Excerpts below are from the first chapter of **Turtles All The Way Down: Vaccine Science and Myth** (pages 40-82).

The Randomized Controlled Trial (RCT)

In a "simple" vaccine clinical trial (one without a control group, as is the case for trials in Phases 1 and 2), researchers face an inherent difficulty in determining whether a specific condition reported during the trial period is actually caused by the experimental compound or not. If a trial subject experiences a severe and immediate phenomenon following the receipt of the test vaccine, such as fainting or cardiac arrest, it could be reasonably assumed that the recently consumed vaccine was the culprit. When the side effect is less pronounced, or appears days or weeks following vaccine administration, however, the researchers decision is less obvious. For example, if the subject's temperature rises to 103°F less than 48 hours after administration of the test vaccine, the researchers do not have enough information to decide whether this is a true side effect or merely an unfortunate coincidence. One option is to have every participant who experiences a health related condition during the trial undergo a series of in depth medical examinations in order to uncover possible links to the experimental vaccine. This strategy is not feasible or economical, however, if only because the vaccine is new and its specific effect on the human body is virtually unknown. Consequently, such an investigation could prove lengthy, costly, and unlikely to yield conclusive results.

A better option is to conduct an "enhanced" clinical trial - a controlled, randomized, and blinded trial (also known as a randomized controlled trial - RCT. In an RCT, subjects are divided into two groups: the trial group, receiving the test compound, and a control group, receiving a dummy or existing compound (whose efficacy and safety profile is well known). Subjects are randomly assigned to the two groups prior to the start of the trial to ensure that the groups are virtually alike in every relevant characteristic (age, gender, area of residence, demographic status, and so on). The term blinded (or blinding), means that the trial subjects do not know which group they are in and thus do not know whether they will receive the test or dummy compound. In a double blind trial, the researchers also do not know which subjects belong to which group. Thus, prior knowledge of which compound a participant will receive is less likely to influence either subjects or researchers and skew the results of the trial. In a non-blinded trial, subjects who receive the test compound, rather than the dummy one, may complain more about side effects, since they expect them to occur. Similarly, a researcher who knows a particular subject belongs to the control group also knows that any reported side effects are not due to the vaccine and may inadvertently (subconsciously underreport medical conditions occurring during the trial period. Only when the trial is over, after all relevant information has been collected, is the specific compound administered to each of the study subjects revealed, and the researchers, with the complete data in hand, can begin the post-clinical data analysis.

When it comes to pre-licensure testing of drugs, vaccines, and other medical products, RCTs are widely considered the industry's "gold standard". The random distribution of subjects to trial and control groups, as well as the minimization of potential biases through the use of double-blinding, facilitates a reliable and meaningful comparison of trial and control group data. As an example, in a vaccine trial in which the control group is receiving a dummy compound, one can measure the level of antibodies produced in trial group subjects and compare it to that of the control group, thus getting a measure of vaccine efficacy.

Similarly, a researcher could compare the incidence of adverse events following vaccination in the two groups, thus getting an estimation of vaccine safety. The larger the number of trial participants and the better the researchers adhere to RCT standard practices, the more reliable and comprehensive the trial results will be.

Due to the high quality and reliability of RCTs, they are the method designated by regulatory agencies (and accepted by the pharmaceutical industry) for evaluating efficacy and safety of vaccines in Phase 3 clinical trials.

The Control Group in a Clinical Trial

As we have seen, the use of a control group in a clinical trial allows researchers to examine the therapeutic effect of the compound (efficacy) and the rate of adverse events it causes (safety) by comparing outcomes in the trial group with those of the control group. This comparative statistical analysis, then, will be influenced by the nature of the compound the researchers give to the control group.

As a general rule, when deciding upon the type of compound given to the control group in an RCT, there are two options. For a trial of a completely new drug or vaccine, i.e. one which does not have an approved equivalent, the control group should receive an inert compound (placebo) that does not affect the parameters measured in the trial. However, if a proven treatment already exists, it may be unethical to prevent control group participants from receiving it. For example, in trials of new cancer drugs, it is considered unethical to prevent the control group's subjects from receiving an existing drug for their illness. In this scenario, then, the control group would receive the current approved treatment. This practice is also the norm for vaccines even though vaccines are used preventatively (not treatment for an existing condition) and are given to healthy individuals.

If we apply the above guidelines to the clinical trials for the two generations of the Prevnar vaccine,' then the original Prevnar, a new vaccine that had no therapeutic alternative at the time it was developed, should have been tested in an RCT in which the control group received an inert injection as a placebo. In the trials of Prevnar-13, the next-generation vaccine, the control group should have received the (original) Prevnar vaccine, assuming that it would be unethical to deprive that group's subjects of the current Prevnar vaccine's protection, whose efficacy is already proven.

So how do researchers determine the incidence of adverse events associated with the new compound being tested in a controlled clinical trial? By comparing the rate of adverse events observed in the trial group to that of the control group. For example, if in a new vaccine's trial group of 1,000 infants there were 20 cases of high fever, and in the control group (which has the same number of subjects) there were only 10 such cases registered, the results would imply the risk of high fever in the vaccinated is twice as high as in the unvaccinated. In absolute terms, the data shows that the vaccine increases the risk of high fever occurrence from 1 in every 100 infants to 1 in 50.

When the control group's subjects are given a placebo, an inert substance not known to cause high fever, it is assumed that the incidence of high fever recorded for the group represents the background rate (or baseline rate) of the phenomenon. In other words, the background rate is the number of subjects who would experience high fever naturally, regardless of any trial intervention. In our example above, we would assume that 1 in 100 control group subjects developed high fever due to random causes (unrelated to the trial). Since the trial group would likely experience a similar background rate of high fever (1 in 100), any significant deviation from this level should be attributed to the experimental vaccine. It follows, then, that an RCT in which the control group receives an inert placebo is designed to answer the critical question of How many adverse events does the new vaccine cause? Of course, we should keep in mind that trial results are no more than a good estimation. If or when the vaccine is released to the market, the actual reported adverse event rate might deviate significantly from that observed in the clinical trial. Still, the results of RCTs are the best estimate of safety available to science during the vaccine approval process, and in many cases, throughout its lifetime.

In a trial in which the control group receives a different vaccine (as in the trial of Prevnar-13 vs. Prevnar, its predecessor), the results obtained are always relative, answering the question How many more (or less adverse events does the new vaccine cause compared to the current vaccine? For example, if (out of 1,000 subjects) 24 cases of high fever were observed in the trial group, while 20 such cases were reported in the control group, the new vaccine would appear to increase the odds of high fever by 20% (relative to the current vaccine). That is an important piece of information as it reveals how the new-generation vaccine's safety fares against that of its predecessor. However, it is impossible to calculate from a trial such as this one the absolute rate of adverse events caused by the experimental vaccine - that is, the rate of adverse events from vaccinating compared to not vaccinating. The absolute rate could not be calculated because the control group received a compound (the current vaccine) which is not inert (neutral), but rather has side effects of its own. In the above example, 24 cases of high fever were observed in recipients of the new vaccine, and 20 cases in current vaccine recipients. But how many cases would have been reported in trial subjects given a true placebo? This trial cannot answer that question; therefore, the absolute rate of adverse events caused by the new vaccine cannot be calculated from trial data. The new vaccine could be said to cause 24 cases of high fever per 1,000 subjects, but this number would not represent a reliable estimate as it does not take into account the background rate of the phenomenon, which was not measured in the trial.

In order to determine the true rate of adverse events of a new generation vaccine, a three-arm trial must be conducted, combining the two methods described above. In this kind of trial, subjects would be randomly allocated into three groups, one trial and two controls: The trial group would receive the new generation vaccine, the first control group would receive the current vaccine, and the second control group would receive an inert placebo. This trial design is considered to be of excellent quality, as it measures both the absolute rate of adverse events (comparing the new vaccine to the placebo) and the relative rate (comparing the new vaccine to the current vaccine). From a public health perspective, the three-arm trial answers two important questions: (1) How many adverse events does the new vaccine cause when compared to not vaccinating? and (2) How many adverse events does the new vaccine cause when compared to the existing vaccine?

Continuing with our Prevnar example, if the placebo-receiving control group reported, say, 8 high fever cases per 1,000 subjects, then the study would indicate that the new vaccine - which, as we recall, had 24 cases of high fever per 1,000 subjects - increased the risk of high fever by a factor of three (or, put differently, caused 16 more cases per 1,000 subjects), compared to not vaccinating.

Another scenario in which a three-arm trial would be appropriate is re-establishing the safety of a legacy vaccine that was originally tested many years ago. The environment into which today's infants are born may differ significantly in crucial health-related aspects from the environment in which a first-generation vaccine was tested decades ago. For example, the current measles-mumps-rubella-varicella (MMRV) vaccine (ProQuad) is the "grandchild" of the original MMR vaccine, which was tested in the late 1960s. Back then, the vaccine schedule consisted of only the diphtheria-pertussis-tetanus (DPT) and polio vaccines, with the first dose administered at age two months. If ProQuad were clinically tested against the original MMR and proved to have a similar safety profile, could we assume it is safe just because its grandparent vaccine was deemed safe 50 years ago? MMR vaccines are typically administered in the second year of life, after most of the infant vaccine schedule has already been delivered.

If, hypothetically, the MMR's risk of harmful side effects were related to the load of previously administered vaccines, then we could not automatically accept the present safety of the original MIMR. Remember that the MMR was first tested when the vaccine schedule consisted of only two other vaccines. If it were tested today, with many more vaccines on the schedule, some of which are given to pregnant mothers, others to newborns and infants one month of age, would it still be proven safe? And the changing vaccine program is just one aspect of the environment that may affect the safety of a given vaccine. Other factors, such as chemical exposure, changing diets, air pollution, radiation, etc., could also play a role. Therefore, a clinical trial comparing ProQuad to MMR alone is deficient, as it would rely on the presumed safety of a vaccine (MM) that might no longer be safe. Once more, a third group receiving a placebo is the proper solution to the problem.

To summarize, in a clinical trial of an (entirely) new vaccine, the control group should receive a placebo so that the absolute rate of the vaccine's adverse events can be determined. This design does not pose an ethical problem, since the vaccine has no existing alternative. In a trial of a new-generation vaccine, one control group should receive the current vaccine and another should receive a placebo (a three-arm trial).

External Control Group

Another important point to consider is that an RCT control group cannot be replaced with data from another trial, or any other externally calculated background rate. In other words, it is not scientifically valid to draw conclusions by comparing the observed rate of any phenomenon in a randomized controlled trial to the rate reported in another trial or to a rate observed in the general population.

For example, if in a particular vaccine trial the reported incidence of sudden infant death syndrome (SIDS or "crib death?) in the trial group were 0.5% (1 in 200), researchers could not then compare this rate to the background rate of the phenomenon in the population (say 0.8%), thus determining that the vaccine lowered the risk of SIDS. This is because trial participants comprise a subgroup which could possess specific characteristics, known or unknown, which are not representative of the entire population. This could potentially yield trial results that are not comparable to rates in the general population. For example, the proportion of infants participating in a trial whose parents smoke may be much lower than the background rate in the entire population, skewing the incidence of crib death in trial participants in a downward direction. Of course, skewing in the opposite direction is equally possible.

Similarly, there is little scientific merit in comparing results from different clinical trials. For example, no significant insights could be derived from comparing the results of a Prevnar trial carried out in infants from the New York area in 2010 with those of a Prevnar-13 trial conducted in Philadelphia in 2005. This is due to the randomization principle of the Randomized Controlled Trial (RCT), which requires that the trial participants be randomly divided between the trial group and the control group. Obviously, groups whose members were selected at different times and places would not satisfy this requirement. In the above examples, any differences in trial results could be entirely due to dissimilarities between the groups, such as different socioeconomic status, environmental exposures, or behavioral characteristics.

The principle described above is well known to the pharmaceutical industry and it appears in numerous vaccine manufacturers leaflets. For example, the package insert for Glaxo-Smith-Kline's (GSK) hepatitis A vaccine (Havrix) reads: "Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared to rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice.

Clinical Trials in Children

Throughout most of the 20th century, the prevailing opinion in the world of medicine was that due to the relative fragility of children (compared to adults), they should be protected from the perils of medical research. The result was a distinct lack of scientific knowledge about the effects of medical interventions (such as medication) on children. Administering medication to children, therefore, was largely a wide-ranging experiment conducted on the public. Circumstances began to change in 1977 when the American Academy of Pediatrics (AAP) published new guidelines regulating the participation of children in clinical trials. In the new guidelines, the AAP said that drugs and vaccines should be tested on the population for which they are intended - in this case, children - and that this requirement is not only ethical, but essential to their health as well.

Over the following decades, various international medical organizations have formulated ethical rules governing the participation of children in clinical trials of drugs and vaccines. According to these rules, children may only be included in experiments intended to achieve an important scientific or public health objective directly related to the health and wellbeing of children. Children should not participate in studies that do not promote such goals, such as studies designed merely to confirm the results of other studies or studies designed to advance scientific knowledge that does not concern children.

In addition, the medical code of ethics states that all parties involved in a trial must carefully weigh the potential benefit to child participants against the potential dangers involved. If the study's children cannot be expected to benefit from the studied intervention, then the intervention's inherent risk must be "minimal', especially if the subject has not consented to participate in the trial (as is the case with infants). For example, if children assigned to the control group of a drug trial were to receive a dummy medication (placebo) and a blood test, then both the medication and the blood draw must present no more than "minimal" risk. And any potential benefit must be substantial enough to justify the intervention's risk. For example, in a trial of a children's cough syrup, the risk associated with the new drug should be relatively low as the potential benefit would be relatively low, while the potential benefit in a trial of a child cancer medication would be significantly higher, thus the risk posed by the drug could be proportionately higher as well.

A more lenient approach holds that even if the experimental procedure has no potential benefit, there may be a "minor increase over minimal risk" if the experiment has the potential for gaining knowledge about the subjects' disorder, that is considered to be of "vital importance". However, even with this approach, the risk associated with the intervention must not exceed the risk a healthy child would face in everyday life and should not cause permanent or irreparable damage. In any case, there must be prior knowledge of the level of risk inherent in the procedure. If the risk is unknown, it cannot be determined to be "a minor increase over minimal risk".

Now that we are familiar with the different clinical phases of the vaccine approval process, the purpose of control groups in randomized controlled trials, and the ethical limitations imposed on children's participation in medical research, we can better examine the deliberately flawed procedure the industry uses to conduct vaccine clinical trials.

A Problem and a Solution

Let's take a moment to examine a hypothetical scenario: A major pharmaceutical company has developed a new drug against a particular medical problem. Following the drug's preliminary trials, the company realizes that the drug is associated with a relatively high incidence of serious side effects that may negatively affect its chances to win FDA approval. Let us suppose that, since the company spent hundreds of millions of dollars developing the drug and the target market segment is worth billions of dollars in sales per year, the company decides to move forward with the licensing process and start a Phase 3 clinical trial.

Given all of the above, what are the company's options, legal and illegal, for ensuring that the trial demonstrates a positive safety profile, thus clearing the way for the drug's approval?

One option is to artificially lower the incidence of adverse events reported in the trial group (the group receiving the new drug), by withholding or modifying data for specific cases. The difficulty with this technique is that for the duration of the trial, because of the enforced double-blinding, researchers do not know which subjects belong to which trial group. Thus, one cannot suppress or dilute reports for a specific group (the trial group, in this case) while leaving those of the other intact. Randomly suppressing reports would not be likely to accomplish the desired effect as the ratio of adverse events between the two groups would probably not change much.

Another theoretical option would be to modify the results following the conclusion of the clinical stage of the trial, at which point the blinding is removed and the data becomes fully available to the researchers. The difficulty with this approach is that falsifying trial data is a criminal offense, which can lead to grave consequences for the company and the researchers themselves, making this an unattractive option.

Another option would be to use various statistical techniques (which will be discussed later in the book), to build a false safety profile for the drug being tested. The difficulty with this approach is that the RCT study design greatly reduces researchers' ability to affect the results since they gain access to the full data set at a time when the data can no longer be altered. With limited ability to control the data, it can be quite difficult to eliminate undesired signals by statistical manipulation while at the same time successfully covering one's tracks.

The last option available to the company wishing to hide their product's undesirable side effects is to design a trial in which the reported rate of adverse events in the control group would likely be very similar to that of the trial group. As described previously, the RCT control group represents the baseline rate to which the trial group is compared. A similar proportion between the two groups would indicate that the adverse events reported in the trial group were the result of "background noise" only and not caused by the experimental drug. This technique has three distinct advantages: (1) It is 100% legal, (2) it is very effective, and, as it turns out, (3) it has the full approval of licensing authorities around the world. As we shall shortly see, this method is exactly the one vaccine manufacturers employ to deliberately obscure the real incidence of vaccine adverse events.

The entire vaccine program is founded upon this deception.

Fake Placebo

It is virtually impossible to state the bottom line of the analysis presented above mildly, so here goes: **Vaccine trials in general, and childhood vaccine trials specifically, are purposely designed to obscure the true incidence of adverse events of the vaccine being tested.**

How do they do this? By using a two-step scheme: First, a new vaccine (one which does not have a predecessor), is always tested in a Phase 3 RCT in which the control group receives another vaccine (or a compound very similar to the experimental vaccine, see explanation below). A new pediatric vaccine is never tested during its formal approval process against a neutral solution (placebo). Comparing a trial group to a control group that was given a compound that is likely to cause a similar rate of adverse events facilitates the formation of a false safety profile. The rate of adverse events of the tested vaccine is said to be similar to the "background rate", hence it is considered safe. The researchers, and the vaccine manufacturer they work for, seem to "forget" that the compound they administered to the control group is a bioactive substance, carrying its own risks and side effects, and hardly represents the baseline or background rate that is essential to an RCT for a new vaccine.

The vaccine is subsequently approved and added to national vaccine programs throughout the world. Then, when the "next generation" vaccine comes along, its pre-licensing clinical trial will always compare the new vaccine to the current vaccine and never to a placebo. Thus, all parties involved ensure that the true rate of vaccine adverse events is never discovered - for either the original or upgraded vaccine - and that rate is never shared with the public, or even the medical world.

The practice of giving a different vaccine to the control group in an RCT of an entirely new vaccine and calling it "placebo" is a deliberate misrepresentation of the term. As explained previously, a placebo is a compound (or procedure) that does not affect the parameters measured in the trial. When testing the efficacy of a new vaccine, researchers measure the level of disease antibodies in both study groups, so the substance given to the control group must not affect that antibody level or the comparison becomes meaningless. For example, in a hypothetical new hepatitis C vaccine trial, it would not make scientific sense to inject the control group subjects with a compound that could increase (or decrease) the subjects' hepatitis C antibodies. Doing so would preclude a valid assessment of the effect of the vaccine on the antibody level, as the substance taken by the controls could have distorted the comparison."

The above analysis holds true for safety testing as well. If the compound given to the control group has its own significant side effects, it cannot be regarded as a true placebo. If the rates of adverse events observed in the trial and control groups appear similar, is it because the experimental vaccine is safe or because the control compound is just as unsafe as the vaccine? It would be impossible to know. Giving the control group an active substance in an RCT intended to test safety would be a bad design decision, then. Yet this is exactly how new vaccine Phase 3 trials are performed: Instead of a placebo, the control group receives a different vaccine, which is certain to cause its own adverse events and can in no way be deemed a neutral substance.

This practice of administering a different vaccine to the control group in a new-vaccine trial has no bearing on efficacy testing: It is highly likely that the control vaccine, which usually targets a different disease, would have no effect on the antibody level of the disease targeted by the test vaccine.

Thus, using our hepatitis C example, if the control group subjects in the vaccine trial were given the Prevnar vaccine, no change in their hepatitis C antibody level would be expected; thus, the true efficacy of the test vaccine could be determined. But this lack of effect is not the case when it comes to safety: Because the Prevnar vaccine has its own side effects, it cannot be considered neutral in this context. Therefore, the true rate of adverse events for the experimental hepatitis C vaccine cannot be determined by comparing it to the rate in the group that received Prevnar since the controls did not receive a neutral compound.

This deliberate distortion of the placebo concept in clinical trials of new vaccines is so prevalent that researchers and vaccine package inserts frequently refer to the bioactive compound given to a control group as "placebo", even when it's clear it is another vaccine or a similar bioactive compound, which in itself is not safety-neutral. Falsely using the term "placebo" allows researchers to conclude that the new compound "was proven safe" because its rate of adverse events was similar to that of placebo - even though the substance the control group received was decidedly not a placebo. For example, in one of the DTaPo vaccine trials, the rate of hospital admissions in the trial group was almost 1 in every 22 subjects. The researchers did not consider this statistic alarming, however, because in the control groups that received different DTP vaccines, the hospitalization rate was similar. 16 Was such a high hospitalization rate in trial participants unrelated to the vaccines used, or were they the main culprit? Only the use of a true placebo control group could answer that question.

No logical explanation can be found for the ubiquitous practice of administering bioactive compounds to control groups in trials of new vaccines other than a desire to conceal the true rate of adverse events of the vaccine. Testing a new vaccine against a placebo in an RCT is the simplest, safest, cheapest and most reliable option. Saline (sterilized salt water), for example, is a safe, reliable, widely available, and inexpensive compound - certainly when compared to a vaccine. Because it does not cause significant adverse events, nor does it produce disease-specific antibodies, it provides a reliable baseline for both safety and efficacy testing and is therefore ideal for control group usage. Calculation of the true rate of adverse events of the test vaccine becomes straightforward and simple. Despite its clear benefits as a placebo, vaccine makers prefer not to use saline in vaccine trials, and the reason for this should be obvious by now.

Mere Coincidence or Deliberately Flawed Design?

As we've clearly illustrated in the preceding sections, not one of the vaccines the CDC recommends all American children receive was tested for safety in a Phase 3 clinical trial where the control group received an inert placebo. All the vaccines reviewed in the preceding pages - of which tens of millions of doses are administered to infants and toddlers in the US every year - were tested in trials which did not include any control group at all, or ones in which the so-called control group received at least one other vaccine.

Is it just coincidence that none of these vaccines has been tested against a true placebo, despite the fact that in many cases doing so would have been easier, cheaper, and yielded more valid results than the testing that was done?

Is it just an accident of fate that the accepted methodology of all childhood vaccine trials obscures the real rate of adverse events of the new vaccine? That seems highly improbable.

As explained at the start of this discussion, testing the safety of a next-generation vaccine against its predecessor is justifiable on ethical grounds: Withholding an existing and proven treatment from control group subjects would be immoral. However, there is no justification for conducting a chain of trials (turtle upon turtle upon turtle) that ultimately stands on nothing but air. Moreover, what possible rationale could justify trials for new vaccines wherein the control groups receive other (sometimes experimental) vaccines? Would a safety trial for a new cigarette have any credibility at all if the "control" group consisted of subjects who smoked a different kind of cigarette?

Whether or not you believe this trial methodology is ethical, its consequence remains the same: The true rate of adverse events of routine childhood vaccines is virtually unknown; therefore, there is no scientific basis for claiming they're safe.

The fact that we don't know how often childhood vaccines hurt the children who receive them casts a dark shadow over the legitimacy of vaccine programs the world over. But that is not all. Even worse, as we shall shortly see, safety trials conducted for some childhood vaccines blatantly and seriously violate the medical code of ethics. In any vaccine clinical trial, a balance must be struck between the vaccine's potential benefits (disease protection) and potential risks (adverse events). When control subjects in vaccine trials receive another type of vaccine, even if it's done in order to obfuscate the real rate of adverse events of the vaccine being tested, the compound they receive is at least of some potential benefit to them. However, in rotavirus vaccine trials this imperative ethical risk-to-benefit balance was blatantly violated.

The Clinical Trials of the Rotavirus Vaccines

Designing clinical trials for the RotaTeq and Rotarix vaccines was particularly challenging for their manufacturers, Merck and GSK, respectively. To begin with, the first rotavirus vaccine brand (RotaShield) was recalled from the market after it was found to significantly increase the risk of intussusception, a highly dangerous condition in infants. This meant that clinical trials for the new rotavirus vaccines had to adhere to higher safety standards. In addition, the companies faced an equally serious problem: With RotaShield off the market, there was no suitable vaccine to give to control group subjects.

A rotavirus vaccine dose, a few drops of an opaque liquid, is consumed orally. Hence, the control group in its clinical trials could not receive a vaccine administered via injection as it would violate the RCT blinding principle. If the trial group were vaccinated orally, while the control group was injected, it would be easy to tell the two groups apart. At the time the rotavirus vaccine trials began, there was no other orally ingested vaccine licensed for use.

The use of the live polio vaccine (OPV), also consumed by mouth, was terminated in Western countries several years earlier.? As a result, there was no oral vaccine available to compare with rotavirus vaccines in clinical trials.

Another option would be to give the control group a few drops of a neutral liquid, such as a solution of sugar or salt water. These compounds are safe, inexpensive and convenient to use - ideal for the purpose of testing the vaccine's efficacy and safety. Because these were entirely new vaccines, which had no alternative, there were no ethical objections to using such a solution.

So, on the one hand, rotavirus vaccine manufacturers did not have a ready-made vaccine available for use in the control group, and on the other, there was no impediment to using a cheap, available and effective substance, such as sugar water. How, then, did they choose to conduct their Phase 3 clinical trials? A preliminary examination of the clinical trial record of the rotavirus vaccine shows that the control groups in the RotaTeq and Rotarix trials received... a placebo! Was this, then, the industry's first breach of the sacred tradition that vaccines never be tested against a true placebo? Were the rotavirus vaccine trials the first to provide reliable and relevant information about the rate of adverse events of a childhood vaccine?

The answer to these questions is, unfortunately, "no and no".

Examining one of the licensing documents submitted to the FDA by GSKs indicates that the placebo received by the control group in the main Rotarix trial (which included approximately 63,000 infants) is nothing but the tested vaccine without its antigenic component. This compound, the vaccine-sans-antigen (sans means without), is well suited for testing the efficacy of the vaccine as it does not produce rotavirus antibodies. However, when it comes to safety, it's a whole different ballgame: The vaccine-sans-antigen is a potentially potent compound whose side effects are likely to be quite similar to those of the vaccine being tested.

And what was the placebo in Merck's RotaTeq vaccine trial? That's difficult to say because Merck deleted its description from the licensing document submitted to the FDA. It appears that the trial's placebo is a trade secret, which implies its contents were very similar to the vaccine's. Further examination of RotaTeg documents supports this hypothesis: In another RotaTeq clinical trial, the control group received the vaccine-sans-antigen, similar to the compound control group subjects received in the Rotarix trial.

The bioactivity of the compounds given to the control groups in rotavirus vaccine trials was seemingly apparent in the rate of adverse events reported in the trials. In the Rotarix trial, about 1 in 30 control group subjects experienced a "severe" medical event (a rate which was even slightly higher than that of the trial group), and a similar proportion of participants was hospitalized. In addition, 16 infants suffered intussusception and 43 died." In the RotaTeq trial, similar rates were recorded in the control group: Serious adverse events were reported in 1 of every 40 subjects, 15 suffered intussusception, and 20 infants died.

Using the word placebo to describe the vaccine-sans-antigen leaves the false impression that it is a safe compound that has no side effects of its own. Formal documents, which reference the rotavirus vaccine trials, rely on the supposed biological neutrality of that "placebo". One example is the Rotarix vaccine package insert, which states in the clause discussing the rate of intussus-ception reported in pre-licensure trials: "No increased risk of intussusception was observed in this clinical trial following administration of ROTARIX when compared with placebo."63 (The trial in question is the same trial referenced above. There are plenty of other examples, too). Nowhere is there any reference to the actual contents of that "placebo".

The rotavirus vaccine makers were evidently able to find a creative solution to the challenge they faced. They gave their trials control groups compounds that were very similar to their vaccines, and, as was no doubt expected, the resultant rates of adverse events were not significantly different from those observed in the trial groups. In future trials of next-generation rotavirus vaccines, GSK and Merck will be able to give their control groups the standard "placebo" - the currently licensed vaccine - whose safety "was already proven" in its pre-licensure trials.

But there's a fly in this sticky ointment.

Unethical Trials

As previously discussed, the ethical standards for using children as subjects in clinical trials are exceptionally high. Clinical trial designers must ensure that planned procedures are balanced with respect to the expected benefit and risk to the participating infant or child. If a child subject is likely to receive no benefit, the potential harm must be "minimal" or only "slightly above the minimum", and by no means permanent or irreparable. In addition, the risks associated with any procedures must be well known in advance.

In stark contrast to the standards above, tens of thousands of infants in the control groups of the rotavirus vaccine trials received compounds that could provide no potential benefit to the recipient yet carried significant risk. Neither GSK's nor Merck's vaccine-sans-antigen could possibly prevent rotavirus as they did not contain the antigenic particles that evoke immune reactions to the virus. On the other hand, these compounds had significant potential to cause harm, as demonstrated in the trials. (Remember, 1 in every 30 or 40 control group subjects experienced a serious adverse event). In addition, the safety profiles for the vaccines-sans-antigens were unknown (and, for all we know, still are) as they were new compounds specifically formulated for the rotavirus trials with no documentation of past safety studies. Hence, the health risks associated with administering them to infants was undetermined.

To sum up, tens of thousands of infants were given an utterly useless compound whose safety was unknown and whose side effects could be (and probably were in some cases) severe and permanent. Thus, the Phase 3 clinical trials of the rotavirus vaccine constitute blatant violations of the medical code of ethics.

This ruthless breach of ethics and morality is highlighted by the fact that there was no scientific justification for giving the vaccine-sans-antigen to the control group other than a malicious intention to conceal the experimental vaccine's true rate of adverse events. Using a real placebo that posed no health risk - a few drops of sugar or salt water - would have cost less and led to more scientifically valid conclusions by enabling straightforward calculations of the true adverse event rates as well as vaccine efficacy.

The manner in which the rotavirus vaccine trials were conducted raises grave questions which should not be directed solely toward the vaccines' manufacturers. The FDA supervises the vaccine approval process, and it is the FDA that approved these trials. The vaccine also received CDC approval and that of other health authorities around the world, even though the vaccine trials unnecessarily endangered tens of thousands of children and may have caused serious harm to hundreds, as well as dozens of needless deaths.

The Declaration of Helsinki is the ethical code governing the conduct of human medical experimentation. The Declaration was formulated for the medical-scientific community by the World Medical Association and is considered the ethical cornerstone of the medical research field. It leaves no doubt as to the ethical violations perpetrated in the rotavirus trials:

> *Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed. When the risks are found to outweigh the potential benefits [...] physicians must assess whether to continue, modify or immediately stop the study.*
>
> *...[A] potential research subject who is incapable of giving informed consent [...] must not be included in a research study that has no likelihood of benefit for them unless [...I the research entails only minimal risk and minimal burden.*

The Nuremberg Code, the medical code of ethics established in the late 1940s to bring Nazi doctors to justice, constitutes the basis of the Declaration of Helsinki. It too underlines the immorality of the rotavirus vaccine trials: "[An] experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury." A similar conclusion was also reached by a World Health Organization (WHO committee that recently examined placebo use in clinical trials.

Ponder it as you will, you won't find a satisfactory explanation for the way the rotavirus vaccine trials were conducted Other than the malicious desire to assist the manufacturers in obscuring and concealing the vaccines' true adverse event rates. This demonstrates that the public health establishment is willing to go to great lengths to maintain the pretense of vaccine safety; casting aside medical ethics and even fundamental principles of morality in the process.

Summary

Vaccines, as opposed to drugs, are given to healthy babies and thus must meet a particularly high safety standard. Clinical trials of new vaccines must be impeccably designed and performed, thereby providing high-quality, reliable data about the products efficacy, and more importantly, about their safety. Anything less is socially and morally unacceptable.

Vaccine manufacturers and health authorities worldwide frequently assure us, the public, that vaccines are tested at the highest possible level and that the rigorous series of clinical trials they undergo as part of the licensing process ensures that vaccines are truly safe and effective.

These assurances, however, are meaningless at best and deliberately misleading at worst.

As we have seen in this chapter, vaccine trials are designed and performed in such a way as to ensure that the true extent of adverse events is hidden from the public. There is not a single vaccine in the US routine childhood vaccination program whose true rate of adverse events is known. The assertion that vaccines cause serious side effects in "one in a million" vaccinees contradicts the results of numerous clinical trials in which serious adverse events were reported in 1 in 40, 30, or even as few as 20 vaccinated infants. After becoming acquainted with the finer details of vaccine safety trials, hearing the familiar tune of "a similar rate of adverse events was reported in the control group (which received another vaccine or similar compound)" comes off as ludicrous, cynical, and patently immoral.

Current vaccine clinical trial methodology completely invalidates the claims that vaccines are safe and that they are thoroughly and rigorously tested. And pulling out that bogus card completely topples the childhood vaccine program's house of cards, as officials' assurances of vaccine safety rely primarily on deliberately flawed, industry-sponsored clinical trials.

Furthermore, some of the clinical trials that have been conducted for routine childhood vaccines, which were approved by relevant health authorities, blatantly violated the medical code of ethics (the Declaration of Helsinki) and fundamental principles of morality. In these trials, infants in the control groups were given completely useless compounds (an antigen-free vaccine) whose safety was unknown and which had the potential to cause serious and irreversible damage to health, including death.

Any reader looking for a quick and definitive understanding of the truth about vaccine safety - well, you can put this book down right now. You have your answer: The entire vaccine program is based on a deliberate cover-up of true vaccine adverse event rates. This seemingly mighty fortress, carefully constructed over many decades and fortified by countless officials, researchers, and physicians - actually stands on nothing but turtles all the way down.