intake, and a high body mass experienced "…a more than threefold elevation in risk." In determining the worker's personal non-occupational risk I have taken into account the worker's vegetarian diet, absence of family history of colon

[27] See Burkitt, D.P. 1984. Dietology and prevention of colorectal cancer. Hospital Practitioner 19: 67-77; Stemmermann, G.N. Nomura, A.M., Heilburn, L.K. 1984. Dietary fat and the risk of colorectal cancer. Cancer Research 44:4633-7; Ballard-Barbash, R., Schatzkin, A, Albanes, D., et.al. 1990. Physical activity and risk of large bowel cancer in the Framingham Study. Cancer Research 50: 3610-3613.

[28] Singh, P.H., Fraser, G.E. 1998. Dietary risk factors for colon cancer in a low risk population. American Journal of Epidemiology 148(8): 761-774.

cancer, lean body mass, non-smoking history, and low alcohol use and Dr. Guidotti's indication of approximately a 33 percent reduction of risk for healthy living habits. I find a reasonable level for the worker's personal non-occupational risk in this case is approximately .30 below that of the general population.

(233) The worker's personal non-occupational risk further reduces the non-occupational risk from the healthy worker effect of .85 by a further .30 to yield a combined non-occupational risk of .55. The worker's personal risk absent his occupation therefore is .55 relative to the general population risk of 1.00. A doubling of the worker's non-occupational risk would require an occupational risk of 1.10 or greater. Given my previous finding that the cumulative risk for firefighters in general is 1.30, the occupational risk for firefighters in general is more than double the worker's non-occupational risk. However, it is still necessary to take into account the worker's individual occupational risk factors to complete the risk analysis.

Are the particular worker's occupational exposures similar to the average exposures for firefighters as a group; if not, to what extent do the worker's occupational exposures impact the worker's individual risk?

(234) I agree with the panel majority that the dose response evidence in the epidemiological literature indicates that the worker's 20-plus year history as a firefighter increases his attributable risk by approximately 0.20. This is consistent with Dr. Guidotti's analysis that indicates "the data shows a 20 percent increase of risk after 20 years of service." I find the 0.20 increased risk, from years of exposure, a reasonable and realistic figure in this case. This would bring the worker's accumulative attributable risk to 1.50 more than double the worker's non-occupational risk level of .55.

(235) I have also considered the nature of the worker's exposures in his 22 years active firefighting (including the atypical theatre fire involving nitrogen dioxide for which he was hospitalized for 48 hours) and his subsequent work as an inspector with the city which involved inspecting a wide range of sites with hazardous commodities (including a range of radioactive materials, PCB's, a range of pesticides, sodium cyanide, zinc cyanide, etc). I consider that the hazardous commodities inspection duties likely exposed the worker to some carcinogenic materials, although I would expect that the non-emergent inspection duties would have allowed the use of protective equipment. I appreciate that it is difficult to attempt to quantify this factor. However, given the nature of exposures likely encountered, I consider an added factor of 0-10 percent would be appropriate in the circumstances of this case. For the purposes of this decision, I find the specific exposure likely experienced by this worker added an additional 5 percent.

(236) The combined occupational risk for this worker is therefore 1.55 taking into account the .25 increased occupational risk factors specific to this worker's exposure as a firefighter. Using the methodology advanced by Dr. Guidotti, I find that the worker's personal risk absent his occupational risk is .55 and his occupational risk is 1.55. The attributable occupational risk is 2.82 well above the 2.0 level required to establish a work relationship in this case.

(237) On the basis of all of the foregoing, I conclude that the worker's exposures as a firefighter, in combination with his healthy living habits and lower than average non-occupational risk, bring the worker's attributable risk above 2.0. I conclude, from the evidence that it is more likely, than not, that the worker's exposure as a firefighter is the most likely cause of the colon cancer in this particular case.

(238) In the final analysis, there is one expert medical opinion in this case that supports a work relationship. I consider that expert opinion to have weight, and provide significant support for establishing a work relationship between the worker's colon cancer and his employment as a firefighter. The opinion of Dr. Howe does not address this worker's individual circumstances, and does not consider the merits and justice of the case, as required by section 99 of the Act.

(239) I would, therefore, allow the worker's appeal.

Paul Petrie
Vice chair

Conclusion

(240) The worker's appeal is denied as we find that his colon cancer was not due to the nature of his employment as a firefighter. We confirm the decision of the case manager.

Randy Lane
Vice Chair

Daphne Dukelow
Vice Chair

RL/hf