**IN THE UNITED STATES DISTRICT COURT**
**FOR THE SOUTHERN DISTRICT OF NEW YORK**

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| CENTRAL RABBINICAL CONGRESS OF THE USA & CANADA, *et al.*, | : | Case No. 12-Civ.-7590 |
| Plaintiffs, | : | Judge Naomi Reice Buchwald |
| vs. | : | |
| NEW YORK CITY DEPARTMENT OF HEALTH & MENTAL HYGIENE, *et al.*, | : | |
| Defendants. | : | |

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**DECLARATION OF DR. DAVID M. ZUCKER, PH.D**

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1. I am Professor of Statistics at Hebrew University, Jerusalem. I received B.A., M.A., and Ph.D. degrees in Mathematical Sciences from The Johns Hopkins University in 1980, 1981, and 1986, respectively. My area of specialty is biostatistics. I have worked in the field for nearly 30 years. From 1983 to 1986 I worked as a statistician for the US Food and Drug Administration. From 1986 to 1992 I worked as a statistician for the US National Heart, Lung, and Blood Institute. Since 1992, I have been a faculty member of the Department of Statistics at Hebrew University. I have conducted and published research on statistical methods, primarily in the area of biostatistics. From 2008 to 2010 I served as one of the three chief co-editors of the journal *Biometrics*, a leading international biostatistics journal published by the International Biometrics Society.

2. I have carefully reviewed the June 2012 report by the Centers for Disease Control and Prevention in its *Morbidity and Mortality Weekly Report* entitled "Neonatal Herpes Simplex Virus Infection Following Jewish Ritual Circumcision that Included Direct Orogenital Suction – New York City, 2000-2011" (MMWR Report). I have also carefully reviewed the affidavits of Professor Awi Federgruen and Professor Andrew Gelman, and a draft of the response affidavit of Professor Federgruen. In this affidavit, I present my professional opinion on some of the issues raised in this documents. I will refer to direct orogenital suction using the abbreviation DOS.

3. A key issue is the size of the group of infant males in the New York City (NYC) population exposed to DOS during the study period. In the MMWR report, the size of the exposed group was estimated at 20,493. The derivation of this figure involved several steps. First, the number of boys entering kindergarten in Jewish day schools in NYC in 2010 was ascertained to be 6,197. Second, data from a national census of Jewish day schools were used to estimate the percentage of these boys coming from specific ultra-Orthodox subgroups; it was thereby estimated that 43% of these boys came from the Hasidic subgroup and 29% from the Yeshiva subgroup. Third, the assumption was made that 100% of the boys in the Hasidic subgroup and 50% of the boys in the Yeshiva

subgroup would have undergone DOS. As a result of these three steps, the annual size of the population exposed to DOS was estimated at 3,564. This figure was then multiplied by the length of the study period, 5.75 years, to obtain the estimate of 20,493 exposed.

4. Professor Federgruen identified several problems with this calculation, including problems with the estimates of the percentages of kindergarten boys in the Hasidic and Yeshiva groups and with the percentage of boys in the various Orthodox Jewish groups undergoing DOS. Based on kindergarten enrollment data, Professor Federgruen estimated the percentage of kindergarten boys in the Hasidic subgroup to be 69% and the percentage in the Yeshiva subgroup to be 23%. I consider these estimates, based on actual enrollment data, to be more accurate than those in the MMWR report. Using these revised percentages, the estimated size of the DOS-exposed population becomes 29,371. Professor Federgruen provided some plausible reasons why this figure may be an underestimate, such as the growing population trend in the Hasidic subgroup.

5. Professor Federgruen noted further that the assumed 50% DOS exposure rate for boys in the Yeshiva subgroup was not based on any actual data, and suggested that this figure is likely to be an underestimate. In addition, Professor Federgruen noted that the MMWR calculation assumed that 0% of the boys in Orthodox Jewish subgroups outside the Hasidic and Yeshiva subgroups underwent DOS, an assumption that is highly questionable. He also noted that a substantial number of Jewish boys outside the Orthodox community undergo DOS (*e.g.*, boys whose circumcisions are done by a Chabad *mohel*). It is evident that the MMWR investigators did not make a concerted effort to ascertain the degree of DOS exposure in the various relevant Jewish groups. This omission constitutes a serious flaw in the study.

6. Professor Federgruen has attempted to correct the estimated size of the DOS-exposed group in the Jewish population outside the Hasidic and Yeshiva subgroups, arriving at an estimated DOS-exposed population size of 35,818. It is unfortunate that the study investigators did not provide a well-developed estimate of this important figure.

7. Another serious flaw in the study was the lack of an a priori specification of a rule for terminating the study. As data are collected over time, the results undergo natural random fluctuations. A proper study design incorporates an a priori termination rule (e.g., specified calendar time, specified total number of cases, or a statistical process control type of rule), in order to foreclose the possibility of the investigators' choosing to stop the study at a point where the results look strong due to a random upturn.

8. In his supplemental affidavit, Professor Federgruen raises the possibility that a heightened awareness of a possible association between DOS and neonatal HSV may have made it more likely that HSV would be tested for and detected in infants from Orthodox families than in infants in the general population. Reporting bias due to more intense scrutiny in one group relative to another is a recognized phenomenon discussed in epidemiology textbooks. The extent of such a reporting bias is difficult to assess.

9. In his supplemental affidavit, Professor Federgruen argues that the method used in the MMWR report to compute the confidence interval for the relative risk of neonatal HSV in the DOS population, a method based on the normal approximation to

the binomial distribution, is an inappropriate method for the case at hand. He proposes an alternate calculation based on the Poisson approximation to the binomial distribution, another well-known classical approximation presented in standard probability texts which is geared specifically to the case of rare events. In Section 3.6.1 of Johnson, Kemp, and Kotz (2005), a classic authoritative handbook on statistical distributions, a rule is presented for choosing between the normal and Poisson approximations. Denoting the sample size by $n$ and the probability of an event by $p$, the rule is to use the normal approximation if $n^{0.31}\,p$ is less than or equal to 0.47 and to use the Poisson approximation otherwise. In the DOS-exposed population, using the figures in the MMWR report, we have $n^{0.31}\,p = 20{,}493^{0.31}\,(5/20{,}493) = 0.0053$, emphatically favoring the Poisson approximation. A similar calculation leads to the same conclusion for the unexposed population. Accordingly, in the case at hand, the confidence interval method based on the Poisson approximation is clearly more appropriate than the method used in the MMWR report based on the normal approximation.

10. Another issue raised by Professor Federgruen is the reliance in the MMWR calculation on a "delta method" argument involving a local linear approximation to the logarithm of the estimated event proportions. Denoting the estimated event proportion by p and the true event proportion by p*, this approximation takes log(p) – log(p*) to be approximately equal to (p – p*)/p*. The "delta method" is an established method for handling transformed versions of parameters which is appropriate when the normal approximation is valid and the database is large enough to make the estimated parameter value sufficiently close to the true parameter value to render the local linear approximation valid. These conditions are not satisfied in the present case. I will present a calculation illustrating the problem, using the figures in the MMWR report. Define the following notation:

n1 = number of infants in the general population = 352,411
m1 = number of cases in the general population = 25
p1 = estimated proportion of cases in the general population = m1/n1
p1* = true proportion of cases in the general population
n2 = number of infants in the exposed population = 20,493
m2 = number of cases in the exposed population = 5
p2 = estimated proportion of cases in the general population = m2/n2
p2* = true proportion of cases in the exposed population

11. Under the normal approximation without the log transformation, the difference p2– p1 is regarded as approximately normally distributed with mean p2*– p1* and variance estimated by v = p1*(1– p1)/n1 + p2*(1– p2)/n2. The null hypothesis that p2*=p1* is tested using the z-statistic z = (p2*– p1*)/sqrt(v), and the 95% confidence interval for p2*– p1* has lower limit (p2– p1) – 1.96*sqrt(v) and upper limit (p2– p1) + 1.96*sqrt(v).

12. Under the normal approximation with the log transformation using the "delta method", the difference log(p2) – log(p1) (natural base logarithm) is regarded as approximately normally distributed with mean log(p2*)– log(p1*) and variance estimated by v = (1– p1)/(n1*p1) + (1– p2)/(n2*p2). The null hypothesis that p2*=p1* is tested using the z-statistic z = (log(p2) – log(p1))/sqrt(v), and the 95% confidence interval for

log(p2*)– log(p1*) has lower limit (log(p2) – log(p1)) – 1.96*sqrt(v) and upper limit (log(p2) – log(p1)) + 1.96*sqrt(v). This confidence interval can be exponentiated to produce a confidence interval for the risk ratio p2*/p1*, and this is the type of confidence interval presented in the MMWR report.

13. If the conditions of the "delta method" hold, the analyses with and without the transformation should yield similar conclusions, and in particular the z-values should be similar. This is not so, however, in the present case. With the log transformation, the z-value is z=2.52, corresponding to a highly significant p-value of p=0.01, the 95% confidence interval for the log risk ratio is [0.275, 2.19], and the 95% confidence interval for the risk ratio is [1.3, 9.0], as presented in the MMWR report. Without the log transformation, however, the z-value is z=1.57, corresponding to a non-significant p-value of p=0.12, and the 95% confidence interval for the risk difference p2*– p1* is [–0.000042, 0.00039], which includes the null hypothesis value of 0. This illustrates clearly the invalidity of the MMWR report's statistical methods in the current setting.

14. Based on his revised estimates of the size of the DOS-exposed population in the NYC study and the use of the more accurate Poisson-based method, Professor Federgruen produced corrected confidence intervals for the relative risk of neonatal HSV in the DOS-exposed group. These intervals are given in Table 1 of his supplemental affidavit. I present here the corresponding p-values for testing whether the DOS-exposed population has a higher rate of neonatal HSV than the general population. The traditional p-value criterion for declaring statistical significance is $p<0.05$. Under the MMWR report's assumption that the size of the DOS-exposed population is 20,493 (first row of Table 1 of Professor Federgruen's supplemental affidavit), the p-value is p=0.023. Under the assumption that the size of the DOS-exposed population is 29,371 (second row of Professor Federgruen's Table 1), the p-value is p=0.077. Under the assumption that the size of the DOS-exposed population is 35,818 (third row of Professor Federgruen's Table 1), the p-value is p=0.193.

15. In other words, using the corrected parameters and appropriate formulae, the data in the MMWR surveillance study do not provide statistically significant evidence according to traditional statistical standards that the DOS-exposed population has a higher rate of neonatal HSV than the general population. In addition, there are concerns about the MMWR study (noted in Points 7 and 8 above) that cast further question on the study report's conclusions.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct to the best of my knowledge.

Executed this 30th day of November, 2012, at 11 Neiman Street, Jerusalem, Israel.

David M. Zucker

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