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From the Editor's Desk

JSS Technical Editor
C. G. Muniak P.hD.

Indexing the JSS

Over the years some authors have asked about whether the JSS was indexed as this would influence their decision to publish in our journal. Unfortunately, the answer was no. We looked into the subject of indexing, but could not muster the resources to make much progress, until now. Stephen Thomas, one of our associate editors, has recently done an excellent job on the indexing issue. The JSS has now been indexed by a number of providers: Google Scholar, Crossref, ROAD, SafetyLit, BASE, Internet Archive Scholar, Dimensions, Unpaywall, UlrichsWeb, OCLC Worldcat and Fatcat. This should increase the visibility of the JSS to a wide audience. We anticipate that this will increase academic interest which will result in more submissions and possibly more membership for the ISSS.

This issue of the JSS contains two papers that push the boundaries of what many of us think of as system safety, while the third paper is a bit more "traditional."

The first technical paper in this issue is "The Delta Variant" by Dr. Richard Zito. Dr. Zito continues his series of articles on the COVID pandemic and discusses the implications of the delta variant.

The second technical paper is "Global Warming and System Safety "by Dr. Malcolm Jones. This paper outlines the system safety application possibilities associated with global warming solutions.

The third technical paper "Assessing the Software Control Autonomy of System Functions in Safety-Critical Systems" by Dr. Vu N. Tran and Viet N. Tran describes the process and rules for assessing Software Control Categories (SCCs) for programs following MIL-STD-882E.

The "TBD" column by Charlie Hoes discusses some of Charlie's opinions concerning the use of the risk matrix.

As usual, I welcome your comments, letters to the editor and article submissions.

Regards,
Chuck

We Want to Hear from You!

Journal of System Safety is seeking papers and articles on many topics where system safety makes a critical contribution, including:

- Explosive Safety
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- Chemical Safety
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TBD

by Charles Hoes

As a long time, System Safety engineer, working on major programs that implement system safety programs in accordance with Mil-Std-882, I understand that the topic of this post is rather controversial since it questions one of the main tenets of the profession – that a formal risk assessment based upon a pre-established Risk Assessment Matrix is a necessary part of the process.

For those that might not be "in the know", in the world of system safety risk is considered to be the probability and severity of the outcome of an "accident" or undesired event. The idea is that if something goes wrong (perhaps the rung of a ladder breaks while someone is using it) it will result in an injury or damage of some kind. Thus there is a severity (damage or injury) aspect, such as a broken bone, and a probability aspect – the probability of the hypothesized outcome.

The system safety process is most effective if it is begun while the system being investigated is still just a concept, before the concept has been turned into detailed designs or implemented into a product. Thus, at the beginning it involves the investigation of ideas. The "system" (whatever is being considered) is evaluated or studied in an attempt to find as many hazards, and thus potential accidents, are lurking in the design. Each of these potential accidents is evaluated to determine the severity of an injury and the probability of that injury occurring to determine the potential risk.

The risk is assigned a code typically taken from a table such as this:

RISK ASSESSMENT MATRIX				
SEVERITY / PROBABILITY	Catastrophic (1)	Critical (2)	Marginal (3)	Negligible (4)
Frequent (A)	High	High	Serious	Medium
Probable (B)	High	High	Serious	Medium
Occasional (C)	High	Serious	Medium	Low
Remote (D)	Serious	Medium	Medium	Low
Improbable (E)	Medium	Medium	Medium	Low
Eliminated (F)	Eliminated			

Sample Risk Assessment Matrix

The risk descriptions land somewhere on the table, indicating the "level of risk "of the hypothesized event. A central idea about this process is that level of risk can be the same (or similar) for various combinations of severity and probability. The idea is that a frequent outcome having a negligible injury might be equivalent from the risk management point of view as one that has a catastrophic outcome that is unlikely to ever occur (improbable). The hope is that this approach provides a consistent means for prioritizing efforts to reduce the overall risk. The seemingly obvious result of this is that if resources are scarce (which is always the case), then it is better to put your effort into eliminating "serious" or "high" risks than "low" ones. In fact, it might be a policy that "high" risks are not allowed and must be reduced to a lower level, or the project can't go forward.

This all makes perfectly good sense and gives the appearance of being objective and therefore somehow "scientific." Certainly the idea that risk is related to the combination of severity and probability makes sense. It appears to be a straightforward cost-benefit evaluation. However, there are many problems with actually using a table such as this for making decisions.

The definition of risk being a multiplication of probability and cost comes from financial risk management where all of the severities (costs) are described in terms of economic value (dollars), while probability is taken from a statistical evaluation. Modern economists treat this as a calculus problem of adding (in a calculus fashion) all of the possible outcomes and associated cost to find an "expected" value for the investment. As long as the expected value of the return is greater than the expected value of the costs of the associated risks it is judged to be a "good" investment. Many millions of dollars are invested in the process of estimating the expected values costs and returns in an attempt to find the "optimal" investment choices. The concept behind this process is pretty apparent and "scientific". If you want to understand which option has the least risks, all you need to do is figure out the projected dollars lost and the probability of each. Simple, except that even with economic decisions it is not so easy to predict either of these values or understand the statistics behind them.

However, safety risk assessments are much more difficult when there are illnesses and injuries being considered. Assuming that the probability of postulated outcomes can be determined (no small feat in itself), attempting to put a rational value on the severity of the postulated outcomes is fraught with difficulties and uncertainty. For example, I am not sure how many broken fingers equals a broken foot, or how many broken feet are the same as death. I can't multiply the severity of a broken foot by the probability of that broken foot and get a meaningful answer – in order to perform this operation, the severity needs to be a numerical value, usually dollars. Insurance companies place a value on body parts, but I don't find this particularly satisfying. I am not comfortable about performing cost/benefit analyses based upon my opinion of the value of someone else's foot. I am not convinced that I can properly determine how much each of these types of outcomes is "worth". When I ask the question of how much *my* life is worth there is nothing with a higher value. There is no inherent cor-

"Assuming that the probability of postulated outcomes can be determined (no small feat in itself), attempting to put a rational value on the severity of the postulated outcomes is fraught with difficulties and uncertainty."

Photo: Pexels

respondence between an injury or illness and its dollar value. There are pronouncements, regulations and actuarial tables, but these are just made up by people, there is no inherent measuring stick.

In addition to the problem that you can't actually multiply probabilities by an outcome (even if you find a way to quantify the outcome) the outcomes being investigated almost always have a range of outcomes. Using the previous example of the broken ladder rung, this might lead to a range of injuries ranging from none to death. This would result in a separate risk assessment for each hypothesized outcome – the total risk associated with falling off the ladder is the sum of these risks, but we don't know how to add risk categories because we don't know how to properly quantify severity. A common approach to solving this problem is to use a value that is considered to be the highest "probable" or "credible" risk. I really don't know what the most credible means beyond the probability of the event, it sounds like circular logic to me.

It seems to me that rather than going down the path of trying to find more rational, scientific, or supportable values for the risk assessments, perhaps we should examine the purpose of the exercise to see if we can find a better solution.

A common assumption is that risk assessments are performed in order to prioritize actions to reduce the risks of the overall project. The concept is that resources are always limited, therefore it is important to take care of the high risk concerns first. This "seems" logical, but is it? It implies that we can ignore low risk hazards until all of the higher ones have been resolved. However, in an actual design/development project that doesn't, and shouldn't, happen. Complex design/development programs don't follow a linear process. Instead, many parts and pieces are developed in parallel by many individuals. Features of controls are identified and integrated as the program develops – controls for all levels of risks are not "prioritized" – they are either found and integrated into the design, or not. Therefore, the risk table is NOT an effective prioritization tool. Potential risks need to be identified and controlled to a level that is deemed to be "acceptable" – regardless of the level of risk involved. They are not "prioritized."

If risks are not prioritized using the risk matrix, perhaps the matrix can somehow be used to determine when the risk has been reduced enough to be considered "acceptable." Maybe it can help with determining how much risk is "acceptable." A lot of engineers, managers and regulators like the idea of defining levels of risk that are "acceptable" and therefore don't require further efforts to reduce them. This might be an appropriate solution if we have confidence in the determination of the risk parameters (probability and severity of an unwanted outcome). However, as discussed earlier that is fraught with difficulties and quickly becomes unaffordable. This is seldom a viable solution because of the unknowable aspects of the process.

Even if it were somehow feasible to accurately determine the risk in terms of probability and severity, there is still an open question about how to determine "acceptable" risk levels. Safety risks pose dangers to many different stakeholders in a decision. The company developing the project has financial (and moral) risks, the program manager another set of concerns, the development team another, the user another, society in general yet another. Those that might be directly injured may have different acceptance criteria than those that intend to make a profit from the program/product. Not only that, but there are many different things that come into play when making the determination of "acceptability" including things such as utility, perceived value, dread of the type of injury, social norms, and many others. There is no single, universally agreed upon method to determine "acceptable." It always involves opinion, ethics, morality, cost, and perceptions – in other words, personal judgment.

Instead of using the risk matrix as s measure of acceptability, perhaps it might be useful as a communication tool assisting the safety engineer to express an opinion about the resulting risks. The risk code and/or position on the risk matrix table can't be used to determine "acceptability", it can't be used to determine a "priority" for action – it really can't be used for much, except that it might help inform the decision makers about the "importance" of an identified hazard. That in combination with a lot of other information can help make the ultimate decision about whether or not to spend time and money to fix a potential problem.

I wonder if there is sufficient value in doing "false" risk quantification to offset the many abuses to the process that have occurred in the past. The reason that I call them "false" isn't that I think anyone is attempting to hide or obscure anything. My conten-

tion is that they are seldom more than an expression of "engineering judgment". It might be better to express that judgment in a format that clearly identifies it as a judgment, rather than in a form that has the appearance of a "quantified truth."

Most managers and regulators are looking for a quick, simple and responsibility-free (and hence liability-free) means of deciding the question of acceptability. Abuses abound, showing up as a regular feature of in-depth accident investigations showing that the "acceptable" decision was determined by whether or not the anticipated risk code fell within an essentially arbitrary criteria. While the criteria may have been met, the risks were not acceptable as evidenced by the outcome. There are far too many examples of these categories being converted to elements of a cost/benefit analysis showing that solving the problem is more expensive than the cumulative costs to the unknown future injured parties. Unfortunately this use of the risk codes can lead to rationale along the lines of, "I can't afford to reduce the risk because it would cost me more than your cost of your injuries." This is a rather odd risk acceptance criteria, but common.

I wonder if it might not be better to drop the risk matrix entirely and instead use an interactive process where "experts" (stakeholders) with a range of points of view come together to achieve a unified decision concerning the acceptability of the risks. All of the stakeholders need to agree that the risks are acceptable, not just a subset – and definitely not because they met an existing criteria. This idea is close to the "old" approach of "concurrent engineering" in that all of the stakeholders are included in the decision making process at the same time, rather than each group working separately and then "throwing" a finished project "over the wall" to be accepted or rejected by the using community. The idea of "consilience" comes close to what I have in mind. One definition of consilience is, "the perception of a seamless web of cause and effect." This is opposed to the often used idea of a single cause and effect genesis leading to accidents. A single cause is seldom "the" cause of an accident, it is much closer to a seamless web of cause and effect.

Perhaps the risk matrix might be used as a communication tool, but the real risk acceptance process brings into consideration many, many important considerations that were not included in that part of the safety assessment. To minimize confusion and misuse, perhaps it would be best to drop the use of the matrix entirely, using well thought out rationale statement and studies instead of attempting to over-simplify the process.

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The Delta Variant

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ABSTRACT

Nothing is harder than to realize when you are living through *history*. For most of us, each day is pretty much like another. There is nothing historically remarkable about that. Occasionally, however, our lives are punctuated by events, both natural and man-made, that are apocalyptic and often (but not always) beyond our control – natural disasters, war, pestilence, and famine. These are the events that the historian must recognize. At this time, it is the COVID-19 pandemic that demands to be recorded by "his-story" so that posterity will know what we did right, and what we did wrong. This author has taken up the challenge of producing accurate, unbiased, comprehensive, technical annals of the global coronavirus pandemic that began in 2019. "The Delta Variant" is the third publication in this series. We are now near the end of the third year of the pandemic (summer/fall 2021). As predicted by this author, it has been a draconian year. Last year's peak in the number of active cases was not a global maximum for the pandemic in the U.S., since this year the number of active cases has already surpassed it. Without knowing where the global maximum lies, no accurate predictions can be made about the magnitude and duration of this modern plague. The "Delta Variant" (δ-variant) of COVID-19 has greatly complicated efforts to combat the virus. The "anti-vaxxer" movement, uncontrolled migration of people into and within the U.S, and the relaxation of safety measures during the late spring and early summer in the U.S. also contributed difficulties. All of these problems were foreseen by the author and were discussed in the second paper ("Vaccine Safety") of this series on the COVID pandemic. However, our biggest problem in the U.S. was an over confidence born of a natural summertime trough in the daily infection rate. We wanted to believe the infection was past, so we ignored the experience of India, and our administrators fueled our hopes with their words and actions. We believed because we wanted to believe – *except for this author*. So, what went wrong? What is a δ-variant, and why is it so dangerous? That will be the topic of this publication.

INTRODUCTION

There are so many places where one could begin describing this year's events that it is difficult to choose one. Nevertheless, there is only one terrible ending – the devastating number of new infections this year. So, perhaps the author should tell the δ virus story backwards. Figure 1 shows the number of active cases since the pandemic began.

At this point in time, it is impossible to know what type of statistical model (Gaussian, Rayleigh, Weibull, something else?) to apply to the global (long-term) data set because a global maximum (for the entire data set) has not yet been reached. However, short term predictions based on extrapolation of linear and quintic polynomial trends in the available data

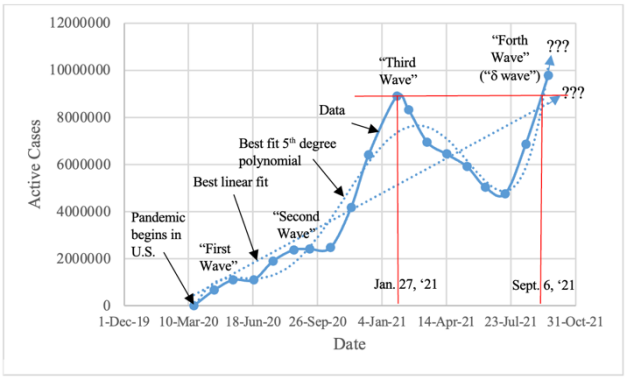

Figure 1: Active cases of COVID in U.S. versus date. *From Worldometer, (https://www.worldometer.info) Sept. 28, 2021. Linear and quintic polynomials are the best trend models for the data curve.*

(capturing seasonal trends, behavioral trends, technological trends, etc.) suggest that the number of active cases will continue to rise after Sept. 19, 2021. A series of peaks with decreasing amplitude (active cases vs. time) will be needed before the U.S. can be reasonably confident that the pandemic is waning. And that may take a few years. Once a global maximum has been established after a time tmax from the beginning of the pandemic, it will take another time interval tmax after the maximum before an approximate model can be adopted for active cases. Furthermore, it will take a time interval 2tmax after the maximum before that model can be refined to a reasonably accurate form. Even if this winter's local peak were the global maximum we are all looking for, it will still be 2 more years before approximate projections for active cases can be made. Furthermore, accurate projections will not be available for at least 4 years (Zito, 2020a). The outlook for total deaths is just as discouraging (Figure 2). As of Sept. 19, 2021, it looks like a simple linear increase with no horizontal plateau in sight! Globally, the outlook for daily deaths is considerably brighter due to ongoing vaccination and the use of post-infection therapeutic agents. These statistics and drugs will be covered in detail in another publication of this series.

At this point one might reasonably ask, "How did the author know that this outbreak would happen given that the authorities, including health care authorities, were so confident that an end was near?" The answer is that the opinion of the authorities, although important, does not constitute proof by itself. Only mathematics, and especially experimental evidence, are the arbiters of truth.

In this case, all the experimental evidence from the δ-variant outbreak in India (Li, Agarwal, 2021) suggested that we were making a *huge* mistake. It must always be remembered that the author's job is to tell the truth. Although the authorities are usually right, it is *not* the author's job to make excuses for them when they are wrong! Even if it's the CDC!

S-PROTEIN MUTATIONS AND THE δ-VARIANT

Starting in this section, it would be best for the reader to examine the first two coronavirus papers in this series (Zito. 2020b, 2021). That background information will be invaluable, and it cannot all be repeated here other than to make a few brief statements intended more to reawaken the memory than to be pedagogic.

In Figure 1 of the "COVID-19" paper (Zito, 2020b), the "S-protein (the binding protein) of the coronavirus envelope was depicted schematically as a slender triangular needle. Actually, the S-protein looks more like the "club" in Figure 3 below, and the scale of this cartoon is now 100x smaller than that of Figure 1 in the "COVID-19" paper (Zito, 2020b).[1] Each S-protein is composed of two protein subunits, S1 and S2, each a complete protein in its own right. The two proteins stick together because the amino acid residues (building blocks) that compose these proteins (Zito, 2020b) poses chemically active side chains. These side chains can interact with one another through disulfide bonds (from a sulfur atom in one subunit to a sulfur atom in its neighbor subunit), as well as hydrogen bonding, Van der Walls forces, and other types of non-permanent interactions.

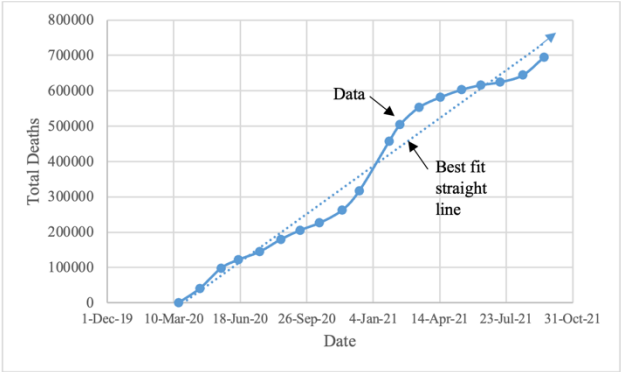

Figure 2: Total Deaths versus Date for the U.S. *There is no indication of any negative curvature as of Sept. 16, 2021. The author's sobering predictions for this year from "Vaccine Safety" (Zito, 2021) have come true.*

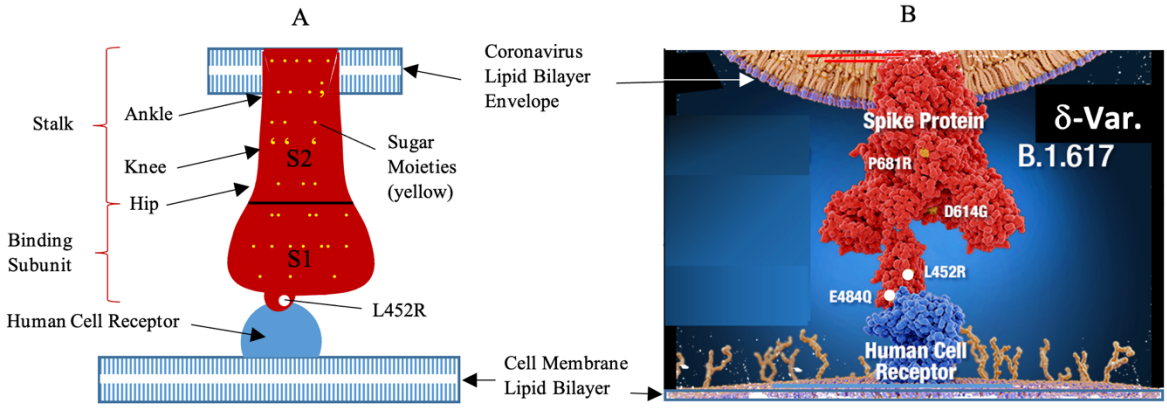

Figure 3: A) Cartoon of a coronavirus spike protein *(red) interacting with a cellular binding site, or human cell receptor (blue sphere). The S1 subunit contains the binding site, while S2 is used to support S1 above the viral envelope. The subunit structure of a protein is called its quaternary structure. The yellow dots are sugar moieties while the white dot marks the location of an important amino acid mutation site.* ***B) Computer simulation of a spike protein*** *interacting with a cellular binding site (modified by author from Ayass Biosciences, 2021). Individual atoms can be discerned. The view is about 1000 Å (or 0.1 μ) across. Several δ-variant (B.1.617) amino acid mutation sites are shown (where L = Leu = Leucine, R = Arg = Arginine, P = Pro = Proline, D = Asp = Aspartic Acid, G = Gly = Glycine, E = Glu = Glutamic Acid, Q = Gln = Glutamine). The things that look like red "weeds" on the cell surface are cellular proteins. The structure of all of these proteins is based on X-ray diffraction studies of these complex biological molecules.*

Recall from "Vaccine Safety" (Zito, 2021) that hemoglobin has four such subunits.

The tip of the S1 subunit is responsible for binding, whereas S2 is called a stalk and is used for support. The stalk is broken up, imaginatively, into an ankle, knee, and hip. The ankle anchors the S-protein in the virus's semi-fluid lipid bilayer envelope. And, as the name "ankle" might suggest, some S-protein movement can take place (like the tubes, or spines, on the back of a sea urchin). In the first publication of this series (Zito, 2020b) it was noted that the spike protein (S-protein) was a glycoprotein, meaning that the S-protein has sugar moieties (molecular fragments) attached. These are the yellow spots in the cartoon of Figure 3A. The reason for this can now be explained. Sugar is not normally recognized by the immune system as "not self" because the body needs sugar. So, the dusting of sugar fragments over the surface of the S-protein is an insidious disguise, or cloaking device, to make the coronavirus invisible to antibodies and white blood cells (much more will be said about this later)! Fortunately, the disguise is imperfect, as we will see!

Next, we must increase our magnification by another factor of 10 and focus in on the structure of the S1 subunit. A protein, when first created, is nothing more than a string of various amino acids chemically linked together by polypeptide bonds like a string of pearls, each with a letter on it that represents a particular amino acid (and there are 20 types) (Zito, 2020b). This linear sequence of amino acids is called the primary structure of a protein. After creation, the protein folds into its secondary (local) and tertiary (long range) structure, which may look, for example, like the S1 protein in Figure 3. Folding occurs for the same reasons (and involves the same types of bonds) that make subunits stick together.[2]

Sometimes, however, a mutation occurs in the primary amino acid sequence, for reasons that will be explained in the next section. When that happens, one letter (label) can change to another. Therefore, to specify a particular mutation it is necessary to specify the original letter, the location of the mutation from the beginning of the amino acid sequence, and the new mutated letter. Hence, L452R means that leucine (denoted by L), the 452nd amino acid in the S1 subunit, has changed to the amino acid arginine (denoted by "R"). Similarly, E484Q means that glutamic acid (E), the 484th amino acid, has changed to glutamine (Q). To understand why such changes are important, it is necessary to look at the structure of these amino acids (Figure 4).

Figure 4 shows the molecular structure of leucine and arginine. It can be seen that arginine has a much larger side chain than leucine. In fact, arginine is the largest (dimensionally) of all 20 amino acids in its

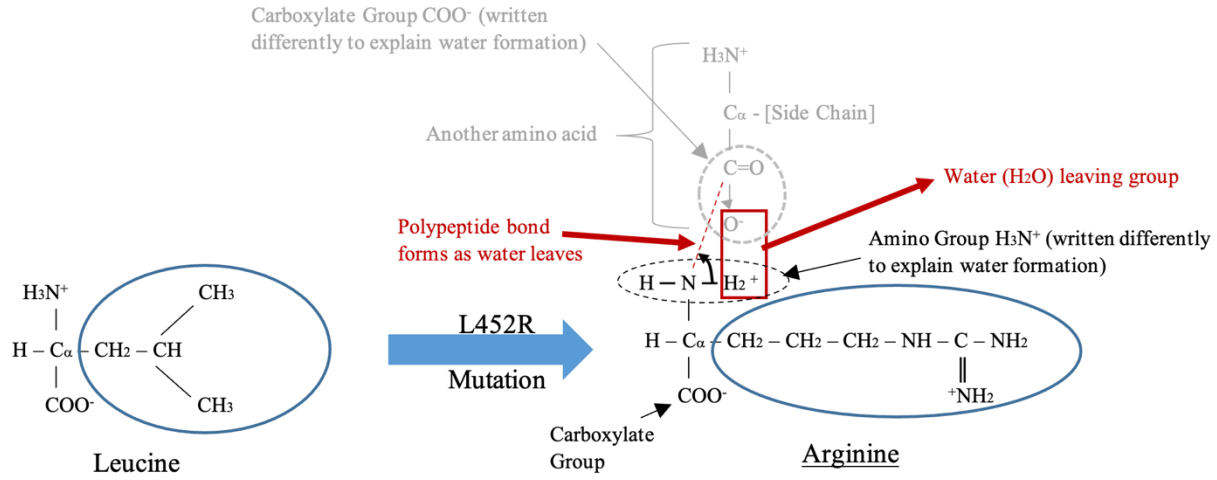

Figure 4: The structure of the amino acids in the δL452R mutation (leucine to arginine). *Side chains are encircled in solid blue lines and are attached to what is called the α-carbon atom of each amino acid. At neutral (~physiological) pH, the carboxylate group will have lost a proton in solution (cellular cytoplasm), and the amino group will have gained a proton from solution. The net result is a structure called a zwitterion, and it is the usual form in which an amino acid is displayed. A Polypeptide bond (shown only for arginine as a dashed red line) forms when the amino group (encircled in dashed black) of one amino acid (arginine) reacts with the carboxylate group (encircled in dashed gray) of another amino acid (in gray) (Mathews, van Holde, 1996). A water molecule is created as a leaving group (a waste product) (boxed in red). When many such reactions (polypeptide bonds) form in sequence, a protein (or polypeptide) is formed. The "backbone" of the protein can be written as $(-C_\alpha\text{-N-C-})_n$, and each C_α is associated with a particular side chain structure that is unique to each type of amino acid. This is how the primary structure of a protein polymer is formed. The field of view is now 100 Å across. – At this point the reader should ask, "If the process of polypeptide formation is so complex, how can one amino acid be clipped out of a protein chain and replaced by another?" That will be explained in the next section.*

conformation of maximum extent (i.e., when the molecule is all stretched out). Perhaps the steric hindrance (stand-off distance) imposed by this side chain keeps antibodies from binding to this critical contact point of the S1 subunit of the S-protein (see Figure 3). The E484Q mutation is similar, but glutamine (Q) is a smaller molecule than arginine (it looks just like R except that one -CH_2- moiety is missing in the side chain), and that may explain why this mutation is less important. L452R has turned out to be one of the two most significant mutations that makes the δ-variant such a "super-strain". It is worth noting that both L452R and E484Q occur along the edge of the binding domain (area of the S-protein where it makes contact with the cellular binding site – blue sphere in Figure 3) and not *in* the binding domain. In this way the viral S-protein can still bind to a cell, but it can keep large antibody molecules from binding to, and covering, the binding domain. A virus whose binding domain is protected from antibody attack by further encircling bulky mutations might out-compete one that is not so protected, thereby favoring the generation of resistant strains! So, what can be done to fight it? A new vaccine (a δ specific booster) needs to be developed. It induces the human immune system to produce an S-protein with the L452R mutation in place. When antibodies are developed against this new (mutated) S-protein, assuming the steric hindrance model is correct, a pocket will be present in the new antibody molecules to accommodate the arginine side chain and allow intimate bonding with the δ S-protein. Once the binding domain is capped or blocked by an antibody, an invading coronavirus is neutralized! It is for this reason that a δ specific booster is needed. *It is of central importance to understand that although the current boosters are NOT δ specific, they do boost the waning (weakening) immunity of the original vaccines as a function of time* (Neergaard, 2021). Because of the limited advantage of a booster based on the original vaccine, experts at the CDC initially decided to scale down its distribution to the immunity-compromised and those over 65.

The δ-variant possesses another important S1 mutation (hence, the appellation "Double Mutant") over its parent called Δ157-158 (not visible in Figure 3). The capital Δ (delta) stands for "deletion", while 157-158 stands for the position of the deleted amino

acids from the beginning of the primary chain. These deletions can change the folding of the S1 protein and, therefore, its shape. It's just one more factor that prevents antibodies tuned to the classical COVID strains (Wuhan and α) from successfully binding to the δ-variant S1 protein. Again, this underscores the need for a δ specific booster. Exactly how, mechanically, amino acid deletions, and the previously discussed substitutions, take place will be the topic of the next section.

Eventually, if a δ specific booster is not widely distributed, the successful δ-strain will continue to mutate further and further out of range of the original two-shot series (it has already bifurcated into B.1.617.1 and B.1.617.2). And, although further mutations may not be that harmful to someone who has received a δ specific booster, the consequences for someone who skipped such a booster may be grim, and cumulative deaths (Figure 2) may continue to rise.

Like influenza, annual boosters for the latest coronavirus strains may become a necessary feature of the nation's vaccination program. Until recently (up until Oct. 2021) the prevailing wisdom was to separate any flu and COVID vaccinations by at least one month, and to take the current booster no sooner than 6 to 8 months after the initial series of two injections. However, because the original coronavirus series entered the market so late in the cold and flu season, many people are currently out of synchronization with nature's natural infection cycles.

It may be time to start thinking about migrating one's vaccination schedule so that immunization for *both* diseases takes place prior to the onset of the cold and flu season; say late August for the current flu vaccine and late September for any coronavirus booster. Although, as of Oct. 2021, many people are taking both shots close together in time, or even simultaneously, since the side effects of the flu vaccine are quite mild. The current booster can be harsher. Typically, for the first 12 hours after vaccination, all you get is tired and a sore arm. Then, for the next 5 hours you might get chills, headache, joint aches, and perhaps a slight fever. Finally, recovery occurs in the last 7 hours. In summary, full recovery can take about a day. Consequently, for vaccines other than flu, the one-month rule should be observed. Furthermore, as discussed in "Vaccine Safety" (Zito, 2021), a time may come in the near future when an mRNA flu vaccination will be combined with an mRNA coronavirus vaccine. When that happens, people who have successfully modified their vaccination schedule will be in an ideal position to replace the vaccinations for the two diseases with a single "combo" shot. It is unfortunate that these issues have not been fully discussed in the media.

mRNA, CODONS, tRNA, THE RIBOSOMAL PROTEIN WORKBENCH AND rRNA

This section will be primarily concerned with a detailed look at the translation process (Mathews, van Holde, 1996). Recall from the first report (Zito, 2020b) that the process of producing a protein from the RNA viral code is called translation. That is because the nucleotide language of RNA (with alphabet A, C, G, U) must be translated into the amino acid language of proteins (with alphabet A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, V – each letter representing one of the 20 amino acids).

So, how is this translation accomplished? First of all, since the nucleotide code consists of only 4 letters, and the amino acid code consists of 20, a one-to-one correspondence between nucleotides and amino acids is impossible. What if two nucleotides corresponded to one amino acid, would that work? No, because two nucleotides can only produce 16 ordered pairs, at most. What about three? Yes, that will work because there are 4x4x4, or 64, possible *ordered* triplets (e.g., GCA refers to alanine while its reverse ACG refers to threonine – order counts). However, 64 is larger than 20, what about the extra triplets? Well, some amino acids are specified by more than one triplet of nucleotides, and some triplets are signals to start or stop making a protein string. Each triplet of the RNA nucleotide code that specifies an amino acid of a protein's primary structure, or a start/stop signal, is called a codon. The codon for leucine is CUA, but the codon for arginine is CGA! Therefore, a single genetic error (point mutation) that changes a U to a G is enough to direct the cellular protein machinery to replace a leucine with an arginine, thereby turning the old (Wuhan, α strain) S-protein into something that looks more like the new δ strain protein.

What about the Δ157-158 mutation? How do you explain that? There are three ways to say STOP in the nucleotide language; UAA, UGA, and UAG. If, for example, the amino acid preceding 157 and 158 were serine (coded by UCA), and if a point mutation

changed the middle C to an A, then the UCA codon would be changed to the UAA STOP codon. In that case, if amino acids 157 and 158 were at the end of a protein chain (for S they are not), they would simply be clipped off the end of the protein chain in the new (δ) version of the S-protein during cellular manufacture (Zito, 2021). It is for all these reasons that the probability for a significant mutation in the second paper of this series (Zito, 2021) was set at ~ 2.5 x 10^{-8} per year per infected person (~ the product of the probabilities for two point mutations).[3] Once the cell's protein manufacturing centers, called ribosomes, produce all the necessary proteins for the new δ-variant, the pieces self-assemble in the cell's cytoplasm to form new δ-virions that can infect other cells upon release. At this point the reader may say, "All this theory ties up a lot of loose ends from the previous publication, but what exactly do these ribosomes and related protein manufacturing tools look like?"

Figure 5A shows a molecular "stick-figure" (bond) model of the most important tool. It is called transfer RNA, or just tRNA (Anon.a, 2021). Recall from the first publication in this series (Zito, 2020b) that, in the beginning, life was based on RNA. There were no proteins – these came later in evolutionary time. Therefore, all the tools used to make proteins for more modern life forms had to be made of RNA. The tRNA in Figure 5 came from a yeast cell, not a human cell. Human tRNA is a more complex cruciform. However, the author's goal here is to elucidate principles, not obfuscating details.

The reader's first observation should be to note the hairpin turn at the bottom of the stick- figure model. This allows the originally linear strip of RNA to fold in upon itself and form the double helical structure shown below. It suggests that the DNA double helix may have evolved from a structure of this kind, except that RNA contains uracil (U) instead of the thymine (T) of DNA. However, U and T have a very similar molecular structure. In fact, they differ only by the replacement of a hydrogen atom in U with a -CH_3 group in T. It is easy to imagine that such a replacement could have taken place in Earth's early methane (CH_4) rich atmosphere. Finally, if the strained, chemically reactive, bond at the hair-pin turn should snap due to heat or interaction with its chemical environment – *voilà*! You have DNA! The story of how cellular life on Earth evolved has been an interest of the author's since he was 15 years old and will be the subject of a future book.

For now, the reader only needs to note that at the site of the hair-pin turn, three open bonding sites are available that match the codons of viral RNA (vRNA). That is to say, the tRNA fits into the vRNA like a plug into a socket. Still more amazing is the fact that the open end of the tRNA double helix is capable of binding an amino acid! And each amino acid has its own type of tRNA. Therefore, tRNA acts like a "taxi", transporting free amino acids to the codons of a vRNA molecule that is trapped on a cellular ribosomal workbench where proteins will be manufactured. The operation of that workbench will be discussed next.

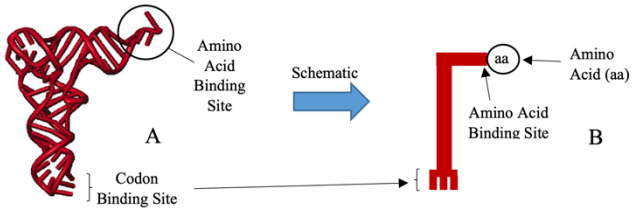

Figure 5: A) "Stick-figure" (bond) model of tRNA *showing its codon plug (bottom) and its amino acid binding site (top) (Anon.a, 2021).* ***B) Schematic representation of tRNA binding an amino acid.***

Ribosomes are also made of RNA (called rRNA), and each comes in two pieces (subunits); one is called a 30S subunit (or "small" subunit) while the other is called a 50S subunit (or "large" subunit). The 30S and 50S designations are called sedimentation coefficients and refer to how these subunits separate after centrifugation. Together, the two subunits form a complete ribosome, whose sedimentation coefficient is 70S, where the sum of the sedimentation coefficients of the parts is not necessarily equal to the sedimentation coefficient of the whole. In solution (cytoplasm) an equilibrium exists between the 30S and 50S subunits, and the 70S ribosome; 30S + 50S ↔ 70S. Whenever a strand of mRNA (or vRNA) is trapped between the two subunits, protein production can begin. This biological "hammer (50S) and anvil (30S)" is diagramed in Figure 6.

The 50S subunit contains three cavities, or chambers. From right to left, the first is called "A" for "amino acid chamber". The second is "P" for "polypeptide chamber", and the third is called "E" for "exit chamber". It used to be thought that there were only two chambers, but it is now known that there are definitely three. The entire process of protein chain initiation, elongation, and release is very complex. However, the basic steps can be outlined easy enough.

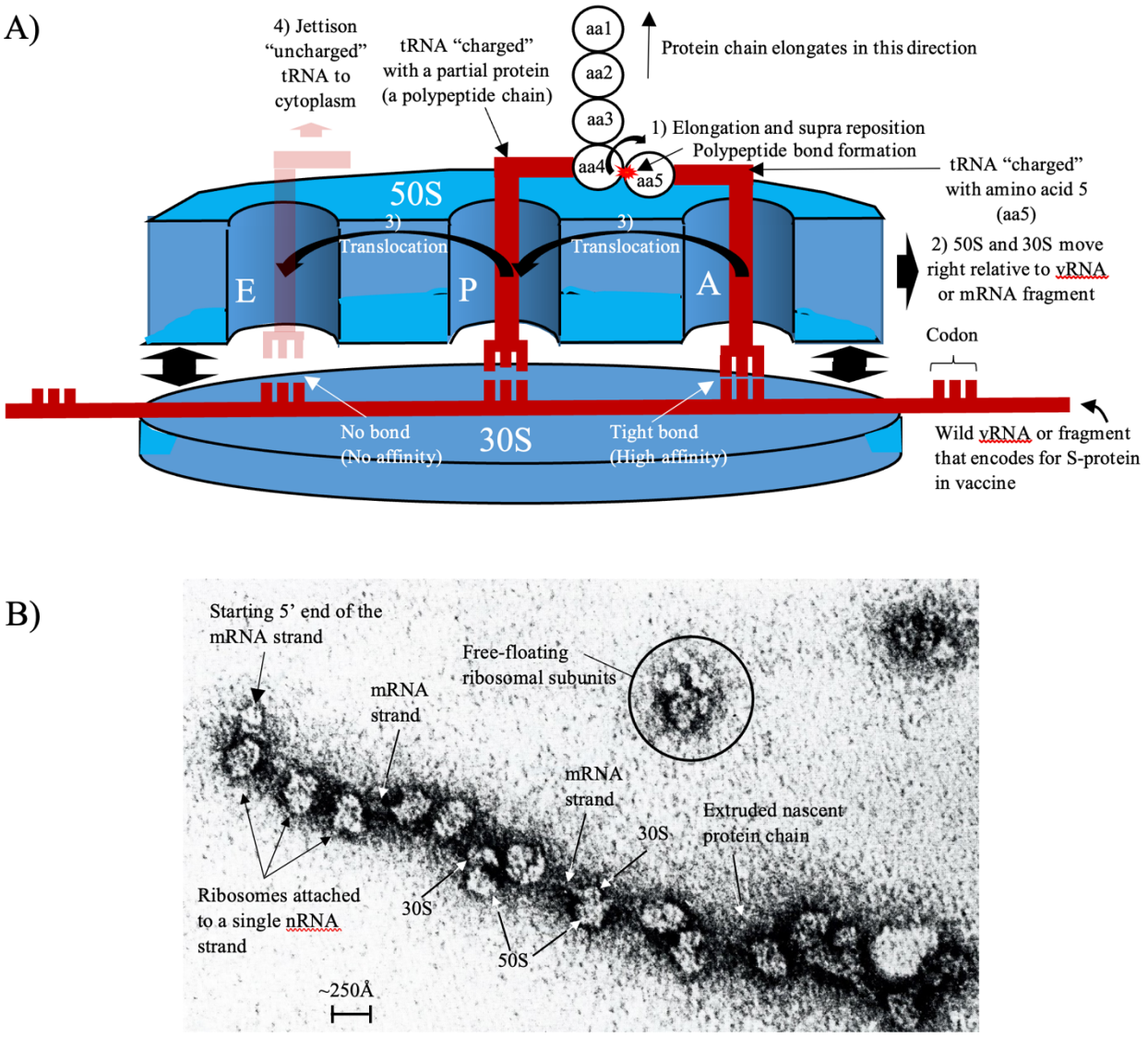

Figure 6: A) Schematic of the 70S ribosomal workbench showing the elongation of a protein chain. *"aan" stands for "amino acid n" in a protein chain. This figure ties together Figures 4 and 5 of this publication with figures 1 and 6 of the first publication of this series (Zito, 2020b). Like moving missiles between silos, tRNA (either "charged" or "uncharged") can be moved between chambers A, P, and E. tRNA's can also enter or leave chambers.* ***B) An astounding electron micrograph*** *by Barbara Hamkalo (Mathews, van Holde, 1996), modified by the author, showing sixteen E. coli ribosomes translating a strip of mRNA from its starting end (called the 5' end for technical reasons). About 50 ribosomes can be attached to a single mRNA; a fact that will prove important for the calculations that will follow. All ribosomes are moving to the right as in A. Some ribosomes are floating free, sometimes individual subunits can be discerned. In one case an extruded nascent protein chain can be detected. Although the cartoon in A is not to be taken too literally, it is not too far from the literal truth either!*

As the reader might have guessed, the initiation of protein manufacture is signaled by a START codon (AUG). After that, Figure 6 shows the crucial steps in polypeptide (protein) chain elongation. When chambers "P" and "A" are filled, two amino acids, one from the elongating protein chain, and one attached to a tRNA, are close enough to each other that a polypeptide bond can form as depicted in Figure 6A (Step 1).

Therefore, the ribosome acts like a catalyst facilitating bond formation. The entire chain is now transferred to the "A" chamber, and the tRNA in the "P" chamber is now uncharged (i.e., it has lost its polypeptide chain). If 50S and 30S momentarily lose their mutual grip on each other and move to the right one codon relative to the mRNA (or vRNA) (Step 2), two translocations occur (Step 3). That means the uncharged tRNA that is in the "P" chamber moves to

exit chamber "E", where it is eventually released into the cytoplasm too pick-up another amino acid (Step 4). And the tRNA, with its protein chain, that resides in chamber "A" moves to chamber "P". Empty chamber "A" now has a strong affinity for a new tRNA that will match the new codon. Termination and protein chain release occurs when one of the STOP codons is reached, as discussed above. This is how vRNA hijacks the cellular machinery to produce more viral proteins. It is also how vaccine RNA fragments induce the cell to produce the S-proteins that eventually produce the immune response. The vaccine RNA fragments, however, eventually wear out and are cleared from the body in a few hours. The same is *not* true for the complete viral RNA because the proteins that are produced self-assemble into new virions to continue the wild infection. Vaccination and the infection process will be discussed further in the next section, but first there is one detail that demands discussion and one curiosity.

Recall from the first publication in this series (Zito, 2020b), and from Figure 3A above, that the coronavirus S-protein is dusted with sugar to make it (at least partially) invisible to the human immune system. So, the S-protein is really a glycoprotein (or sugar-protein) and not just a pure protein. How does that happen? That is now easy to explain. Look at Figure 7. Arginine contains an $-NH_2$ group at the end of its side chain (where the "-" represents a bond), and that group can bind to a number of different sugars by simply forming a water molecule as shown in Figure 7. The process is called glycosylation. Normally, very few proteins manufactured by free floating ribosomes in the cytoplasm are glycosylated, and those that are, usually only have a single N-acetylglucosamine sugar ring added. But the ribosomes bound to the intra-cellular membrane called the endoplasmic reticulum (ER) are different (Alberts et al, 2002). The ER contains an enzyme called oligosaccharyl transferase that allows an entire block of connected sugar molecules (like the one depicted in Figure 7) to be transferred to the nitrogen atom of an amino acid side chain. Up to a point, the larger the block of sugar molecules, the better the S-protein camouflage. It is for this reason that the ER plays such an indispensable role in coronavirus replication (see Figure 4 of Zito, 2020b).

Finally, it is worth noting that neither tRNA nor rRNA are pure RNA. Each comes with protein attached. It is as if evolution is not satisfied with a pure RNA protein-making-micro-machine and is trying to develop a more versatile protein protein-making-micro-machine. Perhaps an all-protein protein-making-micro-machine will be the future of all life on Earth in another few billion years!

DEFINITIONS AND RUMORS

Before beginning the calculations of the next section, a few definitions are necessary. Some of these precise definitions were devised by the author to clarify paradoxes that arise when a vaccine is not 100% effective. Most are forms of definitions from "Melloni's Illustrated Medical Dictionary" (Dox, 1979), a standard medical reference. Other definitions come directly from the U.S. Center for Disease Control (CDC). As will be demonstrated, a great deal of confusion, acrimony, and misery has been generated by misunderstanding vocabulary.

Infectious Agent = A microbe, such as a coronavirus particle, that is capable of replicating within a host. The existence of such an agent has been proved experimentally and will be taken as axiomatic.

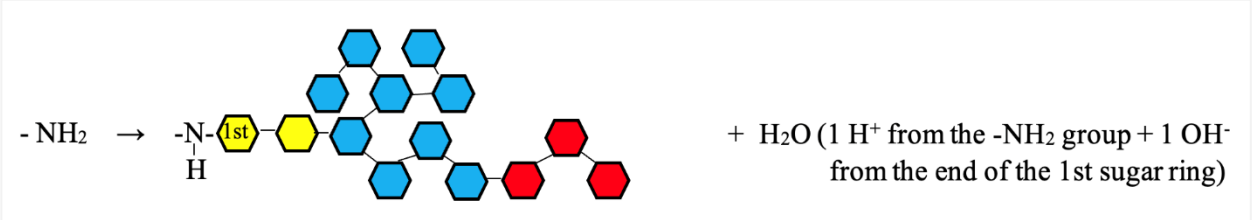

Figure 7: Forming a glycoprotein from a protein by reaction of 6-carbon (hexose) sugar rings with an amino acid side chain. *Red rings are glucose, blue are manose, and yellow are N-acetylglucosamine sugars. The network of sugar rings is called an oligosaccharide, and it will contribute significantly to the steric hindrance that an antibody will encounter when trying to block the S-protein binding domain of a δ-variant virion. Other amino acids (besides arginine) can also have a sugar network, most notably glutamine (Q) of the δ-variant's E484Q mutation, and asparagine (the abundant amino acid found is asparagus), but not leucine! If, however, the S-proteins oligosaccharides becomes too ornate and bizarre, the immune system will recognize it as something foreign and can build an antibody to fit around it like a glove and bind to it. A δ specific booster gives the human immune system an opportunity to adapt itself to the arginine and glutamine oligosaccharide networks. Just one more reason why it is so important!*

Infection = A condition in which an *infectious agent* is actively replicating within a host.

Immune = A condition in which an *infectious agent* cannot replicate within a host. Note that the intersection of the set of all people with an *infection* induced by a specific *infectious agent* with the set of all people *immune* to that *infectious agent* is the null set.

Artificial Inoculation = The entry of a live attenuated *infectious agent*, a killed or inactivated *infectious agent*, a protein from the *infectious agent*, or even part of a protein from an *infectious agent*, into a host via controlled artificial means (injection, ingestion, subcutaneous administration, etc.).

Wild Inoculation = The uncontrolled entry of a viable "wild" (not attenuated) *infectious agent* from another host (via a sneeze, cough, contact with urine, stool, or epidermal eruptions, etc.).

Infectious = A condition in which the titer of *infectious agents* within a host is high enough to cause the *wild inoculation* of another host. *Immune* and *infectious* are mutually exclusive conditions by these definitions. (Note that external mechanical transport of an *infectious agent* by an *immune* intermediary to another host does not make the intermediary infectious by these definitions, since the agent was never replicating *within* the intermediary).

Fully Vaccinated = A host that has received all *artificial inoculations* of a series. See Figure 8.

Partially Vaccinated = A host that has not completed all *artificial inoculations* of a series (including any required boosters). See Figure 8.

Unvaccinated = A host that has not received any *artificial inoculations* of a series. See Figure 8.

Successful Vaccination = Antibody levels, induced by *full vaccination* (only), that are sufficient to render a host *immune* to any likely *wild inoculation* by a given subtype, strain, or sub-strain. Successful vaccination status is not necessarily lifelong and must be maintained by periodic *artificial inoculations* ("boosters"). See Figure 8.

Unsuccessful Vaccination = Antibody levels, induced by *full vaccination* (only), that are insufficient to render a host *immune* to any likely *wild inoculation* by a given subtype, strain, or sub-strain. U*nsuccessfully vaccinated* hosts do not include the *partially vaccinated* but are a subset of the *fully vaccinated*. See Figure 8.

Vaccinated = a nonspecific colloquial term that could mean, *successfully vaccinated*, *unsuccessfully vaccinated*, *fully vaccinated*, *partially vaccinated*, or the union of any of these sets, depending on context.

Breakthrough Infection = Infection of a host *fully vaccinated* against one or more circulating strains (CDC.gov).

Vaccine Effectiveness (VE) = The percent (%) of cases below what would be expected of an *unvaccinated* population. All data are collected under typical field conditions; not the ideal controlled conditions of a clinical trial (CDC.gov). Therefore, any resistance to infection due to natural immunity (innate and wild acquired), behavior, age, etc. in the *unvaccinated* population has already been taken into account. VE is defined only in terms of observables.

Potentially Infectious Superset = the union of the *unsuccessfully vaccinated*, the *partially vaccinated* and the *unvaccinated*. People in the *potential infectious superset* are at risk of infection but, when infected, the symptoms of the *unsuccessfully vaccinated* and the *partially vaccinated* will generally be milder than those who are *unvaccinated.*

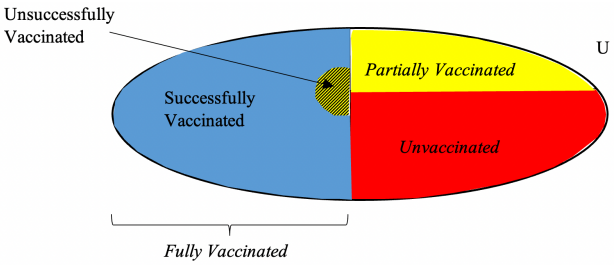

Figure 8: Venn diagram (Meyer, 1970) for a population *(blue = safe, yellow and yellow shaded = at risk, red = unsafe). The intersection of any pair of mutually exclusive subsets is the empty (or null) set ∅, while the union of all mutually exclusive sets is the Universal Set (U) equal to the entire population. Furthermore, {Fully Vaccinated} = {Successfully Vaccinated} ∪ {Unsuccessfully Vaccinated}, {Successfully Vaccinated} ∩ {Unsuccessfully Vaccinated} = ∅, {Potentially Infectious Superset} = {Unsuccessfully Vaccinated} ∪ {Partially Vaccinated} ∪ {Unvaccinated}, {Unsuccessfully Vaccinated} ∩ {Partially Vaccinated} ∩ {Unvaccinated} = ∅, and {Potentially Infectious Superset} ∩ {Successfully Vaccinated} = ∅. Finally, if # represents the number of elements (people) in a given set {…} then, for the Pfizer and Moderna COVID vaccines, #{Successfully Vaccinated} >> #{Unsuccessfully Vaccinated} for all strains from Wuhan to δ (Halmos, 1960). Note that the notion of "successful" and "unsuccessful" vaccination has not been extended to the partially vaccinated because the VE is generally low and short lived.*

With this ladder of precise definitions, each depending on a previous definition, we can begin to talk. First of all, if vaccines were 100% effective, full vaccination, successful vaccination, and immune

would all be synonymous terms, and the unsuccessfully vaccinated would not exist. However, as Table 1 shows, most common vaccines are *not* 100% effective.

In that case, the definitions above allow the reader to draw several conclusions. First of all, by definition, successfully vaccinated people are unlikely to develop an active infection or spread an infection to others because an infectious agent cannot replicate within these hosts to any significant extent. They are effectively immune. Basically, by the definitions above, the spread of disease is through those who are unsuccessfully vaccinated, partially vaccinated, or unvaccinated, because these are the sets that contain hosts who have insufficient antibody levels to prevent infection (disease) from any likely wild inoculation. Furthermore, breakthrough infections of the fully vaccinated are almost exclusively confined to unsuccessfully vaccinated people, and tend to be milder, involve less hospitalizations, and the period of time during which they are infectious is shorter compared to those who are unvaccinated. The same is true of partially vaccinated people, although little has been said about them in the literature.

The author was asked the following very practical question during his August 2021 live presentation, "How does one know if they have been successfully vaccinated against COVID?" To be *assured* of successful vaccination, the fully vaccinated must wait two weeks after their last artificial inoculation. Then an S-protein specific antibody titer test must show a level of antibodies high enough to assure effective immunity (numerically, a titer of 100%, or something close like 99%),[4] while a virion test shows a negative result (indicating that the patient has no current asymptomatic active infection that is responsible for high antibody levels). It goes without saying that antibody levels must be maintained (not allowed to expire) for any circulating strains to stay successfully vaccinated.[5] As a practical matter, if a patient has had a reaction to the required series of injections, including boosters, that is an indication that the patient's immune system has recognized the S-protein produced in cells after vaccination as "not-self" - an essential step for successful vaccination.

What if someone gets no reaction from vaccination? In that case, an S-protein specific antibody test is warranted. If the test is positive after 2 weeks, there is no obvious reason for concern,[6] although a *titer test* would have been more informative. The lack of reaction may have been due to a previous contact with the coronavirus S-protein. But, if the test is negative, then a trip to one's primary care physician is warranted, as this may be an indication of some underlying problem. Such problems may include impaired immune response due to disease, prescription drugs, age, or other factors. There is even the remote possibility of a spoiled batch of vaccine (Paduano, 2021; Chuck, Kesslen, 2020).

A patient's physician is the best person to decide what the next step should be in the vaccination process. But, if an antibody titer is not too low, the attending physician may just suggest another inoculation (with the same composition and strength, or a booster). That has been the common practice recently in cases of both weak immune response and waning immunity (say, less than 60% below peak – a benchmark used by many physicians). Remember, just because you are in a state of unsuccessful vaccination does not mean that you must remain so. Furthermore, some people refuse to be vaccinated because they claim they are allergic to a particular vaccine's ingredients. In that case, switching to

Table 1: Vaccine vs. Effectiveness. *The word "any" means all infections regardless of severity, whereas "severe" means only the most life-threatening cases. The Moderna vaccine is among the most effective vaccines. Strangely, none of these "imperfect" vaccines, other than that for COVID-19, currently excites even the slightest public passion.*

DISEASE	VACCINE	EFFECTIVENESS	REFERENCE
Tuberculosis	BCG Vaccine (Bacillus Calmette-Guérin)	70% for children 5-15 yrs ~30% for adults	Stulpin, 2019 Katelaris et al, 2020
Cholera	OCV (Oral Cholera Vac.)	52% (any), 71% (severe)	Firdausi et al, 2018
Varicella (Shingles)	Varivax (1 dose)	82% (any), 100% (severe)	CDC.gov, Oct. 21, 2021
Varicella (Shingles)	Varivax (2 doses)	98% (any), 100% (severe)	CDC.gov, Oct. 21, 2021
COVID-19 (Wuhan, α)	Moderna (mRNA-1273)	~95% (any)	CDC.gov, Oct. 22, 2021
COVID-19 (δ)	Moderna (mRNA-1273)	~80% (any)	CDC.gov, Oct. 22, 2021
Smallpox (Variola)	ACAM2000	95%	CDC.gov, Nov. 11, 2021
Polio	IPV (2 doses) (Inactivated Polio Vaccine) IPV (3 doses)	90% 99% → 100%	CDC.gov, Nov. 11, 2021 CDC.gov, Nov. 11, 2021

another type of vaccine with a different composition may help. Many are available (Zito, 2021). An allergist should be consulted.

A less rigid, less definition and logic driven, more analogue, way to understand infections and vaccination dynamics is in terms of antibody titers and infection probabilities as described by D. Bhattacharya, Chairman of the Department of Immunology at the University of Arizona, (Bhattacharya, 2021a). All available evidence to date (using the Moderna and Oxford-AstraZeneca vaccines) suggests that the higher the COVID antibody titer, the lower the probability of infection by a wild inoculation of given dose and strain (Gilbert et al., 2021; Chau, 2021). "Someone who mounted a robust immune response is less likely to get infected in the first place, less likely than an unvaccinated person to develop serious symptoms if they do get infected, and less likely to transmit.", (Bhattacharya, 2021b). When the antibody titer rises to a level that is sufficient to produce immunity against any likely wild inoculation by a given subtype, strain, or sub-strain, then breakthrough infections, and therefore transmission, are unlikely. At that point the fully vaccinated host is successfully vaccinated. But what if a successfully vaccinated host receives a massive number of virions through some unusual incident (e.g., having a very sick child or spouse sneeze or cough in their face while not wearing masks). Then, will they get sick? Possibly, if they are that unlucky. However, as we will see, most wild inoculations are much smaller, therefore infection is unlikely. Similarly, some unsuccessfully vaccinated people, with low antibody titers, may escape a marginal wild inoculation. However, on the average the statistics in table 1 must be reproduced because, by definition, VE is measured under typical field conditions (see definitions above).

Finally, vaccination dynamics can be understood in terms of vaccine dose. Recall from "Vaccine Safety" (Zito, 2021) that each Pfizer dose contains 30 μg (3×10^{-8} kg) of mRNA, while each Moderna dose contains 100 μg (10^{-7} kg). Let's calculate how many molecules of mRNA are in each dose. As discussed in the first publication of this series (Zito, 2021), mRNA is basically made up of four building blocks, or nucleotides (hence, the N in RNA). These are adenine (or "A" with a molecular weight of 134 Daltons), cytosine (C, with a molecular weight of 111 Daltons), guanine (G, 150 Daltons), and uracil (U, 112 Daltons); where a Dalton is the rest mass of a proton, or 1.67×10^{-27} kg.

Therefore, assuming A, C, G, and U occur with equal frequency in the RNA coding for the S-protein, the average weight per nucleotide is 126.75 Daltons. But the nucleotides are not connected directly to one another in RNA. Instead, all of these nucleotides are connected to a "backbone" of alternating sugar and phosphate moieties (fragments) called a phosphodiester linkage. And each nucleotide is associated with one sugar moiety and one phosphate – a "vertebra" of the backbone one might say. The sugar moiety is called ribose, hence the R in RNA (ribonucleic acid), with a molecular weight of 68 Daltons. The acidic (hence the A in RNA) phosphate moiety has a weight of 95 Daltons. Since the coding of the S-protein requires about 5000 nucleotides (Zito, 2021), the average weight of each mRNA fragment in the vaccine must be about (5000) (126.75 + 68 + 95) = (5000) (289.75) ≈ 1.45×10^{6} Daltons, or 2.42×10^{-21} kg. Therefore, the number of mRNA fragments in each Pfizer dose is about (3×10^{-8} kg) / (2.42×10^{-21} kg) = 1.24×10^{13} mRNA fragments, while each Moderna vaccine dose contains 4.13×10^{13} fragments.

Well, that is certainly a lot of mRNA fragments, but how many S-proteins do these fragments produce? Each fragment is capable of producing about 50 proteins before it "wears-out"; assuming it is used only once after being fully loaded with ribosomes (Mathews, van Holde, 1996; also see Fig. 6B and its caption). Therefore, the human body will produce about 6.2×10^{14} to 2.1×10^{15} S-proteins, depending on which vaccine is used. Eventually, all of these S-proteins are neutralized and destroyed as a vaccinated individual rapidly recovers from the immunological challenge posed by a vaccine. Therefore, each S-protein is eventually captured by an antibody molecule generated by the host's immune system.

The S-protein is large, but so is the antibody. The antibody IgG (also known as γ-globulin, a name that may be familiar to some readers) has a molecular weight of 152,000 Daltons. If the antibody attack on an S-protein fails, then it will be assumed that the antibody is free to try again until successful attachment is achieved. In that case, the total number of antibody molecules produced must *at least* be equal to the number of vaccine-induced S-proteins. Realistically, the number of antibody molecules are probably many times greater. But, as a lower bound,

the antibody molecular titer must be up in the 10^{15} range, or about 27 antibody molecules for each of the $3.72x10^{13}$ cells in the human body (Barth, 2017)!

Recall from the first publication in this series (Zito, 2020b), that the minimal infectious dose (MID) of virions needed for an active COVID infection in an unvaccinated host is in the 10^2 to 10^4 range. Therefore, the total number of antibodies produced about two weeks after vaccination probably exceeds this COVID MID by about 10^{11} to 10^{13} times, or one hundred billion to ten trillion times. When antibodies bind to an antigen (like an S-protein molecule or complete wild virus) one of two things can happen. Either the antigen is precipitated, or it is marked for destruction (digestion) by cells called Macrophages that move in for the kill (Mathews and van Holde, 1996).

All this may sound like a big advantage for the antibodies, and if this massive patrol could be maintained, immunity would be good from even a single vaccination. However, immunity from a single exposure is not long lived, as we know from Figure 3 of the first report (Zito, 2020b). The *second* vaccination convinces the body to maintain antibody levels while boosting them still further. While the *third* exposure (booster) not only continues boosting antibody levels but can convey δ-variant specific immunity if the booster is so designed.

These feats are accomplished by Memory B-cells (created by the first inoculation), which when stimulated by the second (and third) vaccination, begin to divide producing more Memory B-cells, and more Effector B-cells, that then produce much longer-lived immunity (from the excess memory cells) and higher antibody levels (excreted from effector B-cell surfaces). All this is a big plus for a booster! Worse still for the coronavirus is the fact that the antibody distribution after vaccination is not uniform throughout the body. For example, antibodies are 100 to 200 times more concentrated in lung tissue than in the tissues of the nasal passages (Bhattacharya, 2021a), giving another two orders of magnitude of protection to the lungs, the prime target of the coronavirus.

Tragically for humanity, the δ-variant has learned by mutation to offset this last advantage by multiplying ~1000 times more in the lungs than in other tissues (Ayass Bioscience, 2021)! This reproductive proclivity, in addition to the previously described amino acid changes, is what makes δ so dangerous! Nevertheless, given all these numbers, sustaining viral replication seems unlikely, assuming the host has a normal immune response to the vaccine (and any boosters). It would take a wild inoculation many orders of magnitude above the MID to seriously challenge a successfully vaccinated individual. It is for this reason that Pfizer and Moderna have chosen mRNA doses in the 30 to 100 μg range for their vaccines. Still higher doses would have increased the risk of anaphylactic shock,[7] which is already in the 1 to 10 cases per million vaccinated range (Zito, 2021). More is not always better!

The operation of the immune system and its many types of cells[8] and protein signals (e.g., interleukin-2, to be discussed in a future article) is one of the most fascinating stories in all of science, and it is unfortunate that the author cannot discuss it more deeply in this publication.[9] However, it is hoped that these transparent calculations help explain why δ is so dangerous, why the vaccine contains the mRNA doses that it does, and gives the reader a more precise idea of what is meant by the descriptive terms *sufficient antibody levels*, *successfully vaccinated*, and *unlikely*.

In summary, regardless of whether you take the definition/axiomatic logic/set theory view, the titer/probability of infection view, or the direct antibody/virion calculation view, the basic story is the same; viz. *breakthrough infections in successfully vaccinated people (the great majority of those who are fully vaccinated) are unlikely*. Clinically, it is the small minority of people who were unsuccessfully vaccinated, the larger population of partially vaccinated people with limited and rapidly waning immunity, and most especially the much larger population of unvaccinated people (~90-97% of all those entering hospitals and medical centers) who are "the vast, vast majority" responsible for spreading the coronavirus to the levels that are observed in the U.S. today (Innes, 2021). Anything else you might have heard to the contrary, or read in the media, or seen on the television or the internet, or heard from radio talk-show hosts, is a *rumor*. The author hopes that any paradoxes concerning vaccination effectiveness and carrier status, that may have arisen due to imprecise language or different points of view, have been completely, and unambiguously, resolved to the satisfaction of all parties involved in this debate.

Now, a pernicious and often repeated rumor cited in the previous publication on "Vaccine Safety" (Zito, 2021) can be revisited. On May 4, 2021, the City and

County of San Francisco (CCSF) posted the following statement on their website (CCSF, 2021):

"We don't know if the vaccine can stop you from spreading the virus"

From the discussion and calculations above, it is clear that the purpose of a vaccine is to prevent viral replication by immunological destruction of infectious agents after a wild inoculation. It is unlikely that any successfully vaccinated individual, with a normal immune response to the vaccine, will spread the virus. Furthermore, the great majority of COVID fully vaccinated, who are challenged by a wild inoculation that would normally develop into an active infection in the unvaccinated, will also prove to be successfully vaccinated (19 out of 20 for the classical Wuhan and α strains; see Table 1).

Finally, two hundred years of experience with modern vaccination techniques, starting in 1796 with Jenner's first use of Cowpox (as a mild analogue for smallpox) to covey immunity (Zito, 2020b), all suggests that the statement above by the CCSF is problematic. The smallpox vaccine is just about as effective as Moderna's mRNA-1273 (see Table 1). Nevertheless, wild (natural) smallpox no longer exists, although the vaccine is still stockpiled to this day because of the omnipresent risk of bioterrorism (another problem for safety engineers). The specter of wild smallpox was eliminated because the virus cannot replicate within people who are successfully vaccinated. Their antibody titer is too high! Therefore, they are unlikely to develop virion levels high enough to spread the disease.

Eventually, as more and more people are vaccinated, herd immunity is established. At that point, the number N of infected people must approach zero as time t approaches infinity, i.e., $N \rightarrow 0$ as $t \rightarrow \infty$ (Zito, 2021). Polio offers another example of disease eradication. As Table 1 shows, 3 doses of the polio vaccine approach 100% effectiveness. Consequently, Polio is almost non-existent in the U.S (except when introduced from abroad) because people who are successfully vaccinated against polio (essentially the same as the fully vaccinated in this case) are unlikely to spread the disease because, again, the virus cannot replicate within their bodies. In general, once herd immunity is established, there aren't enough susceptible hosts left in a population to maintain an infection chain, and the infection *must* die out! When that happens, even people in the potentially infectious superset are protected. That is how *"the vaccine can stop you from spreading the virus"!* As Oscar Wilde has said, "The truth is rarely pure and never simple." – The Importance of Being Earnest.

So, the naïve statement above by the CCSF is sending the wrong message. A very negative one at that! Normally, the author would not include anecdotal information in a report of this kind, but in this case, since all the facts are directly known to the author, the following tragic story shows how *some* people interpret statements like those of the CCSF.

The author has a colleague who is an ardent "anti-vaxxer", as is his wife. Both are educated people, neither would wear masks, practice social distancing, or vaccinate. Neither were old nor had any underlying conditions, except that the husband was allergic to air-born pollen. Then, given enough time and contact, it happened. The husband contracted COVID, was hospitalized, and was put on a ventilator, where he remained for some weeks with his life in the balance. His wife was understandably frightened, confused, and angry. It was all someone else's fault. It was the government's fault, it was the CDC's fault, it was Dr. Fauci's fault. She felt her husband's care wasn't good enough. It was the hospital's fault, the doctor's fault, the nurse's fault. Then, finally, she pointed to the author and made the following astounding accusation, "It's vaccinated people like you that are spreading this disease!"

That is how some people interpret ambiguous official statements like the one by the CCSF. The result is suspicion, confusion, fear, superstition, resistance to vaccination, wide-spread public anger against safety rules designed to keep the scourge from spreading, and hostility, threats, and violence against health care professionals (Hollingsworth, Schulte, 2021). Exactly what the public authorities are trying to avoid!

By contrast the CDC website (CDC.a, 2021) currently (Sept. 14, 2021) states "Vaccines are playing a critical role in limiting spread of the virus and minimizing severe disease. Although vaccines are highly effective, they are not perfect, and there will be vaccine breakthrough infections." This is sending the right message. Furthermore, the CDC website goes on to say, "Given what we know about the Delta variant, vaccine effectiveness, and current vaccine coverage, layered prevention strategies, including wearing masks, are needed to reduce the transmission of this variant." This also is a correct statement and is precisely what the author stated under "Rumor #14" of the previous "Vaccine Safety" publication in this

series (Zito, 2021). Now, fortunately, the newspapers are also finally getting onto the right track. On October 2-3, a quote in *The Wall Street Journal* (Kamp, 2021) said,

"Given that by far the vast majority of severe illnesses and deaths is occurring in the unvaccinated, that this really is now a pandemic of the unvaccinated, most of the deaths we have seen in this surge were entirely preventable." – Robert Kim-Farley, epidemiologist and professor at UCLA Fielding School of Public Health.

The authorities and the media now have the formidable task of trying to correct previously misleading news releases and re-instill public confidence in vaccination science (Figure 9). Precise language is important for public releases if misconceptions are to be avoided. Consider the following simple statement, "You can't give a nuclear reactor too much water." What does that mean?

Again, the reader might reasonably ask how the author knew so soon that some of the "official" statements concerning the spread of infection by vaccinated individuals were misleading? As before, official statements, although important, do not constitute proofs by themselves. The requirements of

***Figure 9: "The Cowpock"**, an 1802 etching (hand colored with aquatint) by James Gillray, was published by "y Ana-Vaccine Society", and now resides in The Morgan Library and Museum, New York, NY (www.Themorgan.org). It vividly portrays the public's nightmarish fears about vaccination, as smallpox ravaged England. The caption sarcastically reads, "The Cow Pock _ or _ the Wonderful Effects of the New Inoculation!" A sly looking Edward Jenner, left of center, is about to vaccinate a very worried woman. Jenner is dressed in the best fashion of the day, with coiffured white hair, formal long coat, white hose, and buckled shoes, prosperous from the new pharmaceutical's profits. While his boy-servant remains in tatters. Ghoulish, mutilated, and bovinely transfigured spectators lurk in the background, victims of the new vaccine! One woman in the crowd (right) has been transmogrified into a kind of cow-woman. Hilariously, hanging on the rear wall, is the picture of a multitude worshiping the biblical Golden Calf! - By the end of the 20th century, vaccines (although only 95% effective, similar to mRNA 1273 – Table 1) not only stopped the spread of smallpox, but they completely eliminated that virus from the planet! Although we may all laugh at the anti-vaxxer cartoon above, the movement was just as vociferous in the 1950's during the Polio epidemic in the U.S. and is still with us today! "There is nothing new under the Sun" – Ecclesiastes 1:9.*

logic, mathematics, scientific experience, and experimental verification must still be satisfied.

Before concluding this section, the author would like to make one last comment concerning public release of information. The Chinese authorities have received a great deal of criticism in the western press concerning their purported withholding of information in the initial days of the pandemic. However, when one considers the behavior of people in the U.S. during the first 9 months of the outbreak here – the artificial shortages created by the hording of basic commodities (canned food, toilet paper, sanitary supplies, cleaning agents, etc.) and the potential violence created by a run on weapons and ammunition by survivalists – it is clear that the potential for public panic is very great indeed.

One must also remember that China has four times the U.S. population. That doesn't just mean their problems are four times greater. Not at all! Consider a population of just two people. Clearly, there is only one way for them to interact – directly with each other. Now, consider a population that is four times greater (8 people). The number of two person interactions is now 7 + 6 + 5 + 4 + 3 + 2 + 1, or 28. That is to say, there are now 28 ways for a dispute to arise among two people (perhaps over a roll of toilet paper in a supermarket)!

This calculation gives the reader some idea of what the Chinese authorities are really up against. They needed to be sure before making an un-retractable public statement to a population of 1.3 billion people. Remember, not all infections spread out of control. If the lethality of an infectious agent is sufficiently high, and its transmission sufficiently low, it may kill off its hosts before a disease can spread very far.

INFECTION CALCULATIONS

VAERS:

Before the number crunching begins, the reader needs to understand what the Vaccine Adverse Event Reporting System (VAERS) is. VAERS tracks post vaccination side effects (including death) for many different vaccines. It is a joint effort by the U.S. CDC and the FDA (Food and Drug Administration). Although anyone can report an incident, there are usually specific rules. For example, consider influenza. Anaphylaxis (discussed above) can only be reported for 7 days after vaccination by Influenza-IIV, IIV3, IIV4, RIV3, ccIIV3, or LAIV4 vaccines (VAERS, 2021). However, VAERS has also been a source of pandemic misunderstandings.

In a July 21, 2021 page-update, the U.S. Centers for Disease Control and Prevention (CDC) said "VAERS received 6,207 reports of death (corrected downward from 12,313) among people who received a COVID-19 vaccine between Dec. 14, 2020 and July 19, 2021" (CDC.b, 2021; Reuters, 2021) - the parenthetical inserts added by the author. This misleading statement has been interpreted by some anti-vaxxers as meaning that the COVID-19 vaccine has *caused* the death of thousands of people. After all, isn't it VAERS' job to track side-effects and deaths?

The current (Oct. 18, 2021) CDC web site also contains several disclaimers separated from the CDC/VAERS claim above. One states, "The FDA requires health care providers to report any death after COVID-19 vaccination to VAERS, even if it's unclear whether the vaccine was the cause". Another states, "**Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem**. A review of available clinical information including death certificates, autopsy, and medical records, has not established a causal link to COVID-19 vaccines. However, recent reports indicate a plausible causal link between the J&J/Janssen COVID-19 Vaccine and TTS, a rare and serious adverse event – blood clots with low platelets - which has caused deaths" (bold-face, underline, and blue highlight, used by the CDC for emphasis). Finally, VAERS "reports may include incomplete, inaccurate, coincidental, and unverifiable information" (wonder.cdc.gov). The only "wonder" is that the CDC/VAERS would allow such "hear-say" evidence (not admissible in court) into a public database!

In order to reconcile all these conflicting statements, implications, and accusations, the author deemed it necessary to call the CDC and VAERS directly on Oct. 19, 2021 (1-800-822-7967) to ask for clarification and guidance. However, after being shuttled around to various departments, the author could discover nothing, other than excessive confusion and uncertainty, concerning the hodge-podge of statements above. Furthermore, a CDC phone representative promised to send the author an explanatory email from a staff "expert". On Oct. 20, 2021, the author did get an email from the CDC, but it contained nothing more than what was on the CDC website. So, where does the truth lie? Can a COVID-19 vaccine cause death?

As far as is known to date (Oct. 19, 2021), there are only a few possibilities. The first is anaphylactic shock discussed above and in "Vaccine Safety" (Zito, 2021). This risk is on the order of a few cases per million people vaccinated. Death is rare due to adrenaline (epinephrine) intervention (no U.S. deaths, 1 death in India).

The second is blood clots (thrombosis). This also occurs at the level of a few cases per million, and it can be life threatening. Thrombosis is only a risk with the Johnson & Johnson vaccine (47 confirmed cases reported total, but only 3 U.S. deaths according to the CDC; 10/18/21) as discussed in "Vaccine Safety" (Zito, 2021).

The third risk is myocarditis, inflammation of the heart, discussed in the author's August 2021 lecture for the ISSC (926 cases reported total, but no deaths; 10/19/21). It is primarily a problem for young men under 30 and involves the Pfizer and Moderna vaccines. The risks are again a few cases per million vaccinated (less than for the smallpox vaccine). Death would be a rare event.

The fourth risk is Guillain-Barre Syndrome (GBS). This disorder involves the Johnson & Johnson vaccine (a total of 228 preliminary cases reported (no U.S. deaths, 1 death globally reported by the European Medical Agency- EMA, 10/19/21), and occurs at the level of about 10 cases per million vaccinated (CDC, 10/19/21). GBS involves damage to nerve cells by the body's own immune system causing muscular weakness and sometimes paralysis. Most people fully recover from GBS, but sometimes the nerve damage is permanent. As far as the author knows, no deaths have yet occurred from vaccine induced GBS. Clearly, all four of these risks together (3 U.S. deaths; J&J vaccine only) account for 0.048% of the VAERS deaths reported on July 21, 2021. So, what accounts for the other 99.952% of VAERS reports?

Several factors are probably involved. First of all, excluding malicious lying, death after vaccination could have been coincidental after distribution of about 400 million doses (10/19/21). Death could have been from an accident (e.g., a plane crash)[10], old age, cancer, or any number of pre-existing conditions. It is only necessary that the death be *after* receiving a COVID vaccine and within the stated time interval to enter the VAERS database. Just because you were vaccinated does not mean you will never die!

VAERS deaths can also be related to waning immunity (the loss of immunity as a function of time), "too-late" vaccination, weak partial vaccination, unsuccessful full vaccination, or (rarely) spoiled vaccine. Undoubtedly, some people will call into VAERS claiming that the vaccine gave someone an active case of COVID that killed them. As discussed in "Vaccine Safety" (Zito, 2021), this is impossible. However, many people believe this rumor, and will enter a datum with VAERS. The belief is particularly tenacious when a person already has a latent infection and then receives the vaccine within the 5-day incubation carrier window. In this case, vaccination was too late. A few days later, the vaccinated person becomes sick, and may even die. No one can convince the surviving family and friends that the moribund was already infected before vaccination! There is also the very remote possibility of being vaccinated with a spoiled batch of vaccine (rare). Anyone vaccinated with mishandled or expired vaccine is still unvaccinated. However, even if a person is healthy when partially *or* fully vaccinated, they may not develop sufficient antibodies to prevent disease. Calculation of the total number of people who develop a COVID-19 infection after vaccination, and who die of that infection, will be next.

During most of the time interval cited by VAERS (Dec 14, 2020 – July 19, 2021), δ infections were not an important factor in the U.S., and as of July 27, 2021, about half the U.S. population (49.1%) were fully vaccinated (Anon.b, 2021; CDC.c, 2021) while 17.9% of the population were partially vaccinated (Kirzinger et al, 2021). That leaves about one third of the population (33.0%) unvaccinated (Kirzinger et al, 2021). On July 25, 2021, the total (cumulative) number of COVID cases (T) was ~34,600,000 in the U.S. (Johns Hopkins, 2022). If n_{uv}, n_{pv}, and n_{fv} are the total number of unvaccinated, partially vaccinated, and fully vaccinated cases respectively, then:

$$T = n_{uv} + n_{pv} + n_{fv}. \qquad \text{Eq 1}$$

Let e_{pv} be the vaccine effectiveness (in decimal) of a single dose of Moderna or Pfizer vaccine. These are the partially vaccinated, and from "Vaccine Safety" (Zito, 2021) the reader knows that e_{pv} usually lies in the 60 to 85% range. For this report, e_{pv} will be set to 0.6 (or 60%), the lower end of its range, because partial vaccination results in rapidly waning immunity, and because some estimates of e_{pv} are even lower than 60% as will be cited below. Furthermore, for the classical Wuhan and α strains, $e_{fv} \approx 0.95$ after full vaccination (see Table 1). Since vaccine

effectiveness (see the above definitions in the section "Definitions and Rumors") is defined as a (percent) decrease in cases relative to the number of cases in an equally large unvaccinated population (n_{uv}), it is clear that n_{pv}, the number of infections following weak partial vaccination is proportional to $(1\text{-}e_{pv})\ n_{uv}$. But wait, the set of partially vaccinated people is smaller than the set of unvaccinated people by a factor of (0.17 / 0.330). Therefore, the partially vaccinated will contribute proportionally less cases to the total T. Therefore,

$$n_{pv} = (0.179 / 0.330)\ (1\text{-}e_{pv})\ n_{uv} = (0.542)\ (1\text{-}0.6) n_{uv} = 0.2168\ n_{uv} \quad \text{Eq 2}$$

Similarly,

$$n_{fv} = (0.491 / 0.330)\ (1\text{-}e_{fv})\ n_{uv} = (1.49)\ (0.05)\ n_{uv} = (0.0745)\ n_{uv} \quad \text{Eq 3}$$

This is the number of unsuccessfully vaccinated of the fully vaccinated, essentially equal to the number of breakthrough infections by CDC definition. When the results for n_{pv}, and n_{fv} are plugged into the basic expression for T, the following equation results:

$$T = n_{uv} + 0.2168\ n_{uv} + 0.0745\ n_{uv} = (1 + 0.2168 + 0.0745)\ n_{uv} = 1.2913\ n_{uv} \quad \text{Eq 4}$$

Therefore, n_{uv} = 26,794,703 cases. Therefore, the unvaccinated contribute 26,794,703 / T = 26,794,703 / 34,600,000 = 0.7744 or 77.44% to the total case load. The partially vaccinated contribute n_{pv} = 5,809,092 cases or 16.79%, while the fully vaccinated contribute n_{fv} = 1,996,205 or 5.77% (these are the breakthrough infections by CDC definition). Note that 77.44% + 16.79% + 5.77% = 100.00%, as it should. It is also important to recognize that $n_{uv} >> n_{pv} > n_{fv}$, as stated in the section on "Definitions and Rumors". The next task is to translate infection figures into death figures.

On the average, an American who is infected by COVID has a 1.26% chance of dying (worldometers, 2022). Let $\%_{uv}$, $\%_{pv}$, and $\%_{fv}$, be the post-infection death rates (in percent) of the unvaccinated, partially vaccinated, and fully vaccinated respectively. It is certainly true that

$$1.26\% = (0.330)(\%_{uv}) + (0.179)(\%_{pv}) + (0.491)(\%_{fv}) \quad \text{Eq 5}$$

where each percentage is weighted by the fraction of the population it represents. It is also known that (Mathieu, Roser, 2021):

$$\%_{fv} = (0.155)(\%_{un}) \quad \text{Eq 6}$$

Now comes a real problem. There is very little data on the partially vaccinated, in spite of the fact that they form an important part of the population. Therefore, an assumption will have to be made. It will be assumed that $\%_{pv}$ lies between $\%_{un}$ and $\%_{fv}$, so that

$$\%_{pv} = [(0.155 + 1)/2]\%_{uv} = (0.577)(\%_{uv}) \quad \text{Eq 7}$$

Therefore, putting equations 6 and 7 into 5 yields:

$$1.26\% = [(0.330) + (0.179)(0.577) + (0.491)(0.155)](\%_{uv}). = (0.5094)(\%_{uv}). \quad \text{Eq 8}$$

Therefore, $\%_{uv}$ = 2.473; that is to say, the unvaccinated have a 2.473 percent chance of dying from an active COVID-19 infection. While $\%_{pv}$ = (0.577)(2.473) = 1.427 percent, and $\%_{fv}$ = (0.155)(2.473) = 0.383 percent. Note that $\%_{pv} = (\%_{un} + \%_{fv})/2 = (2.473 + 0.383)/2 = 1.428$, as it should aside from a round-off error in the fourth significant digit. Also note that (0.330)(2.473) + (0.179)(1.427) + (0.491)(0.383) = 1.26%, as it should.

Finally, according to these calculations, the death rate for the unvaccinated after infection is six and a half times higher than the death rate for the fully vaccinated after infection (i.e., 2.473/0.383 = 6.457)[11] – another reason why full vaccination is important even if you have been unsuccessfully vaccinated. Now, these VAERS calculations can be finished because the number of deaths following unsuccessful (low titer) full vaccination is

$$(\%_{fv}; \text{ in decimal})(n_{fv}) = (0.00383)(1{,}996{,}205) = 7645 \quad \text{Eq 9}$$

The number of deaths following weak partial vaccination is

$$(\%_{pv}; \text{ in decimal})(n_{pv}) = (0.01427)(5{,}809{,}092) = 82{,}896 \quad \text{Eq 10}$$

Finally, the number of deaths due to lack of vaccination is:

$$(0.02473)(n_{uv}) = (0.02473)(26,794,703) = 662,633 \quad \text{Eq 11}$$

The total as of July 27 should be about 7645 + 82,896 + 662,633 = 753,174 dead. But wait, the graph in Figure 2 shows that the total deaths on July 19 to be about 630,000. So, the calculated value is 19.6% larger than the actual value. Why? It is primarily because theory calculated all the deaths that will *eventually* result from the total number of infections as of July 27. In reality, some of those who were infected near the end of the VAERS time interval, may not have died yet! Also, it has been tacitly assumed that the percentage of unvaccinated, partially vaccinated, and fully vaccinated remained the same from Dec. 14, 2020 to July 19, 2021. This is clearly not true for the first month after vaccination began, but there were also relatively few cases at that time. Therefore, the calculated number of people who died due to unsuccessful full vaccination should be downwardly revised by 19.6% to 6,147 deaths. This figure differs by only 1% from the VAERS figure of 6,207 deaths! Therefore, enough unsuccessfully vaccinated people died to explain the VAERS data. Actual deaths from the vaccine are negligible! What about the partially vaccinated, those who were vaccinated "too-late", coincidental deaths, preexisting conditions, malicious lying, etc.? Those were probably contained in the original VAERS figure of 12,313 deaths but were removed prior to downward revision. Until the CDC/VAERS is more transparent about how they select, filter, and revise data for the VAERS database, nothing more can be said. Finally, the reader may reasonably ask, "Wouldn't it have been easier to have started from total deaths rather than total infections?" Yes, but then how would you partition the dead into those who were unvaccinated, partially vaccinated, and fully vaccinated?

Although VAERS data may be useful to experts looking for potential vaccine trends, these complex data are just confusing to the general public and lead to rumors, misunderstanding, and *resistance* to vaccination. Just the opposite of what the authorities are trying to accomplish! The reader can now understand why imprecise and confused language and thoughts have caused so much bickering and prevented calculations! The readers may also wish to compare these more precise VAERS calculations to the approximate calculations presented at the August 2021 annual meeting of the ISSS (conference video available from ISSS). Those calculations were performed in a different, simpler, but less precise way. However, the results were similar.

CASES ENTERING HOSPITALS AND MEDICAL CENTERS (AUG. 2021):

On July 21, 2021, the total number of active COVID cases (T′) was about 5,000,000 in the U.S. (see Figure 1). If n_{uv}', n_{pv}', and n_{fv}' are the number of unvaccinated, partially vaccinated, and fully vaccinated active cases respectively, then

$$T' = n_{uv}' + n_{pv}' + n_{fv}' \quad \text{Eq 12}$$

As before, let e_{pv} be the vaccine effectiveness (in decimal) of a single dose of Moderna or Pfizer vaccine; $e_{pv} \approx 0.6$. Again, let $e_{fv} \approx 0.95$ for the classical strains after full vaccination (see Table 1). Therefore, in analogy to the previous calculations, the number of infections following weak partial vaccination is $n_{pv}' = (0.179 / 0.330)(1\text{-}e_{pv})\, n_{uv}' = (0.542)(1\text{-}0.6) n_{uv}' = 0.2168\, n_{uv}'$. Similarly, $n_{fv}' = (0.491 / 0.330)(1\text{-}e_{fv})\, n_{uv}' = (1.49)(0.05)\, n_{uv}' = (0.0745)\, n_{uv}'$; this is the unsuccessfully vaccinated subset of the fully vaccinated set for the active cases circa July 21, 2021. Substituting these results for n_{pv}', and n_{fv}' into the basic expression (equation 12) for T′ yields:

$$\begin{aligned} T' &= n_{uv}' + 0.2168\, n_{uv}' + 0.0745\, n_{uv}' \\ &= (1 + 0.2168 + 0.0745)\, n_{uv}' \\ &= 1.2913\, n_{uv}' \end{aligned} \quad \text{Eq 13}$$

Note that equation 13 has the same form as equation 4, except that unprimed variables have now been replaced by those that are primed. That is because both equations are dealing with cases, not deaths. Therefore, $n_{uv}' = 3,872,067$ cases. Therefore, by the end of July, the unvaccinated contribute 3,872,067 / T = 3,872,067 / 5,000,000 = 0.7744 or 77.44% to the total active case load. The partially vaccinated contribute $n_{pv} = 839,464$ cases or 16.79%, while the *fully vaccinated* contribute $n_{fv} = 288,469$ or 5.77% (these are the breakthrough infections by CDC definition).[12] The USA Today article cited above (Innes, 2021) did not discuss the partially vaccinated. They may have been considered part of their "unvaccinated" population. However, by the definitions used here, the union of the unvaccinated

and the partially vaccinated would account for 94.3% of all cases. A figure that is close to the center of the ~90 to 97% range for their so-called "unvaccinated" (probably meaning *not* fully vaccinated, or the *complement* of the fully vaccinated set; Halmos, 1960) entering hospitals and medical centers during the month of August 2021 (Innes, 2021). Furthermore, it is precisely the unvaccinated (no vaccinations at all) who are most likely to be hospitalized with life-threatening infection, as demonstrated by the previous VAERS calculations. Now the reader can understand why Dr. Kim-Farley called the current situation in the U.S. "a pandemic of the unvaccinated". Mathematics has a way of exposing the truth, and sharpening understanding, in a way that verbal arguments never can!

THE δ-VARIANT AND HERD IMMUNITY:

On Sept. 9, the *Arizona Republic* (2018 Pulitzer Prize winner) reported a breakthrough infection rate of approximately 15% for Aug. 9 to Sept. 9, 2021, in Arizona, the author's home state (Innes, 2021). Whereas the *Arizona Daily Star* reported 25% breakthrough infections for October in Pima County (Machelor, 2021). How can this be if the Moderna and Pfizer vaccines had a 5% breakthrough rate during testing? That is to say, these vaccines were about 95% effective during trials.

Are successfully vaccinated people spreading the infection? No! Two factors are involved. One is the lower vaccine effectiveness of the two popular vaccines against the δ variant. The other is waning immunity. Let's consider each of these in turn.

A recent article in Medical Life Science, although claiming vaccine effectiveness was "barely affected" by the δ variant, also stated that the average vaccine effectiveness (e) of the two common vaccines used in the U.S. was only 84.1% for the δ virus (Solis-Moreira, 2021). That is approximately a 10% drop from test results involving the classical strains. However, it should also be noted that the data points had a large standard deviation and were scattered over the 70 to 95% range. The study involved the following U.S. populations: Washington D.C., Contra Costa Co. CA, DuPage Co. IL, King Co. WA, San Diego Co. CA, Santa Clara Co. CA, Connecticut, Massachusetts, New York State, Oregon, South Carolina, Utah, and Virginia. So, quite a lot of the U.S. was involved in the study. Another study in the New England Journal of Medicine cited a vaccine effectiveness figure of 30.7% after the first dose, and 79.6% after the second dose (Bernal, et al. 2021). So, although the results of these studies are reassuringly close, they are not exactly the same due to differences in experimental procedure and populations. It is also known that by Aug. 2021, almost all COVID infections in the U.S. were δ variant (~ 100%; Bhattacharya, 2021c). Therefore, the number of breakthrough infections among fully vaccinated people must be in the range of 15.9% to 20.4% (the compliment of the effectiveness; 100% - e in %). These are the unsuccessfully vaccinated. As one would expect, this range overlaps nicely with what has been reported in the press.

The other important factor to consider with regard to breakthrough infections is *waning immunity*. That is to say, immunity does not last forever after vaccination. "Two weeks to four months after a patient received their second dose, the Pfizer vaccine was 91% effective at preventing δ variant hospitalizations. After 120 days (four months) the effectiveness fell to 77%. Moderna's vaccine showed much less of a decrease in protection over the same time interval (LaFraniere, Weiland, 2021). We must always remember that, like the story of Lazarus (John 11:1-44), just because the successfully vaccinated have been saved from the Grim Reaper for a while, does not mean that such protection lasts forever!

With the precise definitions established in the previous section, the general requirements of herd immunity can be established. Recall from "Vaccine Safety" (Zito. 2021), that the multiplicity factor m is the number of people that each infected person will infect in turn before they are quarantined. For the classical Wuhan and α strains, the average is about 3, in rural communities close to 1, and in an urban setting perhaps 5. However, the δ-variant is 2 to 4 times more infectious, depending on which researcher you ask (Innes, 2021). Therefore, in the city, we might expect m = 10 to 20 for δ. Let f be the fraction of people in a population that are members of the potentially infectious superset and, for the moment, consider a vaccine that is 100% effective (so that there are no unsuccessfully vaccinated). Then herd immunity is established if $mf \leq 1$. That is to say, the multiplicity is offset by the scarcity of potential hosts (who are members of the potentially infectious superset) so that a vector can only infect no more than one other person, maximum. For example, consider a δ infection with m = 10. If 90% of the population is fully vaccinated (in this case, synonymous with being

successfully vaccinated), then 10% remain in the potentially infectious superset; i.e., f = 0.1 in decimal. Then mf = (10)(0.1) = 1. That is to say, in this case, an infected person can only infect one other person before they are removed from the population. The infection can be maintained, but it cannot spread. If mf < 1, the infection will eventually die out as time approaches infinity. Now, define F as the fraction of people who are successfully vaccinated, then for the ideal 100% effective vaccine f = 1 – F, and the condition for herd immunity becomes m(1 – F) ≤ 1. What if a vaccine is not 100% effective, but has effectiveness e (expressed as a decimal fraction)? By CDC definition, the fraction F of successfully vaccinated is e$\mathcal{F}$, where $\mathcal{F}$ is the fraction of a population that is fully vaccinated. That is to say, the set of successfuly vaccinated will be smaller than the set of fully vaccinated by a factor of e. Therefore, the condition for herd immunity becomes m(1 – e$\mathcal{F}$) ≤ 1. Solving for $\mathcal{F}$ yields,

$$\mathcal{F} \geq (1/e)\,[1 - (1/m)] \qquad \text{Eq 14}$$

This simple, but powerful, equation will expose the difficulties that the δ-variant presents to public health officials.

First, however, equation 14 must pass the test of logic. Suppose m → 1. That means an infected individual cannot pass their infection on to more than one other person. Such a disease can maintain itself, but it cannot spread. Therefore, vaccination is unnecessary for containment. What does equation 14 have to say about this situation? Substituting unity for the value of m in equation 14 yields $\mathcal{F} \geq 0$ for any positive non-zero value of e. That is to say, the fraction of people who need to be fully vaccinated can be zero, as expected. Of course, if some people *are* vaccinated, that will do no harm. Suppose m → ∞. That means we are dealing with an infinitely contagious disease (say, as an approximation, a germ weapon genetically optimized to be exquisitely infectious). In that case, $\mathcal{F} \geq (1/e)$. Therefore, if e → 1 (i.e., a vaccine approaches 100% effectiveness, like 3 doses of the IPV – see Table 1), then $\mathcal{F} \geq 1$. That is to say, the spread of such an artificial infection can be stopped only if everyone is fully vaccinated with a perfect vaccine - common sense! However, if e < 1, then $\mathcal{F} > 1$, and the infection cannot be stopped because $\mathcal{F}$ can never be greater than unity (or 100%). What if m → 0? That means an infected person cannot infect anyone else (e.g. tetanus). Substituting a limiting value of zero for m in equation 14 yields $\mathcal{F} \rightarrow -\infty$. Therefore, not only is vaccination unnecessary, but the disease cannot spread even if you artificially introduce it into a population (the negative of full vaccination). Suppose m > 1, but e → 0. That means a vaccine is totally ineffective (e.g. gonorrhea; VE → 0 for trial vaccines). In that case, $\mathcal{F} \rightarrow +\infty$, and heard immunity is impossible since $\mathcal{F}$ can never be greater than unity. Finally, if e → 1, then $\mathcal{F} \geq 1 - (1/m)$. Hence, equation 14 has desirable properties and passes the logic test.

Now, let's consider a few practical examples. Suppose the δ-variant is three times more infectious than the classical COVID strains so that each infected city dweller can infect 15 other people before they are quarantined. This is easy to do in a crowded rush-hour subway car in New York. And suppose a δ specific booster is available that is 95% effective against δ. What fraction $\mathcal{F}$ of the population needs to be fully vaccinated to achieve herd immunity? Setting m = 15, and e = 0.95, in equation 14 yields $\mathcal{F} \geq 98.24\%$. Sometime about Sept. 30, 2021, the author heard an official of the Pima County Health Department (Tucson, Arizona) on KUAT (PBS) radio declare that, at that time, virtually the entire population of the county would have to be fully vaccinated to achieve herd immunity. Amazingly, as these numbers show, this statement is completely accurate for the City of Tucson – provided such a δ specific booster is available! The good doctor was probably severely reprimanded by her supervisor for candor.

One more specific example is instructive. Suppose the δ-variant is only twice as infectious as the classical strains so that m = 10. Also suppose that a δ specific booster is *not* available, so that the population can only rely on the protection given by the original formulation as discussed in "Vaccine Safety" (e = 0.8). In that case $\mathcal{F} \geq 1.125$. How can that be? This figure for $\mathcal{F}$ implies that 112.5% of the population would have to be fully vaccinated in order to achieve herd immunity. In other words, herd immunity is impossible for the given conditions (see Figure 10)! This is still one more reason why a new δ specific booster is necessary. If δ is only twice as infectious as the classical COVID strains (optimistic), and if e = 95% for a δ specific booster, then $\mathcal{F} \geq 94.7\%$ in the cities to establish herd immunity (see Figure 10). Vaccination levels of 95.5% have been reached

among the hospital staff of the Strong Memorial Hospital in Rochester, New York (Otterman, Goldstein, 2021), but it is uncertain if they can be reached in the general population given the observed resistance in the U.S. to vaccination.

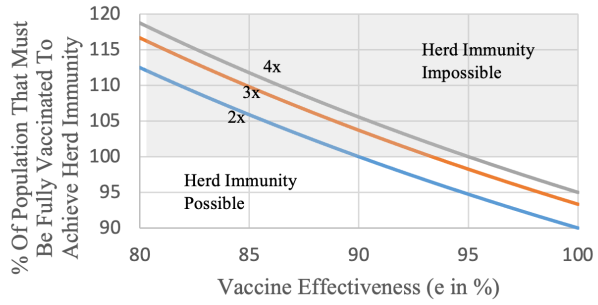

Figure 10: The requirements for herd immunity. *Only (Vaccine Effectiveness, population %) ordered pairs that lie in the unshaded part of the diagram are achievable. Infectiousness levels are labeled 2x, 3x, and 4x, over the classical COVID strains (Wuhan and α). Urban crowding has been assumed. For δ, e ≈ 0.8 for the current vaccine. Therefore, herd immunity is not possible, but fully vaccinated individuals will receive partial to full protection.*

The Biden Administration proposed re-vaccination of the adult population in the U.S. with a δ non-specific booster, based on the formulation used to combat the original COVID strains, 8 months after the initial 2-shot series. However, the plan was insufficiently convincing to "experts" at the FDA and CDC (16 to 2 against; LaFraniere, Weiland, 2021). It was claimed that the old vaccine series is still good enough for most people to prevent "severe disease"; actually, you don't want any disease at all! Others argued that reducing the spread of the disease is also important. In the end, the original proposal was scaled down to only cover people with certain medical conditions and those 65 and older. These limitations were another CDC *faux pas*.

Pima county, Arizona, along the southern border of the U.S., a major corridor for medically unscreened illegal entry into the U.S., has opened booster shots to all adults "because of the high transmission rate" there (Machelor, 2021). Some other states and counties in the U.S. have done the same (Machelor, 2021). As of Nov. 15, 2021, the U.S. government was on the verge of making all those 18 and older eligible for the booster (Walker, Holder, 2021), as the administration originally wanted. However, in the author's *opinion*, eligibility for the current δ non-specific booster should also have been extended to anyone who received the Pfizer vaccine more than 4 months ago because this is the vaccine for which waning immunity has been most pronounced in the U.S. (Walker, Holder, 2021). A 6-month rule (current) is alright for the Moderna vaccine.

This CDC comedy of errors highlights a very important fact. Some of the "experts" named in the *New York Times* article by LaFraniere and Weiland seemed, after an internet search, to be primarily career administrators, not active researchers, or practitioners at the top of their profession. The result was that the CDC was overwhelmingly *wrong*, in spite of early Israeli experience with waning immunity (Walker, Holder, 2021). Perhaps there is a problem at the CDC, or friction with the administration (LaFraniere, Weiland, 2021). However, if the CDC and the FDA aren't informing the American administration, then who is?

CALCULATIONS SUMMARIZED:

The author hopes that these paragraphs bring some order to the tangled mélange of conflicting and misleading information found in the public domain concerning the vaccine. All aspects of the vaccine's performance can be mathematically understood, and it is doing just what it is supposed to do. What is important is the *statistical* behavior of the vaccine, not individual cases unless ALL the relevant facts are known (e.g., age, occupation, underlying conditions, exposure levels, vaccination dates, antibody levels prior to infection, etc.). The latter is what VAERS attempted to do – how successfully is a matter of debate.

It must always be remembered that the pandemic has become heavily politicized, and there are a great many people in the U.S. who wish to find something – anything – wrong with the COVID vaccines that they can. The anti-vaxxers come from all frequencies of the political spectrum. Some claim that former President Donald Trump is trying to poison them. Others claim that the Biden Administration is trying to control them with microchips in the vaccine. Still others claim that the global pandemic is a hoax, and that the vaccine doesn't work. Finally, there are those who claim that COVID-19 is just another common cold. What Rubbish! The author has heard it all! Furthermore, vague ambiguous statements from the authorities, and the publication of statistics having a complex or uncertain interpretation, just exacerbates the misinformation problem (Wichner, 2021).

Some will complain that this article is too detailed. However, it must be detailed if endless verbal arguments are to be avoided! It's all part of the interminable American cacophony of vitriolic political vituperation that stinks in the ear! The anti-vaxxers should remember that, given a pandermic of sufficient duration, almost all the unvaccinated will contract COVID!

THE BOOSTER: AN ETHICAL DILEMMA

The author struggled with the question of whether or not to include this section on the ethical difficulties posed by the current δ non-specific booster. This is not science, and the author is certainly not a theologian, philosopher, or lawyer (although an attorney was consulted). Nevertheless, if this narrative is to be comprehensive, as purported by the abstract, the author has no choice but to walk were even angels dare not tread.

On the surface, the distribution of a booster seems to be only positive. However, how does one answer Dr. Tlaleng Mofokeng, a South African expert advising the UN, when he says that the booster will have the effect of "advancing and deepening the existing inequalities" when "there are people who are yet to receive a single shot" (Miller, Perrone, 2021)? Or that "[Moderna] has been shipping its shots almost exclusively to wealthy nations, keeping poor countries waiting […]" (Robbins, 2021). Moderna says they are a small company, with only one product, and cannot possibly produce enough vaccines for the whole world. Furthermore, Moderna claims that they have tried to get governments to invest in expanding their scant production capabilities but have failed.

The basic issues are old, but also complex. By implication, racially diverse America and American pharmaceutical companies will be accused of discrimination, greed, and profiteering; all emotional "hot-button" words. It must be remembered that many other countries, like vaccine powerhouse India, produce COVID vaccines as well (Zito, 2020b). Although they may not be as effective as Moderna's vaccine, they are certainly better than going unvaccinated!

So, beyond all these inveterate emotional accusations and corresponding retorts, is there any common ground that everyone can agree upon? The author thinks there is, especially at the personal level. First and foremost, all COVID vaccine doses that have been produced (regardless of manufacturer) should be used. Few would question the morality of distributing (giving away) unused doses to third world countries before they spoil. Here in the U.S., there are some people who believe that COVID vaccination violates their religious rights (Otterman, Goldstein, 2021)! Whether such people truly believe what they say, or whether it is just an excuse not to take the vaccine is a matter of conjecture. Nevertheless, their resistance to vaccination is based on freedom of religion, so it is unlikely that they can be compelled to cooperate. In such cases, remitting their doses to someone in another country seems both prudent and ethical.

What about people who refuse to be vaccinated? Some Americans, amazingly, are using counterfeit CDC cards to evade vaccination mandates. Such people are so spoiled and ungrateful that they simply don't realize how lucky they are! In such a case, there is no way to know if a person is compliant, so their doses will either be used by another person or be given away de facto before they spoil.

What about people who voluntarily wish to donate their dose to someone in another country? Shouldn't they be allowed to do so? After all, as the Hindu's would say, our own life is the only life we truly own! The practical answer to this question depends on whether vaccination is legally voluntary or compulsory. If voluntary, their doses can be given away. If compulsory, then refusal, without constitutional exemption, could be fined and their doses given away before they spoil. The fine money can be used to purchase a new dose should they later decide to comply. Nothing is truly free, and the object here is to *persuade* rather than punish!

On a national level, the author would be remiss if he did not raise the controversial question, "Can an employer in the U.S. 'persuade' an employee to be vaccinated by using the threat of dismissal, given that vaccination is *not* the law of the land?" Is this disease control, or "threats and intimidation"? What about the risk to other employees? Who has the liability if someone gets infected? According to current U.S. law, an employer has the right to make vaccination a condition of employment. Thereby mitigating the risk to other employees and reducing an employer's liability. However, as a practical matter, the risk of losing essential employees needs to be balanced against the risk of infection. Furthermore, it is not clear if a government agency has the right to "mandate" vaccination for all companies having more than 100 employees, essentially making

vaccination law. It is an issue that is currently before the U.S. Supreme Court. The government will undoubtedly argue that the mandate is an Occupational Safety and Health Administration (OSHA) rule. The opposition will undoubtedly argue that the pandemic is not occupation related, and that only legislative approval can make vaccination law. What the justices will decide is anyone's guess.

What about on an international level? Should the U.S., or any other country, that manufactures vaccines, distribute them to other nations before vaccinating their own people, who paid for the technology through their taxes?

Regardless of where COVID may have originated, the U.S. is now the most infected country in the world by a very substantial 11.3 million more total cases, 61% more total deaths, and a shocking 45 times more *active cases* than the runner-up (sorted by total cases), India as of Oct. 11, 2021 according to *Worldometers* (worldometers, 2021). These figures are all the more appalling when one considers that India has four times the population of the U.S.! On September 27, 2021, *Medical Life Sciences* (Solis-Moreira, 2021) declared that "The United States remains the country with the highest number of cases and deaths from coronavirus infection 19 (COVID-19)", and that makes the U.S. the primary source of COVID disease for the rest of the world, by far. Clearly, we are doing something very wrong!

Our inability to vaccinate the population (especially minorities) in a timely fashion, and to achieve herd immunity, has taken its toll. Our politicians do a splendid job of manipulating every media outlet when they want to win an election, but where is the corresponding commitment to public education about vaccination? Why doesn't every billboard in the land say, "*Uncle Sam Wants You To Get Vaccinated!*"?

Furthermore, our inability to control the flow of infected people across our international and interstate borders (Jervis, 2021), complacency and over confidence born between waves of infection, and the current political civil cold-war with its concomitant lack of public cooperation over everything from wearing masks and social distancing to the mitigation of stock-piling behavior, have all exacerbated America's problems. Additionally, governmental internecine battles over whether or not to deploy the δ non-specific booster, didn't help matters either. Our efforts were too little, too late, not to mention the fact that we still do not have a *truly* δ specific booster that would maximize our ability to fight that strain. The U.S. needs to put in place, and fund, an infrastructure capable of developing and distributing vaccines for the new COVID strains on an annual basis – perhaps even faster. Perhaps *this* country should be the focus of the global effort to stamp out the pandemic, not South Africa (17th for total cases). These are all issues and questions to stir the passions and, undoubtedly, we will all be arguing about their answers for many years to come. For now, each reader will have to decide for themselves what constitutes ethical national and international public health behavior.

CONCLUSION

"May you live in interesting times" is purported to be an ancient Chinese curse. Actually, it is a modern paraphrase of a Chinese lament from a collection of short stories published in Suzhou in 1627 (Anon.c, 2015). The words may have been different, but the sentiment is the same. Well, these certainly are interesting times, but like so many interesting periods of history, it is filled with a great many tribulations. The current "hot-buttons" of controversy seem to center around the definitions used for infection calculations and how to ethically distribute vaccine doses. *Can* a vaccine stop the spread of an infection? *Should* we get vaccinated? If so, *who* should get vaccinated? These questions all have clear answers as discussed above. So, why are we still fighting about them? Well, this *imbroglio* clearly has nothing to do with the facts. It is emotional, but not without parallel in history. Something similar was going on in the Italian city states starting from the very earliest days of the Renaissance ("re-birth"). It is a story well-known to the Italian members of the ISSS. In 1300 you were either *Ghibelline* (yielding political allegiance to the Holy Roman Empire), or you were *Guelf* (yielding political allegiance to the Pope). But rather than the author retelling the story, let's read the words of the eminent historian Will Durant (Durant, 1953):

"Partisans of the popes and partisans of the emperors not only divided Italy, they split almost every city into Guelf and Ghibelline, and even when that strife subsided the old labels were used by new rivalries, and the lava of hate flowed into all the avenues of life. If Ghibellines wore feathers on one side of their caps, Guelfs wore them on the other; if Ghibellines cut fruit crosswise, Guelfs cut it straight down; if Ghibellines wore white roses, Guelfs wore

red. In Crema the Ghibellines of Milan tore a statue of Christ from a church altar and burned it because its face was turned in what was considered a Guelf direction; in Ghibelline Bergamo some Calabrians were murdered by their hosts, who discovered from their way of eating garlic that they were Guelfs. The timid weakness of individuals, the insecurity of groups, and the delusion of superiority generated perpetual fear, suspicion, dislike, and contempt of the different, the alien, and the strange." – Will Durant

Does this story sound familiar? Although the passage above may seem comical to modern readers far removed from the passions of that time, the character of man has not really changed in 700 years. Today, we fight over masks, vaccinations, and post-infection therapeutics. These, however, are not the real reasons for animosity any more than the way they ate their garlic in Renaissance Italy. No! These are little more than excuses for a confrontation, as each side turns a *faccia tosta* (a hard or impudent face) toward the other. This author doubts very much that the modern American "Ghibellines" and "Guelfs" in Washington know, or even care, about the science and the public health issues of the day. It's going to take a lot more than how we cut our fruit to put an end to the pandemic in the U.S. In the end, Americans are going to have to get control of their borders to stop the flow of medically unscreened, possibly infected, undocumented immigrants into the U.S. In the end, the government will have to institute mandatory adult vaccination for all circulating strains (including δ and now Omicron*)*. And in the end, public health measures are going to have to be enforced with fines. All very unpopular "hot-button" issues that will offend both the "Ghibellines" and the "Guelfs". But until these controversial measures are implemented, total deaths in the U.S. may continue to mount with each cold and flu season at a frightening rate as we approach 1 million deaths in the U.S. (about 20% of the global total). Equally as important, our infected travelers will continue to be a source of disease vectors for the rest of the world! - Stay Well.

FOOTNOTES

1) There is an interesting and instructive piece of video (with a companion booklet) worth examining at this point called "Powers of Ten" by Charles and Ray Eames (Eames, 1989, 1982).

2) There is an interesting piece of experimental music called "Dance Folding" by Augusta Read Thomas (augustareadthomas.com) that debuted on PBS radio (KUAT – Tucson, AZ). It aired on Friday evening, September 3, 2021, and was from the BBC Proms Concert. It is an acoustic rendering of what happens when a protein folds. Each "click" might be interpreted as the contact of two amino acid side chains. It's worth listening to!

3) If the probability for a significant mutation per year per infected individual (2.5×10^{-8}) is multiplied by 1.8 years (the duration of the pandemic as of Oct. 30, 2021), you get a probability of significant mutation of 4.5×10^{-8} per infected person. However, the global number of infected people is 246,000,000 as of Oct. 30, 2021 (Wikipedia). Therefore, the total number of significant strains worldwide should be about $(4.5 \times 10^{-8})(2.46 \times 10^{8}) \approx 11$. In fact, the number of significant strains is 7 as of Oct. 30, 2021 (Wuhan, α, β, γ, δ1, δ2, λ). This actual number of significant strains implies a probability of 1.6×10^{-8} per year per infected individual. Therefore, the error between theory and experiment relative to the theoretical value is $100 \times (2.5 - 1.6)/2.5 = +36\%$, where the "+" sign means that theory has overestimated the observed number of significant strains. So, the virus is mutating with mathematical precision. The coronavirus is just a machine. An unconscious, parasitic, biological killing machine. As such, it is subject to the rules of mathematics. Like smallpox, the sooner COVID is wiped off the face of the Earth (if that is even possible – it may not be since the virus is mutating faster than the rate at which vaccines are currently being developed and distributed), the better off, and safer, humanity will be. Just one more reason why a δ specific booster is needed and should be widely distributed!

4) The units used for titer vary, but typically a successfully vaccinated person should have a titer of 1, or 100%, or 1000, depending on where you wish to put the decimal point. Unsuccessfully vaccinated people will have a titer well below these figures, say, 0.6, 60%, or 600. While a few people who have just received a booster or have just recovered from a wild infection may have a titer of almost 2, 200%, or 2000.

An experimental understanding of successful vaccination begins with an understanding of titer (from the word titrate). Antibody titer is a measure of antibody level relative to the mean antibody levels found in unvaccinated patients convalescing from the wild infection. This latter group has enormous antibody levels because they have just destroyed a full-blown infection, and the concomitant temporarily

uncontrolled proliferation of virions within their bodies. Therefore, these are the antibody levels capable of destroying any likely initial wild inoculation that has not yet started to proliferate in the receptive host. The base-line titer of 1 (or 100% or 1000) refers to this enormous antibody level and it is visualized by a biochemical tool called ELISA (Enzyme Linked ImmunoSorbent Assay) (Khoury et al., 2021). There are many variations on the basic ELISA scheme (Mathews, van Holde, 1996), but the most direct procedure for an antibody analysis would be to create a titrant by covalently linking an antigen (like the S-protein) to a (colored) dye molecule. Note that copious amounts of antigen can be produced by a yeast using the methods outlined in the first report of this series (Zito, 2020b). Now, if a standard amount of blood serum is taken from a convalescing COVID patient, and it is mixed with an *excess* of titrant, the antigen-antibody conjugate will also be colored. The intensity of that color, after removal of any interfering unreacted titrant, is defined as a unit standard titer (or 100%, or 1000). All other titers are measured relative to this baseline. Therefore, if a patient has a blood serum displaying half the color saturation of the standard (as measured by a photodensitometer or visual inspection after serial dilution), then the patient has a titer of 0.5 (or 50%). It is essential to understand that the titrant will not conjugate with just any antibody, but only the S-protein specific antibody (or antibodies if there are more than one). A variation on the ELISA procedure involves the use of a fluorescent dye (usually fluorescein) covalently bonded to the S-protein (Mathews, van Holde, 1996). In either case, the trick is to remove any *excess* titrant. There are many ways to do this. However, since the S-protein is small compared to an antibody, it is probably best to simply pour the mixture through an appropriate chromatographic column; a glass cylinder containing beads (usually made of polystyrene) coated with permanently bonded S-protein specific antibodies. The liquid that is eluted (comes out of the bottom of the column) is the solution to be spectrophotometrically analyzed (the analyte).

Clearly, it is important to keep personal immunity as high as possible (Read, 2021) because massive infections can occur (e.g., if a seriously infected person coughs in your unprotected face). However, baring such unlikely circumstances, a wild inoculation will not be able to seriously challenge a successfully vaccinated person. Experiment, clinical experience, logic and set theory arguments, infection probabilities vs. titer, and calculations of antibody levels, all tell the same story: viz, healthy successfully vaccinated people are unlikely to contract or spread disease!

Naturally, there will always be rumors. An amusing "hear-say" story was related to the author about a wine tasting event attended by 11 supposedly fully vaccinated people. Shortly thereafter, it was claimed that 9 of these got the COVID. As usual, there was no proof of any of this. Cognoscenti must patiently smile at such fables. Their purpose, like that of Aesop's fables or any religious parable, is not to convey facts, but to preach a sermon. In this case, the erroneous anti-vaxxer sermon that "vaccination is futile". Furthermore, such stories are elaborated upon as time progresses through the natural processes of storytelling. So, why do some people believe such rumors? Perhaps one of Oscar Wilde's witticisms captures their sentiment, "I'll believe anything, so long as it's absolutely incredible!" There are no limits to human gullibility!

5) Waning immunity was suspected to be a problem with the BNT162b2 vaccine used in Israel, the first country vaccinated, and has resulted in a sharp increase in COVID cases (Levin et al., 2021). It is for this reason that a booster was prepared for the American population. Because its formula was unchanged (not δ specific), rapid production was possible, vs. a booster with δ specific activity and a longer development time. Finally, it should be noted that waning immunity is a necessary natural process. Very few artificial or wild inoculations convey lifelong immunity. Otherwise, the energy cost to the human body required to maintain a standing army of antibodies at maximum strength against every occasional biological invader would be so great when summed over the years that either premature death would result from the complete exhaustion of the body's energy currency, or species extinction would result from "eating-out" our food supply to furnish the necessary ever-increasing energy demands. Strangely, on a macroscopic scale, the nations of the world are doing the same thing today with their money, their military expenditures, and their ever-increasing populations and energy consumption. Guess what the result will be!

6) This statement assumes the antibody test yielded a "true" positive. Real tests, however, are imperfect. Nevertheless, test repetition is a valid way of removing doubts as described in the first paper of this series (Zito, 2020b). It should also be noted that

an antibody test will only turn positive when the antibody levels reach the levels seen in a person about two and a half days after a wild type infection begins. Therefore, any verified "+" antibody test following vaccination of a healthy person means that the vaccinated has at least a 60-hr. head start in combating the establishment of a new infection. Realistically, it is probably a lot more than that!

7) Anaphylactic shock involves still other types of immune system cells called basophils and mast cells (Wessells, Hopson, 1988; Cowan, Talaro, 2006). Both of these cell types have a similar structure. In particular they contain granules filled with chemicals like histamine, the agent responsible for many unpleasant allergies. In fact, these two cell types were once considered the same. However, we now know that they are quite different. Basophils are a line of immune system cells (0.5% of all white blood cells) that originate from the bone marrow, and, like all such cells, they are mobile in the blood. By contrast mast cells are immobile cells bound to connective tissue around blood vessels, nerves, and epithelia. If the immune system is overstimulated, these cells (especially mast cells) will release their granule contents all at once. If that happens, anaphylaxis is the result. It is a condition that can kill in just 15 minutes from complete airway blockage (Cowan, Talaro, 2006). It should be noted that more health care authorities are moving toward the author's more conservative recommendation of waiting 30 minutes after vaccination before departure to reduce the possibility of anaphylactic shock.

8) The human immune system is very complex. It contains cells for clotting, cells for phagocytosis (digesting foreign substances), cells for inflammatory response, cells to destroy worm and fungal infections, cells to produce antibodies, and cells that produce chemical messages to induce other immune system cells to replicate. The whole menagerie starts from hematopoietic stem cells in the bone marrow ("hem" is Greek for blood, and "poietic" is also from the Greek meaning "having the character of"). Some of these stem cells develop into erythroblasts and then into erythrocytes, or red blood cells. However, it is the remainder that are of interest to us here; megakaryoblasts, myeloblasts, monoblasts, monocytes, macrophages, dendritic cells, megakaryocytes, granulocytes, platelets, neutrophils, basophils, eosinophils, natural killer (NK) cells, lymphoid stem cells, lymphoblasts, and lymphocytes (types T and B) (Cowan, Talaro, 2006). Mast cells are also part of the human immune system, but they are part of another cell line.

9) At this point one might reasonably ask, "Why doesn't the immune system normally attack one's own body?" When immature B-cells in a fetus encounters substances that bind to their surface antibodies, they are not stimulated to replicate. Instead, these cells are destroyed. Therefore, cells producing antibodies against all potential "self" antigens to which we might react are eliminated before birth! The only B-cells that mature are those that produce antibodies against "non-self" substances (Mathews, van Holde, 1996). Welcome to the astounding worlds of biochemistry, cellular and molecular biology, immunology, and modern medicine.

10) Some have speculated that a small aircraft might crash because the pilot suffered heart failure during flight after vaccination. It seems improbable, but any excuse will do for the anti-vaxxers. Presumably some coincidental deaths are eliminated from the data base by postmortem investigation. However, the author has not yet been able to get anyone at the CDC to admit to that (CDC.d, 2021).

11) Although a factor of 6.5 may be reasonable for the entire (pre-δ) VAERS period when only the two-shot basic vaccination series was available, it is too conservative for the δ-predominance period that followed in the U.S. Statistics for October – November 2021 show deaths were 12.7 times higher for the unvaccinated relative to those who had received the basic two-shot series (Johnnson et al., 2022). The increased lethality of the δ-variant among the unvaccinated probably accounts for the factor of 2 difference in deaths since the vaccinations were the same. Furthermore, there were 53.2 times more deaths among the unvaccinated relative to those who received the basic series plus the booster (Johnson et al., 2022). As previously discussed, the booster produced such a massive increase in antibody levels that the death rate among the boosted fell by almost half an order of magnitude compared to those who only received the basic series!

12) Note that the ratio of unvaccinated cases to fully vaccinated cases is 13.4; a figure close to the truth. Statistically, the incidence rate ratio (IRR) was 13.9 at the end of the pre-δ period. The error between theory and experiment is only 3.6%.

ADDENDUM (JAN. 2022)

This report primarily covers the narrow time interval from mid-August 2021 to the end of October 2021. Since then, the Omicron strain has been detected. That will be the subject of a separate publication. There is simply too much to say in a single publication! It should also be noted that active COVID cases in the U.S. (Figure 1) stand at 15,288,098 cases as of Jan. 4, 2022 (Worldometers). This case figure is 8.4% above what is projected by an updated 5th degree polynomial fit to the total data set, and a very substantial 28% above an updated linear model. Furthermore, total deaths in the U.S. are still rising at a linear rate as of Jan. 4 (Worldometers). Although the best fit 5th degree polynomial was a good short-term predictor, it says nothing about when the current surge in cases might reach its peak or, on an even longer time scale, when the pandemic might end. It is likely, however, that cases in the U.S. will ameliorate as the northern hemisphere reaches the warmer spring and summer months.

Also significant is that The Wall Street Journal ran an article entitled "CDC Aims to Revamp Covid Moves" (Schwartz, 2022). Although the article is not completely fair to the CDC, and contains one important error in its science, it does highlight the fact that "Confusion has further undermined faith in the nation's public-health system at a critical moment", just "before the δ variant emerged", when the CDC "suggested people stop wearing masks". It was a replay of what happened in India!

Finally, on Jan 13 the Supreme Court declared the Biden Administration's "vaccine or test" mandate for private companies having more than 100 employees exceeds the authority of the Occupational Safety and Health Administration (Totenberg, 2022).

COMPETING INTERESTS

The author declares that from July 1, 2021 to January 31, 2022 he had no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Global Warming and System Safety

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ABSTRACT

We are currently confronted with the existential challenge of global warning. Because of its nature it is a challenge that confronts the entire globe both in terms of contributing factors and bearing the consequences. In both aspects there is an inevitable balance of responsibilities and consequences. In the former, some national entities are bigger contributors to the problem than others and in a similar manner some global areas suffer relatively more significant negative consequences. Another major challenge has been that of generating a better scientific understanding of the relationships between greenhouse gas emission, global warming, and the resulting environmental consequences. The remaining challenges that follow are how best to prevent or minimise greenhouse gas emissions, how to store them safety and how to mitigate the potential negative consequences. These are now global level responsibilities. At first sight this appears to be a problem restricted to big science, technology, and engineering alone in terms of finding more acceptable forms of energy production, as a counter to our current dependence on fossil fuels and that it might not be an area where system safety can play a prominent part. However, this is not the case, and this paper explores the system safety application possibilities, because all new developments require to be implemented in a safe manner.

INTRODUCTION

The world is currently facing an existential threat as a result of global warming. The seriousness of this problem was recently aired for all to see at the global COP26 meeting in Glasgow, UK in November 2021. The debate about global warming has had a chequered history, which has broadly followed the lines of: It is not really occurring it's a scam. It might be occurring, but this is a normal part of the natural earth cycles. Human activities are not a significant cause. Human activity does appear to be a significant contribution. To cut a long story short, the science has now overwhelmingly demonstrated that global warming is in fact occurring with human activity a prime cause through harmful greenhouse gas emissions, Figure 1. This trend has significant negative consequences for society in the global sense (for example Figure 2). Of course, there are many industries whose commercial success is based on energy production from fossil fuels, which presents the major source of greenhouse gas emissions. There are obviously major conflicts of

interest in the challenge of tackling global warming between commercial interests and those parts of the world which bear the greatest environmental risks.

Figure 1: A Primary Contributor to Global Warming

Traditional System Safety has a long history of safety applications, safety assessment methodology, risk tolerance standards and established criteria. It is now accepted as one of the critical requirements for ensuring the success of any industry. System safety will be intrinsically linked to the nature of the technology to which it is being applied and how to remove or minimise such risks down to generally accepted tolerance levels. That is, they are generally no more significant than those suffered from other sources.

Of course, there is always a difference in what is meant by the implementation of safety and the resultant assessment of remnant risk. The former relates to the application of positive measures and constraints to achieve safety and the latter provides a best effort measure of how successful the applications appear to be. The former is primarily related to the application of sound principles which gives a sound basis for safe technology application, ensuring the products, human involvement, associated processes, and usage will be acceptably safe. Making safe is essentially based on fundamental arguments and the application of clear common sense, but this has become more and more difficult to ensure as products and processes become more complex and less transparent. In turn, risk assessment follows from our *best attempt* at qualifying or quantifying such, based on the level of completeness of our knowledge underpinning such assessments. This also continues to challenge us as technology becomes more and more complex. We can never claim complete knowledge and detriments (a penalty or mishap) can still occur as a result of incomplete knowledge, in addition to failure to follow established rules or best practice.

We have also been aware, over many decades, that human harm can occur through harmful alteration of environmental and geological conditions, whether they be naturally caused (e.g., volcanic, earthquake) or through human based process (for example in the 1960s/70s the UK smog problem caused by domestic coal fires, and the radioactive material release from the evolution of the nuclear industries). These latter concerns have led to environmental protection standards and proactive safety monitoring for standards compliance - regulation.

Global warming gives rise to an evolving need for environmental protection but on a global scale and where the cause and effect (the individual cause contribution and where the effects occur) are not easily understood without the application of state-of-the-art science. As noted above, this subject area has passed through phases of doubt, scepticism, uncertainty, and lack of direct evidence. But eventually through mounting scientific evidence and increasing examples of the detrimental consequences, it has become clear that the problem is real, existential in nature and with a major human based causation. We are already seeing substantial direct evidence of the detrimental consequences.

So, what part should system safety play in this subject area, what guidelines should be developed, and should system safety be involved in the establishment of criteria and standards and in what form should they take for enterprises which may be judged as major contributors to global warming, and protection of those who are at the greatest risk.

CONTRIBUTORS AND NON-CONTRIBUTORS

Unlike the more general case where most if not all enterprises have a major stake in the prevention of detriments relating to the design, manufacture, and application of their products, the same is not broadly so for global warming. In this case a more limited number of enterprises are responsible for the major risk contribution, and at first sight it is unclear how the normal processes of system safety can impact on mitigation of the problem, but system safety does still have a role to play, but by more of an indirect nature. Reduction in the quantitative nature of greenhouse gas release will take the form of new technologies for energy production, the application of new more environmentally friendly energy sources and the potential for their greater general application. Many

Figure 2: One of the Detrimental Effects

take the form of already technically available alternative sources, which in principle, do not significantly contribute to greenhouse emissions. These will need to be scaled up with the necessary technical advances to become more commercially viable. Nuclear power is a major example. Cases are currently being made for an enhanced application of nuclear power with new reactor designs, including the alternatives of small modular forms. In the long term, this might even extend to the eventual practical application of nuclear fusion. Other viable alternatives for expansion are based on directly harnessing solar power through enhanced focussing, solar cells technology, and harnessing the winds and tides. These can all ultimately supply domestic, commercial and transport applications. In the latter case alternative sources of energy are already taking the form of high energy density batteries and the potential application of hydrogen cells, all being technically feasible but needing development to extend their coverage in a more commercially viable and efficient form.

The core of these 'developments' will be based on advances in science, technology, and engineering, but no matter what form all will introduce new detriments and risk and, as such, all will require the skills of system safety to identify the detriments, the potential paths to such detriments, together with an ability to find and implement solutions to remove or mitigate risks to acceptable levels.

For example, the case of nuclear fission is already an area where system safety has played a prominent role and will continue to do so especially if this industry is poised for expansion with new technical approaches, which will need to be assessed for safe implementation. The same will inevitably apply to the other new or expanding energy supply sources, which will replace fossil fuels and to the parallel case of new and expanded greenhouse friendly transportation power application. In all cases, the new technologies and methods of application will give rise to new safety challenges and the need to overcome these leading to acceptably safe operations.

The bottom line here is that although system safety may not be a big player regarding the enhanced methods for reducing greenhouse emissions it will be in terms of the safe applications of the new approaches. In addition, the same can be said in principle about those new techniques being developed for the capture, application of and safe long-term storage of greenhouse gas emissions.

WHAT IS A GREENHOUSE GAS?

Greenhouse gas emissions are the fundamental cause of global warming. They are gases that absorb and emits radiant energy within the thermal infrared spectrum, leading to the capture of heat leading to increasing temperature. The principal greenhouse gases in our atmosphere are water vapour, carbon dioxide, methane, nitrous oxide, ozone, and other fluorocarbons, where through quantitative measure of release criterion, carbon dioxide is the major concern. These can have beneficial or deleterious effects. For example, without greenhouse gases in our atmosphere the average earth's surface temperature would be about -18C and this of course would make human life uncomfortable to say the least. Ozone also has a beneficial aspect in that it helps to protect the earth and life from harmful ultra-violet radiation. At the other extreme Venus, which has a major content of greenhouse gases in its atmosphere, has a surface temperature of many hundreds of degrees C. It is

hotter than Mercury, although the latter is significantly nearer to the sun. Additional greenhouse gases in our atmosphere will move us in the general direction of Venus. Or course we are not talking about Venus scale changes, but current science tells us that average temperature increases of the order of 1-2 C above pre-industrial levels can still produce local and global catastrophic conditions with increased frequency. Science now confirms that we are moving in this direction, and this is confirmed by direct experience. Without rectification the situation will continue to get worse, with the additional concern that cliff-edge conditions may ensue. The current trend of increasing greenhouse content will lead to ever more powerful storms, increased rainfalls, mudslides, increased melting at the poles and other icefields, increased rise of sea levels, increased flooding, increased droughts with more extensive fires and more areas of the earth turning into desert conditions. Science has now made it clear that human activity is a major cause of this increasing greenhouse effect and humanity must be responsible to reverse it. The greenhouse gas increases are essentially occurring because of humanity's greater and greater need for energy and the current reliance on fossil fuels, such as coal, oil, and natural gas. So, the challenge is now to move to more environmentally friendly energy sources, coupled with more efficient processes for greenhouse gas capture and safe storage. In the latter aspect, the world is also currently moving in the wrong direction by continuing to reduce the global capacity of carbon capturing vegetation (forests).

SAFETY AND RISK IN THE GLOBAL CONTEXT

SOME OF SYSTEM SAFETY 'DIFFERENCES'

Any venture of system safety into global warming takes one inevitably away from the more locally related responsibility for detriments to a world of distant partial contribution to detriments with no simple direct relationship between individual cause and effect.

The more traditional system safety world relates to somewhat 'local' boundaries within which, cause and effects occur, and where responsibilities more clearly lie, based on the known manufacture and usage of products. This also applies to the case of the more traditional aspects of environmental protection, where the responsibility is clear, and the detrimental consequences are usually restricted to defined and more limited boundaries. Of course, there are exceptions even here, where detriment boundaries can by quite large. For example, nuclear power and nuclear weapon industries, where catastrophic failures can be far reaching but where the responsibilities are clear, and the boundaries can be assessed. Perhaps a more nebulous area in relation to boundaries and responsibilities is exemplified by the current COVID -19 pandemic, where the boundaries are indeed global, and so are the causes and effects but there is as yet no clear accountability.

Global warming boundaries, simply by their definition, are indeed global but there is, and must be, a shared responsibility for causation. The suffering is not globally uniform, and those who suffer from the worst consequences, are not necessarily those causing the problem. As such, the latter will not necessarily have the most powerful resources or powerful voice in ensuring mitigation or removal of the problem. In addition, those enterprises which are the greatest contributors to the green-house emissions will see their industries as key elements of their economy, both at company and national level, and as such will be somewhat resistant to the pleas from the most affected areas of the globe. This self-interest represents a major challenge to an early rectification of the problem.

In turn, apportioning and acceptance of responsibilities and accountabilities by individual countries and enterprises is likely to be confrontational in nature and not an easy task to solve. Especially in the current climate, where individual enterprises have major dependence on fossil sources as their prime source of energy for domestic, industrial and transport applications and indeed where it often forms a key element of a country's economy.

BENEFIT AND RISK

In the case of global warming there will be risks, but not in the conventional form. In this case the additional risk relates to the distributed global elements and is uneven in nature and is difficult to qualify or quantify in the usual sense. Traditionally a single enterprise can establish a conventional benefit/risk balance simply by just considering the local elements of risk associated with its local activities … it bears its own risk responsibility. For example, how does it benefit the enterprise and the customer base it supplies and what risk arises from its own operations and for the customers' use. In this greenhouse gas world, the process for estimating

benefit follows the usual lines but the risk is somewhat more nebulous, in the sense that an enterprise cannot easily estimate its contribution to the global nature of the detriment risk. Hence, individual risk responsibility is difficult to define and quantify in this case. It is the overall emission which causes detriments, and there will be no clear and deterministic relationship between a specific detriment and individual enterprise contribution. At this stage it appears difficult to move far beyond the relatively coarse measure of a nation's relative contributions to the global emission. In addition, the relationship between overall emission and the full range of potential detrimental consequences that might occur is by no means fully understood. Current environmental scientific assessment indicates that one should ideally aim not to exceed an average temperature rise of 1.5C above the pre-industrial level, with major global concerns arising for increases of 2C or more. Many enterprises will be minor contributors and any attempt for further minimisation will be more for moral/PR purposes only, and in line with some general national expectation to do better. The situation will be different for major emitters and these enterprises will be subject to both global and national pressure to look for significant reductions and for compliance with any agreed standards that ensue. The global pressure will inevitably be governed by the proportionate size of the national contribution to overall release. Another risk, or loss of benefit that is already becoming a reality in the cost benefit balance is the so-called carbon tax. Both emission reduction and reduction of carbon taxes will appear in the overall benefit /risk balance

ANOTHER ASPECT OF RISK

A complete process of defining and measuring global warming risk, is itself a very complicated business. Of course, the obvious starters were noted previously as more frequent and greater storms, increased flooding, and increased droughts, etc. But these are simply the first stages of the detrimental consequence. From these will flow a whole range of subsequent detrimental consequences, such as loss of food production, new or more extensive diseases, disruption of transportation, loss of habitable land, starvation, increased international, national, or local tensions, loss of viable areas for occupation, mass movement of populations, etc. These are not typically the areas where system safety activity takes place in relation to risk assessment but nevertheless may still benefit from the logical mode of thinking normally embedded in system safety.

A HIGH CONSEQUENT RISK

Global warning does indeed fall into the high consequent risk category. However, it represents a difference to our normal experience of high consequence risk analysis and assessment where the probability of occurrence is small but is still subject to uncertainty – high consequence low probability. This has been, and still is, a difficult area for assessment and especially in terms of risk quantification. This is certainly true for the quantification of risk in the nuclear weapon enterprise for the worst-case consequences of inadvertent nuclear yield (INY) and inadvertent radioactive (RA) dispersal. High consequence risk is also associated with 'Black Swan' thinking, where the nature of the potential catastrophic consequences has not really been identified and of course with little ability to assess their probability. If we go back some decades, even global warming and its consequences were still not on the horizon, either in terms whether it could lead to an existential threat or whether there were any substantial grounds for estimating the probability of occurrence. In fact, global warming can be categorised as a 'Black Swan', and like all 'Black Swans' it has occurred with a certain amount of surprise and alarm. It is now certainly recognised as of very high (even existential) consequence, and the full nature of the spectrum of consequences is only now beginning to reveal itself. Consequences have already led to major human detriment, but the prognosis is that there is worse to come – perhaps a still evolving 'Black Swan'. This appears to be true even if greenhouse gas content does not increase above the present level and of course this will be exacerbated if content continues to increase, perhaps with still a lack of clarity of the eventual nature and scale of such consequences

ALARP IN THE GLOBAL WARMING CONTEXT

In the UK at least, risks are subject to the As Low As Reasonably Practicable (ALARP) test, which in fact is a Legal Requirement. This states that there should be a continual process of risk reduction until a stage is reached when the cost and effort is disproportionate to the risk reduction achieved. A clear evidence-based case must be made to substantiate this claim. This approach is associated with a Basic Safety Level (BSL) above which the risk

is deemed as not tolerable and a Basic Safety Objective (BSO) which represents a viable aim for a risk level which is small compared with other risks in life. Essentially, the region between the two levels is identified as the ALARP region and where most of the ALARP assessment process takes place. It is assumed that most countries have a similar general strategy of this form. However, how this may be applied to global warming is somewhat challenging. Where partial cause-and-effect relationships for risk 'at a distance' are somewhat unclear and contentious, let alone having any sound quantitative and legal basis. It is not clear at the present time, how such a strategy of this nature could be applied even in skeletal form, given the difficulty of apportioning (and the acceptance of) responsibilities to the overall global contribution and to local specific detriments. Nevertheless, some strategy and framework based essentially on the ALARP concept does appear to be a valid aim for such enterprises and particularly those classed as major emitters.

The Bowtie Safety Concepts

In the grand scheme of things traditional safety approaches are based both on the Swiss Cheese and Bow Tie concepts of prevention of detriments and limiting their consequences. That is, minimising the probability of a sequences leading to potential harm and following this by actions to mitigate the level of the detrimental outcome. This approach can also be applied in principle to global warming in terms of limiting the potential for emissions and taking further precautions for mitigating the level of consequence. The latter can take the form of early warning of impending abnormal environmental conditions, better protection against flooding, reduced potential for fire damage and even processes for safe capture and safe geological lock down storage through enhanced technical means There is a precedent for the latter as exemplified in the nuclear industries in the handling and storage of nuclear waste. However, this example has not been a process without its difficulties… but lessons may be learned here. Although the core elements of this subject area are mainly associated with meteorological, hydrological, and geological sciences and engineering, system safety assessment methodologies will still have a part to play.

The Relevance of Traditional Safety Assessment Techniques

The question arises as to whether the safety assessment methodologies developed in system safety still apply to the risks associated with global warming. In general, they still appear to be, given suitable customising. For example, the top-down Fault Tree Analysis (FTA) approach can be applied at enterprise level, where the tops of the trees will list emission types and quantities. In turn the fault tree analysis can be used to identify the contributing sources to the top-level emissions. This can then be used in the usual way to identify the main contributors and where best effort should be focused to remove or minimise these.

Failure Modes and Effects Critical Analysis (FMECA) can also be used for assessment in an upward direction to assess the emission implications of fault occurrence. As part of this whole process, associated FTAs can be applied in the downward direction from the fault in order to identify the more fundamental reasons for the fault occurrence and the potential sequences that gives rise to such faults, so that mitigation action can be appropriately targeted. From a general perspective, it would still appear that the safety assessment approaches developed for system safety, should play at least some part in the reduction of the greenhouse risk. Although, these will not play a significant role in reducing or eliminating emission from a normally operating fault free process. The latter can only be done through fundamental changes in approach and the associated application of new technologies and where system safety can play a more traditional role.

The whole subject area of global warming, greenhouse gas emission, safe storage possibilities and societal consequences, does look like a subject that would benefit from the holistic approach of System-Theoretic Accident Model and Processes (STAMP) advocated by Nancy Leveson of MIT. Its more universal overarching approach for all possible detriments and all possible causes would seem to be ideally structured for wide-spread risk analysis needs of this type.

Involvement in Traditional Risk Assessment

All enterprises which have an element of detriment associated with products, their manufacture and use will, as part of their interests and

responsibility, apply traditional system safety assessment methodologies as part of normal operations. However, this will not necessarily be true in relation to Global Warming case. Some enterprises will, by their very nature, have a minimal contribution to such emissions and as such application of traditional assessment methods may only be for good moral/PR reasons. However, at the other extreme there will be enterprises which will be major contributors, and in this case appropriate new approaches and technology application will be necessary to minimise emissions. The traditional system safety approaches will be directed to the safe implementation of these new approaches and technology applications. This will open up a whole range of work areas for system safety.

WHAT ARE THE RENEWABLE AND ALTERNATIVE ENERGY SOURCES?

All sources of energy ultimately come from the sun. Even fossil fuels were 'manufactured' by solar energy at some stage during the earth's history. The renewable energy sources are broadly; solar, wind, hydro, tidal, geothermal, biomass, where in some cases the potential energy available is related to geographical/geological conditions, time of year and even time of day. These latter aspects raise the need for efficient and large-scale technology approaches for energy storage and major release when required because of the 'transient' nature of its generation. All of these do not directly result in greenhouse gas emission, although the biomass case has been challenged in terms of its zero-carbon net emission claim. In addition, there are other forms of energy production which are not renewable but result in little or no greenhouse gas emission, such as nuclear fission. Other sources of energy such as chemical rechargeable batteries, hydrogen and hydrogen/fuel cells do not of themselves lead to harmful emissions, but fossil fuels are often the prime energy source used for their manufacture and recharging. Perhaps the holy grail for clean energy production takes the form of nuclear fusion. However, there are still substantial challenges to its success despite many decades of expensive international research and which is still only just at the energy break even stage. Even then further major challenges remain in the transition to practicable power reactors.

Whatever its form, it will involve significant levels of energy and power, and as such will be associated with potential high-level safety consequences and will have to be handled in appropriate way. This is certainly a business area which calls for, and should apply, system safety skills. In the following sections, the arguments are centred around the human risk element, but of course there will also be the parallel detriments related to commercial cost, continuity of supply, reputation, etc.

NUCLEAR FISSION POWER

Although the nuclear power industry has not had a historical smooth ride, because of major accidents and the need for safe decommissioning and handling and storage of nuclear waste, nevertheless the current climate will look again towards its expansion as a low greenhouse gas primary energy source with a continuous 24-hour a day character. System safety can play a major role from two perspectives.

1) Enhancement of confidence to allay the concerns which are traditionally raised about this technology.
2) With the extension of its application and in relation to the development of new design concepts and technical approaches.

Nuclear power will always have its major safety critics, so enhancing the safety case quality and preventing mishaps will be strong elements in supporting its extended use. Stronger system safety involvement is obviously a core element in achieving this. In the second aspect it goes without saying that the introduction of fundamentally differing concepts and new technologies *must be accompanied* by a major application of system safety. Here we will be talking about true system level changes and the need for an associated system level approach for ensuring safety in what is truly a high consequence industry. One newly developing area where this applies is in the burgeoning interest and development activities associated with small modular reactor designs which offer the opportunity for distributed siting for targeted energy requirements or aggregation in central locations. Developments lie in the fields of Light Water (LWR), Fast Neutron (FNR), Graphite Moderated High Temperature (GMHTR) and Molten Salt (MSR) reactor technologies. These are suggested to have several advantages over more traditional approaches; more easily factory built, more passive safety, small radioactive inventories, more protective and easier siting, easier decommissioning. This spectrum of potential new developments provides

many opportunities and needs for system safety work, covering development programmes, subsequent certification, and routine operation. This could be a provide a long-term intensive system safety involvement.

The nuclear weapons industry on the other hand, although critically dependent on system safety approaches, is not a significant contributor to global warming. Its remanent contribution will essentially be based on taking a responsible attitude by limiting and making more efficient use of its energy consumption.

Nuclear Fusion Power

There is a long history of R&D work in this area, for example 80 years for magnetic fusion approaches and 50 years for alternative laser inertial approaches. But, even after this long time only relatively dubious claims of achieving breakeven conditions have been made, exemplifying the extreme scientific and technical difficulties associated with this type of research. Major national and international programmes are underway to harness this form of energy in a safe and manageably way. For example, magnetic controlled plasma fusion (Tokamaks) in France (ITER), UK (JET), Italy (DTT) and Japan (JT-60SA), where this approach currently appears to be the most promising one. The main alternative is in the form of high-power laser inertial confinement fusion (ICF) of targets, both in indirect and direct forms. Major national and international programmes are underway in the US (Omega and NIF), France (LMJ), UK (Vulcan and Orion), China (SG-II and SG-III) and Japan (GEKKO- XII). The follow-on process to a practical fusion reactor still looks unclear. However, claims have been made to suggest that this technology will provide modest supplies to the electrical grid in the 2030s, becoming more widespread by the middle of the century. No doubt global warming will give an extra push in this direction, but previous claims have always been somewhat optimistic. Again, because of the large energy and power associated with these programmes, system safety thinking is essential to avoid catastrophic failure. The only system safety role in the near future would be one in supporting major physical experiments rather than in what is the more traditional role of product manufacture and application.

Wind and Tidal Power

Both will involve the application of and expansion of current or enhanced technologies, in what can be hostile environments. Both rely on environmental forces as the prime source of energy for electrical production, but both may encounter challenging hostile extremes leading to increased technical risk. During normal running, neither will have extensive human presence at the point where the environmental energy to electrical transduction takes place. However, the major electrical loads need to be handled in routine system safety fashion at the receiving and distribution base, where human presence exists at least for monitoring, control, and maintenance aspects. Installation, maintenance, and repair involve human activity at the energy transduction sites and can be a cause of significant human risk and where system safety skills will play a significant role.

Hydroelectric Generation

This is an already well-established technology area but like the case for nuclear energy, there will be pressures to extend its application, where geographically viable, because of global warming. What had previously been seen as inappropriate or uncommercial possibilities will be re-looked at and given a greater incentive to develop and apply more efficient and cheaper approaches. Such extensions and new developments will not occur without the presence of new or enhanced risks. Again, the human element of risk will be mostly focused on the implementation, maintenance, repair, and control activities associated with such major engineering enterprises. Because of the site's scale and the large sources of energy involved, unsafe operation can result in major negative consequences. Not only at the site of a dam but also down- stream, should a catastrophic failure occur. As such, system safety has and must continue to play a major role.

Direct Solar Energy

There are several possibilities here but the two for which most activity is currently focussed on are solar cell technology and light concentration. Both can be applied in centralised or local distributed fashion. In its more centralised form, there will inevitably be large levels of electrical power and energy storage, which will always pose the most significant risks to human health. As these installations grow in size and capacity so will the scale of potential consequences, requiring the need for a matching systems safety approach to manage these risks in an acceptable safe manner.

Of course, there have also been space-based collector versions in this category, but this lies outside the scope of this paper.

BIOMASS

This method of energy production is claimed to be carbon neutral. Unlike coal, oil, and natural gas, where the carbon was previously geologically 'locked up', and where its burning makes a permanent net carbon increase to the atmosphere, burning of biomass is claimed to be different. Biomass burning is claimed to be carbon neutral in the sense that the CO_2 produced is naturally re-aborded by vegetation giving no net carbon increase to the atmosphere. The associated argument is that that unburned waste wood would naturally decay and release its carbon back into the atmosphere anyway. So, the claim is that a carefully managed overall process even if not strictly zero carbon, would still be a far less net carbon emitter than fossil fuels. The degree to which this statement is correct is still somewhat contentious, based mainly on the rate at which carbon is re-absorbed in relation to the scale and rate of release by burning. The former may not compensate for the latter. Again, as installations become more expansive and burning takes place on an industrial scale, this will pose major potential hazards which will continue to need safe management.

TRANSPORT SYSTEMS

These are systems which are energy intensive users and as such are major contributors to greenhouse gases, given their current heavy dependence on fossil fuels. The prospect of and the rate of change in application of alternative sources will depend on the transport type.

AUTOMOBILES

The automobile industry is already well on the way to replacing oil fuel usage with rechargeable electrical battery sources and potential hydrogen fuel cells. This is already making a significant impact, although both approaches rely on external sources of energy to manufacture critical components and to power the recharging processes. Both approaches are bringing along with them new technologies and new safety challenges, which will require system safety scrutiny to identify and manage appropriately. Not only are these risks associated with workers in the associated industries but more so for the general public at large where automobiles are a domestic and industrial necessity.

AIRLINES

Another major greenhouse emitter are civil and military aircraft, again centred almost exclusively on burning oil. At this point it is pertinent to point out that it was pioneers in this industry who originally foresaw the need for a new and better System Safety approach to combat the dangers associated with flight. In fact, these people were instrumental in the original formation of a group of like-minded thinkers, which eventually led to the formation of what is now the International System Safety Society. There is no reason why the system safety approach, which already has a proud record of contributions in this industry, will not continue to be a major player in aircraft safety. Unlike the automobile industry, the application of revolutionary new forms of propulsion energy is still very much in the exploratory stage and may take the form of an adjunct to the traditional oil-based fuel. The application of liquid hydrogen, fuel cells, solar cells and rechargeable batteries are still at the tentative exploratory stage. The continuing exploratory path to more efficient use of cleaner fuels, through the introduction of new technologies and approaches will again introduce new risks which will need to be managed and where safety failure can be catastrophic. System safety will continue to have a prominent role in this industry.

MARITIME

The potential for greenhouse gas reduction here lies somewhat between the automobile and airline potentials. In addition to traditional oil, and of course in the past coal, alternative propulsion approaches are already established in somewhat specialised areas both in terms of nuclear and rechargeable batteries forms. Currently, these are almost exclusively applied to military systems both as primary and adjunct applications. The prospect for using hydrogen as a basic fuel also appears more feasible/practicable than for the airline case. In addition, sea transport can in principle take advantage of the environment it operates in … both from wind and 'tidal' energy. In the former case not only as an adjunct in the traditional sail form, but also by using the motion-based wind effect to generate turbine-based electrification. In similar fashion motion through the water can be applied similarly. Of course, these latter approaches will be subject to the fact that extracting

energy in this form will introduce a penalty to the efficiency of the main propulsion element of the vessel. So efficient application will be critical. There are many cleaner energy alternatives for the maritime sector, each raising its own requirement for safe application.

CONCLUSIONS

It is now clear that we have a global level existential safety problem where all the science indicates that human activity is playing a major role in creating the problem through the increased rate of fossil fuel burning. As such, globally we should be accountable for finding solutions to combat the problem. We are already beginning to see the detriments that arise from global warming, as witnessed by the continuing reports of increased frequency of more severe environmental conditions. These take on the form of; storms, droughts, increasing deserts, melting of icecaps and glaciers, flooding, increased sea levels, etc. These all gives rise to serious impact on the health and well-being of the human race. These extreme conditions are predicted to get worse, even given the current level of global warming, whereas further increased levels of greenhouse gases in the atmosphere herald an even greater frequency of more severe eventualities. These concerns, by their very nature, are already producing both international and national action to look for solutions to prevent their escalation. The response will be in the form of changing our prime energy sources, methods of application and storage, new applied technologies, and efficiencies of usage, in order to minimise our reliance on and the impact of burning fossil fuels.

Although being an existential science and technology scale problem, it nevertheless presents an expanding opportunity for those engaged in the application of system safety, given the new technologies and engineering processes that will be developed. A whole new world of opportunities, or perhaps more correctly needs, will open up for those with these skills, noting the scale and urgency of the needs which confront us. The content of this paper has only scratched at the surface of where these opportunities and needs will arise. Certainly, a greater consideration of this subject area will be appropriate to more fully scope the opportunities and needs. It is also a time and opportunity for system safety practitioners to be more proactive in self-advertising and stating the crucial role they can play in the inevitable new safety concerns that will arise. In a similar vein, this is also an opportune time for the International System Safety Society to advertise its *key* contributory role in the safe solution to the new problems we face.

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Assessing the Software Control Autonomy of System Functions in Safety-Critical Systems

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ABSTRACT

Software Control Category (SCC) denotes the degree of control autonomy, command and control authority, and redundant fault tolerance software has over hazardous system functions of safety-critical systems. The use of SCC for determining the software contribution to system risks is a unique feature of the MIL-STD-882E System Safety Standard. A lower SCC designation means that the software system has a greater control autonomy over hazardous system functions, whereas SCC 1 means complete autonomous control. Software with greater control autonomy over hazardous system functions require greater effort to assure reliability and safety. Correct assessment of the SCC level of hazardous system functions is crucial for optimizing the safety property of a system developed under budget, schedule, and resource constraints. Beyond the categorical definitions provided by the MIL-STD-882E Standard, there is little information on conducting an SCC assessment. To close this knowledge gap, we present an SCC assessment method. Our paper will describe in detail the process and rules for assessing SCC. For illustration, we apply our method to assess the SCC of several safety-significant functions of an automobile's brake-assist system.

INTRODUCTION

The two crashes of Boeing airliners model 737 MAX that took 346 lives are a stark reminder of the risk of embedded software in safety-critical systems (Wikipedia, 2022a). As software controllers continue to replace specialized hardware devices in safety-critical systems, the risk of software-induced system failure continues to grow. This trend repeats across multiple industries, including transportation systems, traffic control systems, medical surgery equipment, nuclear power centers, power grid infrastructures, industrial robots, and military weapon systems. Eliminating and controlling the contribution of software to system hazards, i.e., the software risk, is

an objective of system safety engineering. Software system safety, or software safety, is a subdiscipline within system safety that focuses on applying system safety principles and practices to software systems development (Wikipedia, 2022b). Software safety controls the risk of defective embedded software systems triggering consequential system mishaps. Software safety's vital role in system safety engineering continues to grow (Danhauser, 2014).

To determine the software risk in safety-critical systems, the MIL-STD-882E Standard focuses on three risk factors: 1) the system mishap severity, 2) the software control autonomy, and 3) the level of rigor (LOR) of the safety quality assurance process. The mishap severity factor measures the magnitude of the consequence of a system mishap. This factor is well-known in system safety and reliability with established methods for estimating. LOR represents the required level of safety analysis and assurance of hazardous or safety-significant system functions (SSFs). The MIL-STD-882E Implementation Guide (JS-SSA-IG, 2018) provides detailed information on the different LOR levels and tasks. Software Control Autonomy (SCC) expresses the degree of control autonomy, command and control authority, and redundant fault tolerance software has over the SSFs (Safety, 2012). How to assess this risk factor is not discussed in the Standard and its related handbooks and guides. It remains a knowledge gap to be addressed. The need for a systematic and rigorous assessment approach is apparent when dealing with systems with many software controllers supporting many SSFs (JS-SSA-IG, 2018). For instance, a high-end automobile system today can have hundreds of independent processors with software controlling hundreds of SSFs. The code size of such a system can easily exceed one hundred million lines of code (Charette, 2021). A SCC assessment method ensures that the resulting SCC of the SSFs are correct, consistent, and explainable.

We propose a functional approach to assessing the SCC of hazardous system functions. Our approach is aligned with the overall functional approach to hazard analysis in the MIL-STD-882E FHA method. We will provide a detailed description of our SCC assessment method, including the process and rules for systematically and consistently deriving the SCC level of individual SSFs. For illustration, we will use our method for assessing several system functions of an automobile's brake-assist system.

REVIEW OF LITERATURE

To support our review, we started by asking, "How does one approach assessing the control autonomy of the embedded software supporting safety-critical system functions?" In addition to looking through the MIL-STD-882 Standard and supporting documents, we performed a literature search on the IEEE Computer Science Digital and ACM databases, using keywords such as "software control category" and "SCC" "MIL-STD-882", "software control level." The list of relevant papers on the software control category within the last ten years is negligible. Below are notes from our literature review.

The MIL-STD-882 Standard plays a central role in military weaponry, aerospace, and nuclear center system safety. The latest revision E of this Standard emphasizes software system safety by adopting the Functional Hazard Analysis (FHA) method. Within the FHA, the SCC is introduced as a risk measuring factor. The SCC designation describes the software contribution risk associated with an SSF; thus, it is a system function-level designation.

The MIL-STD-882 Standard remains widely adopted within the defense, nuclear, and aerospace sectors. A new revision of the MIL-STD-882, revision F, is under development. We expect that SCC will remain critical in considering the software risk in safety-critical systems.

Several related documents mention the adoption of the SCC but provide little additional information on how to conduct an SCC assessment. The Joint Software System Safety Engineering Handbook (JSSSEH, 2010) provides this concise guidance: "the analyst identifies the software safety-significant functions early in the analytical phase and assigns a mishap severity and software control category to each." The Joint-Services Software Safety Authorities Software System Safety Implementation Process and Tasks Supporting MIL-STD-882 (JS-SSSA-IG, 2018) emphasizes that "accurate assessment of the SCC based upon the complexity of the system, autonomy of the system's functionality, and/or its command-and-control authority is imperative." Both the NATO Guidance on Software Safety Design and Assessment of Munition-Related Computing Systems (AOP-52) (NATO, 2016) and The Nuclear Regulatory Commission's Software Safety Hazard Analysis document (Lawrence, 1996)

adopted the MIL-STD-882 Standard. However, neither discusses how to conduct an SCC assessment.

Literature research in safety requirements engineering reports limited publications on modern software-based system safety methods (Martins and Gorschek, 2017; Martins, L. and Gorschek, 2020). Most system safety methods in practice today are derived from hardware-based methods such as Fault Tree Analysis (FTA), Failure Mode Effect Analysis (FMEA), Failure Mode Effects Analysis and Criticality Analysis (FMECA), and Preliminary Hazard Analysis (PHA). Several reasons for the lack of adoption of software-based hazard analysis methods, including Functional Hazard Analysis, are 1) the lack of software safety teaching in computer science and software engineering curricula, 2) the lack of familiarity with software-based methods among system safety professionals, 3) the lack of published information on the effectiveness of software-based methods, and 4) the slowness in the adoption of software-based methods in safety standards.

One interesting publication is from Robert Smith, where the author uses Fault-Tree Analysis to verify that the different proposed MIL-STD-882E SCC designations are distinct (Smith, 2018). However, the paper does not address the issue we seek to address, which is how to systematically assess the SCC of SSFs.

The Guidelines for Development of Civil Aircraft and Systems (ARP4754A, 2010) outlines a method for assessing the Functional Development Assurance Level (FDAL) of system functions. This method first decomposes individual system functions into subfunctions and allocates these subfunctions to the subsystems that make up the system architecture. The system functions are then assigned an FDAL level based on the structures of their subfunctions. For instance, if a function classified as an FDAL A is decomposable into multiple redundant and independent functions, that function may be reclassified as an FDAL B, i.e., a lower risk function. This FDAL assessment method, supporting the software safety activities in civil aviation, has steps similar to our proposed SCC assessment method.

Our previous papers on software safety (Tran et al., 2016; Tran et al., 2016b; Tran et al., 2016c) describe different aspects of the MIL-STD-882E Functional Hazard Analysis method. However, we did not cover how to conduct an SCC assessment.

SCC AS A RISK FACTOR

The system risk associated with an SSF failure is typically expressed as the product of two risk factors: the mishap severity and the probability or rate of occurrence. For quantitative estimation, historical data, system analysis, and simulation studies are used to quantify the probability of occurrence. For qualitative estimation, likelihood categories are used in place of the numeric probability of occurrence. A risk matrix is then used to combine the two risk factors into a single risk level (Safety, 2012).

SYSTEM RISK = SEVERITY x PROBABILITY (or LIKELIHOOD)

With the use of software to control SSFs, attempts have been made to maintain compatibility between software and hardware reliability calculations for joint system reliability assessment (IEEE-1663, 2016). Software reliability methods such as Software Fault-Tree Analysis and Software Failure-Mode Effects Analysis provide software failure probabilities for use in system risk assessment. The MIL-STD-882E Standard, however, moves away from using probabilistic estimation of software risk. The Standard uses alternative factors to approximate the software contribution to system risk: the degree of software control of an SSF and the level of safety quality assurance rigor. The failure risk of an SSF is deemed higher if the function is controlled by a single software controller (an autonomous control structure) instead of a redundant set of independently built and operated controllers (a redundant fault-tolerant control structure). Similarly, the failure risk of an SSF is deemed higher if the safety quality assurance process employed was less rigorous than required.

SOFTWARE RISK = SEVERITY x SOFTWARE CONTROL CATEGORY x LEVEL OF RIGOR

Figure 1 provides an overview of how the SCC is used in software contribution risk assessment. SCC assessment, i.e., determining the degree of software control autonomy of an SSF, is performed after identifying the SSF as a software-controlled SSF. The output of the SCC assessment is used in conjunction with mishap severity to determine the software safety criticality of the SSF, i.e., the Software Safety Criticality Index (SWCI). The SWCI of an SSF then drives the determination of the initial software risk, the development of risk mitigations, the level of rigor

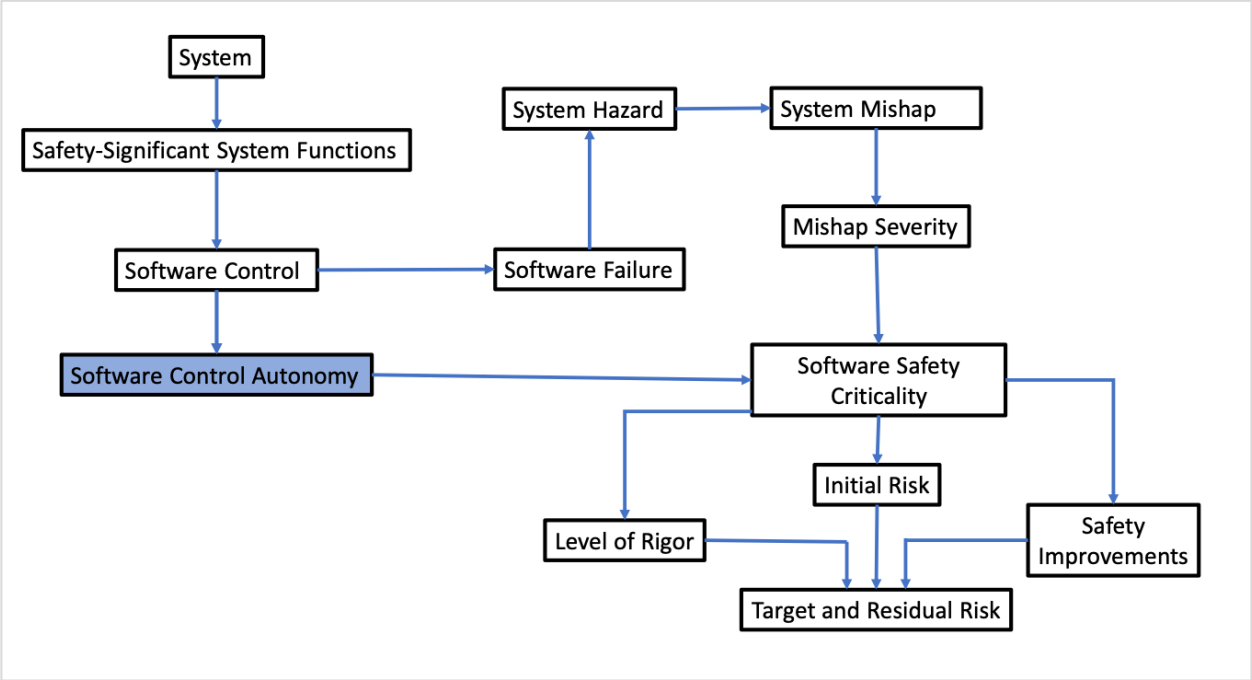

Figure 1: How the SCC is Used to Determine the Software Risk

(LOR) of the safety assurance effort, and ultimately the target and residual risks. Wrong SSC assessment could lead to the erroneous determination of LOR, the third factor of software risk, ultimately resulting in the incorrect software risk assessment. This paper focuses on assessing the SCC of SSFs.

THE SCC CATEGORIES

The MIL-STD-882E Standard defines five Software Control Categories (SCC); some categories have two subcategories (Safety, 2012). The SCC designation is not applied to SSFs controlled strictly by non-software, e.g., hardware or human actions. This section provides our interpretation of each SCC as described by the Standard, emphasizing the distinguishing features of the software control category while adhering to the Standard's definitions. The Standard assumes that the SCC risk factor is only relevant when the software fails to perform its intended control functions.

SCC Level 1: Autonomous (AT)

The AT (SCC 1) designation applies to SSFs controlled by autonomous software functions. Controlling complex system functions could be performed by networked software functions running on independent processors. Failure of any part of the software control puts the system into a hazardous condition leading directly to a system mishap. Autonomy means that there are no external means to detect and intercept the system to prevent a mishap once the software controlling an SSF fails.

SCC Level 2: Semi-Autonomous (SAT)

The SAT (SCC 2a) designation applies to SSFs controlled by software functions that run autonomously, similar to the AT designation. Failure of any part of the software control can put the system into a hazardous condition leading to a mishap. The system, however, is designed to provide a window of opportunity for an independent external actor, e.g., hardware, software, or a human, to detect and intercept the hazardous condition, in a timely manner, thus preventing the system mishap. The external actor does not rely on the faulty software controller to carry out the time-sensitive control action to bring the system back into a safe state.

The SAT (SCC 2b) designation applies to SSFs monitored by software monitoring functions that provide timely safety-significant information to an external actor, allowing the external actor to control a hazardous condition. The monitoring software may or may not control the system function. System mishaps can occur when the monitoring software fails to provide safety-significant information correctly or in a timely way. The independent external actor can also

initiate control actions to prevent a system mishap despite the failed monitoring software.

SCC 3: Redundant Fault-Tolerant (RFT)

The RFT (SCC 3a) designation applies to SSFs controlled by redundant and independent controllers, including hardware, software systems, human actions, and combinations. Independent controllers mean controllers that: 1) receive data from different sources, 2) make independent decisions, 3) take independent actions, 4) are built independently, 5) operate independently, and 6) fail independently. Independence enables redundancy and fault-tolerance. The RFT is assigned when redundancy and fault-tolerance are sufficient to ensure all identified hazardous conditions caused by software failures are controlled. System failure occurred when all redundant controllers failed.

The RFT (SCC 3b) designation applies to SSFs controlled by software functions that depend on an external independent actor's concurrence to initiate control actions. System failure occurs when the software controller accidentally initiates control actions without an agreement. The RFT is assigned when redundancy and fault-tolerance are sufficient to ensure that no control action can be started without external concurrence. Failure of either controller prevents further control actions.

SCC Level 4: Influential (INF)

The INF (SCC 4) designation applies to SSFs relying on software system functions for capturing non-time-sensitive safety-related information. While software functions are responsible for collecting, logging, or displaying safety-related information, they do not control the SSFs, e.g., these SSFs are controlled by hardware. Failure of an INF software function will result in the loss of valuable safety-related information but does not induce a system mishap. The external actor that receives the safety-related information is not expected to initiate any immediate safety action.

SCC Level 5: No-Safety-Impact (NSI)

The NSI (SCC 5) applies to system functions that are not safety significant, i.e., system functions that are not supported by safety-significant software. Failure of the software controlling the system functions will not induce a system mishap.

SCC ASSESSMENT: A FUNCTIONAL APPROACH

SAFETY-SIGNIFICANT SOFTWARE FUNCTIONS (SSSFS)

Each system is functionally composed of a set of system functions. System functions that are of interest to system safety are the safety-significant system functions (SSFs). Software Control Category (SCC) is a system-level property of an SSF. This property is derived from assessing the degree of control software has over the SSF. A software controller could comprise multiple networked software functions running in different subsystems. Each software function could be further decomposed into sub-functions and allocated to different components within a subsystem. Thus, each SSF can be functionally decomposed into a tree where the lowest-level allocated software functions, or safety-significant software system functions (SSSFs), reside at the bottom of the tree. Also, at the bottom are the non-software functions allocated to hardware and human to support the SSF. The assessment of the SCC of an SSF requires understanding the roles and structure of these allocated SSSFs and their relationship with the non-software functions through the lenses of system safety. Figure 2 shows a sample functional decomposition of a system to its SSFs and SSSFs for SCC assessment. Each top-level SSF is decomposed into a set of safety-significant software and non-software functions. A software controller comprises all SSSFs supporting an SSF.

THE SCC ASSESSMENT PROCESS

The SCC assessment process consists of three steps: First, decompose an SSF into a set of software functions and allocate them to the components of the system. Second, assess the SCC level of individual SSSFs supporting the SSFs. Third, adjust the SCC of the SSFs.

In Step 1, Identify the Safety-Significant Software Functions (SSSwFs), each SSSF is decomposed into low-level subsystem functions. System functions that are deemed not hazardous are not analyzed in this step. Decomposing SSSF reviews all the functional elements that support this system function. Multiple SSSFs can share the same low-level subsystem functions. More complex functions

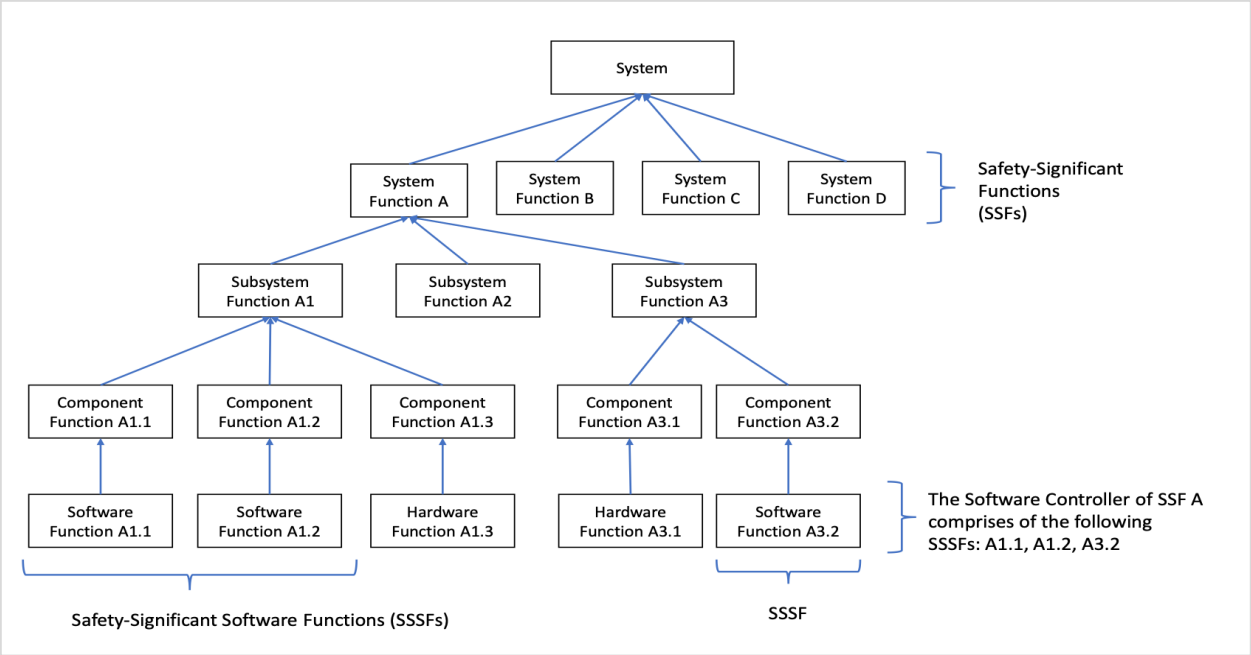

Figure 2: A Functional Decomposition of a System

are further decomposed into smaller functions that could be allocated to the different physical components in the system architecture. Physical components could be hardware, software, or an operator. At the lowest level, the functions allocated to a software component are the SSSwFs that, together with other non-software components, control the SSSF. Step 1 is completed when all SSSFs are functionally decomposed to software and non-software functions allocated to the system architecture components.

In Step 2, Assign SCC to the SSSFs, SCC assessment is performed top-down, starting with the top-level SSF assigned SSC 1, autonomous control. As the analysis progresses down the decomposition tree, each child function inherits the SCC level of its parent function by default. A child function can have a SCC different than its parent function if it is realized by a structure that fits a lower SCC designation. Step 2 is completed when all SSSFs are assigned SCCs.

In Step 3, Reassess the SSF's SCC, the top-level SSF's SCC is reassessed once all the SSSFs supporting it have been assigned SCCs. This reassessment is performed bottom-up until the top-level SSF is reached. At each level, the SCC of a function is reexamined now that the SCCs of its subfunctions are known.

THE SCC ASSESSMENT RULES

There are several rules that guide the SCC assessment of individual functions. These rules can be used in Steps 2 and 3 of the SCC Assessment process.

1. The Top-Level Rule: A top-level SSF is given an SCC 1, i.e., autonomous control, when no other information is available.
2. The SCC Matching Rule: A function whose control structure meets the description of a lower SCC designation is assigned that designation.
3. The Inheritance Rule: A subfunction inherits the SCC level of its parent function by default when no other information is known.
4. The Partition Rule: The SSSFs residing in different physical components can have different SCC levels.
5. The Reuse Rule: An SSSF can have multiple SCCs if it is used by multiple parent functions leading to multiple SSFs. The highest SCC level, i.e., highest control autonomy, will be assigned to the shared SSSF.
6. The Reduced Autonomy Rule: The SCC of a parent function may be lowered if all child functions have a lower SCC than the SCC of the parent function.

In the next section, we will use our method to analyze the rear-ended vehicle collision prevention system for demonstration.

SCC OF REAR-ENDED VEHICLE COLLISION PREVENTION SYSTEMS – A SMALL CASE STUDY

Rear-ended vehicle accidents are among the most common accidents with a risk of vehicle and people injuries (Ryan, 2020). Over the years, many safety braking solutions have been developed to address this problem. This case study will look at a brake-assist system with three safety functions often available in automobiles equipped with the redundant electro-hydraulic brake system. The redundant brake system supports P < 10E-8 probability of braking function loss with a newly introduced electric controlled brake system backed up by a traditional hydraulic brake system. A brake-assist system is designed to augment the vehicle driver, so it remains primarily the driver's responsibility to ensure safe driving. In the rest of this section, we will focus on assessing the SCC level for the SSFs of this simplified brake-assist system.

The three top-level SSFs of our brake-assist system are:

1. The Adaptive Cruise Control (ACC) function controls the vehicle's speed relative to the speed of the front vehicle in a long highway drive without driver interference. While the ACC is more than a brake-assist solution, its Auto-Deceleration function serves to avoid a potential rear-ended collision. Only the Auto-Deceleration function of the ACC will be analyzed.
2. The Autonomous Emergency Braking (AEB) function monitors a potential front collision with obstacles, including another vehicle. When a collision is imminent and there is no driver-initiated braking, the AEB function will initiate braking at full force. It will automatically release the brakes once the vehicle has completely stopped.
3. The Emergency Brake Assist (EBA) function supports the driver in urgent braking. The function monitors the brake pedal to detect a rapid brake attempt by the driver and applies full force to the brake.

Figure 3 provides a simplified illustration of this brake-assist system. The SSFs are identified in the diagram, separated into non-software functions and software control functions, and mapped into a high-level functional architecture. This high-level architectural diagram provides the context for assessing the SCC level of these three SSFs. The assessment will be presented in detail below.

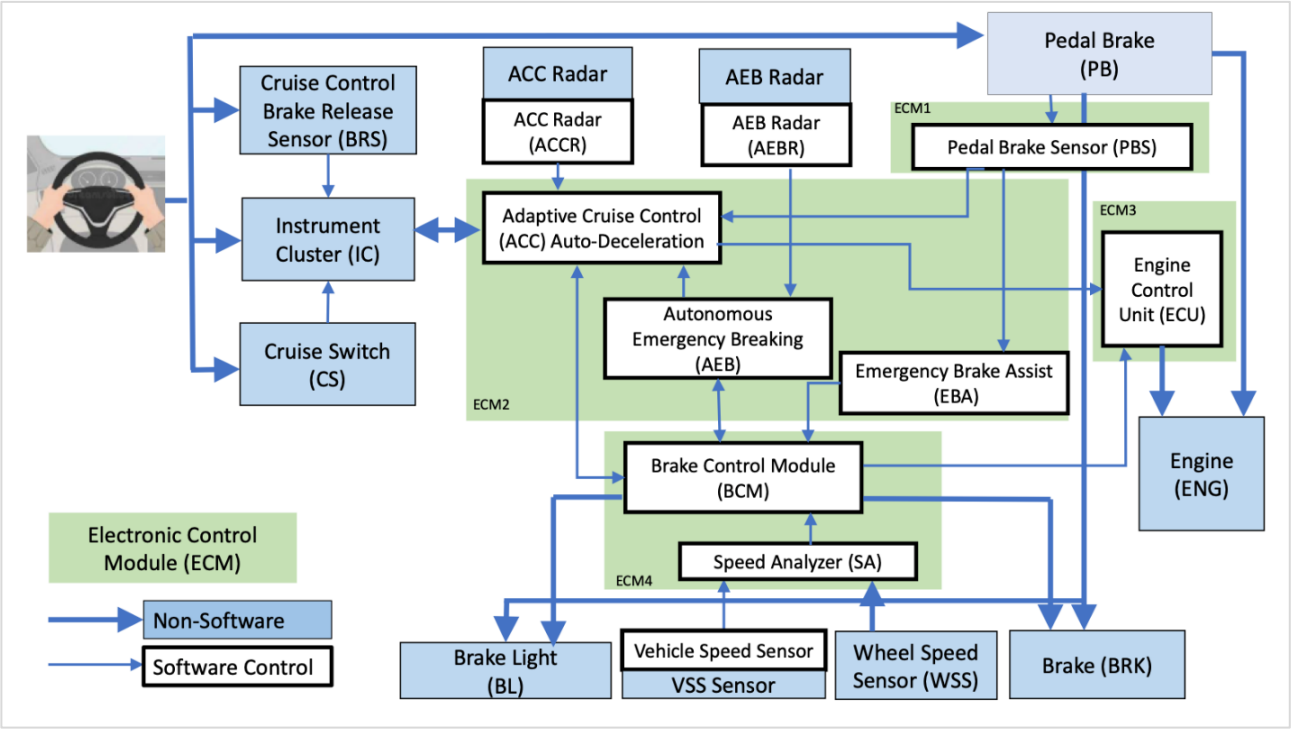

Figure 3: Building Blocks of a Rear-Ended Vehicle Collision Avoidance System

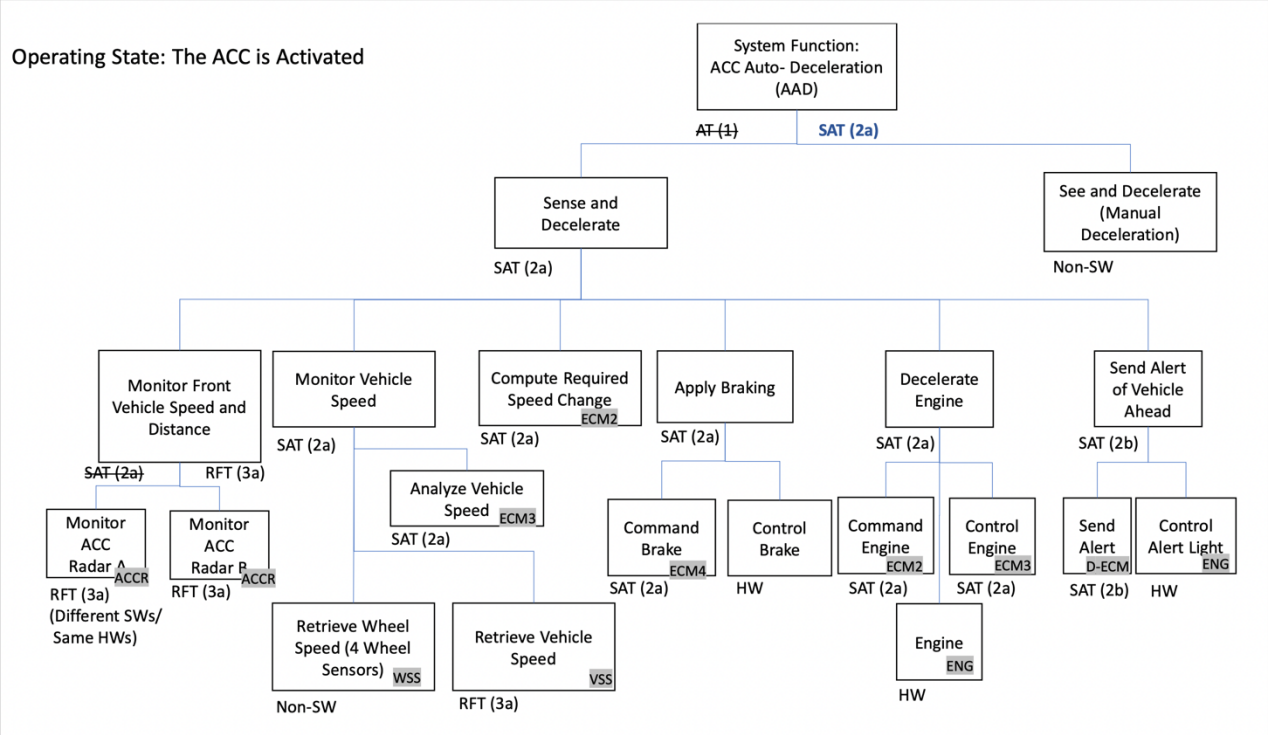

Figure 4: Decomposing Safety-Significant System Function ACC Auto-Deceleration

ACC AUTO-DECELERATION (AAD)

Figure 4 decomposes system function AAD. Function AAD was initially tagged as an AT (SCC 1) function (Rule 1). This function is decomposed into two distinct primary-backup deceleration functions: Sense-and-Decelerate and See-and-Decelerate. Sense-and-Decelerate represents the new computerized function, and See-and-Decelerate represents the manual function performed by humans. The independence of these two functions reflects the requirement that the vehicle driver is responsible for always maintaining visual contact with the front vehicle. The vehicle driver can override the ACC system to slow down the vehicle if needed. Failure of the Sense-and-Decelerate function does not prevent the See-and-Decelerate function from performing the same deceleration. The Sense-and-Decelerate software function thus meets the design criteria of an SAT 2a (Rule 2). The Sense-and-Decelerate function is further decomposed into a set of interacting subfunctions with many to be implemented in software. These software functions inherit their parent's SCC level (Rule 3). The Monitor-Front-Vehicle-Speed-and-Distance function will be realized by a reliable, redundant, fault-tolerant software-controlled radar system, thus qualified for an RFT 3a (Rule 2). Rolling up to the SCC level, the Monitor-Front-Vehicle-Speed-and-Distance function becomes an RFT 3a, according to Rule 6.

Function Monitor-Vehicle-Speed (SAT 2a) comprises three functional components. Function Analyze-Vehicle-Speed determines the vehicle's speed based on the wheel and vehicle sensors. Function wheel speed sensor system is an RFT function with four sensors (Rule 2). The vehicle speed sensor system is redundant to the wheel speed sensor system, thus qualified for an RFT 3a (Rule 2). Function Analyze-Vehicle-Speed, however, is not an RFT function. This function inherits the SAT 2a designation from its parent function Monitor-Vehicle-Speed (Rule 3). Function Monitor-Vehicle-Speed remains an SAT 2a after rolling up the SCC levels.

Functions Control Brake and Control Engine inherit the SAT 2a from its parent according to Rule 3. It may be tempting to classify these functions as AT (1) as they are responsible for controlling the brake and engine systems, respectively. This assignment would be incorrect. Neither function should be given a higher SCC level than its parent function Sense-and-Decelerate (SAT 2a). While the failure of functions Control Brake or Control Engine will fail the function Sense-and-Decelerate, the function See-and-

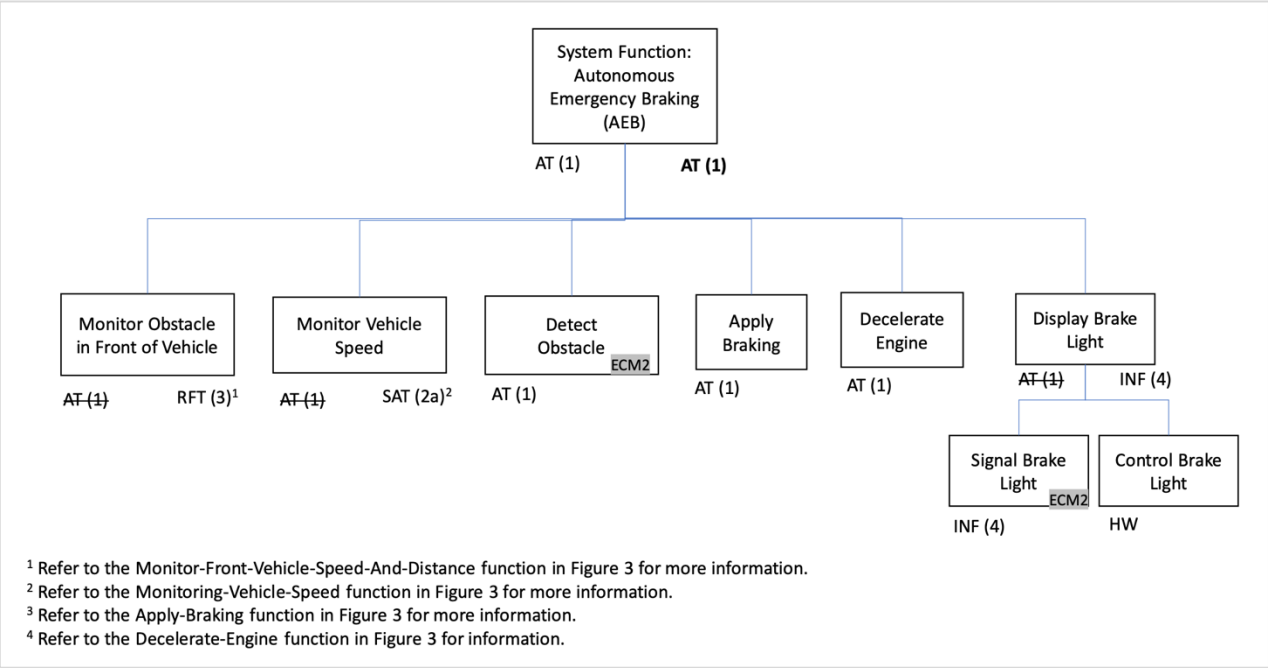

Figure 5: Decomposing Safety-Significant System Function Autonomous Emergency Brake

Decelerate is capable of controlling the hazardous condition. Functions Control Brake and Control Engine are thus SAT 2a functions.

Function Sense-and-Decelerate remains an SAT 2a, making the top-level SSF ACC Auto-Decelerate (AAD) an SAT 2a, according to Rule 6. Function See-and-Decelerate is realized by the vehicle driver and the hydraulic brake system, i.e., non-software.

AUTONOMOUS EMERGENCY BRAKING (AEB)

Figure 5 decomposes function AEB. Unlike function AAD, which is activated manually, function AEB is automatically activated when the vehicle is started. Function AEB function does not assume that the vehicle driver will be responsible for detecting obstacles on the road in front of the vehicle. Instead, the AEB operates autonomously. When function AEB detects an obstacle blocking the vehicle's path, it initiates braking control in full force. Function AEB will not release the brake until the vehicle is completely stopped. Failure of the AEB to detect and brake can lead to a system mishap. The AEB is an AT 1 (Rule 2).

In Figure 6, function AEB is decomposed into subfunctions that scan for obstacles on the road, monitor the vehicle's current speed, analyze the radar signals to detect the obstacles, apply brake and engine control, and display the brake light. Functions Monitor-Of-Vehicle-Obstacles-In-Front-Of-Vehicle, Monitor-Vehicle-Speed, Apply-Braking, and Apply-Engine-Control are decomposed and assigned SCC levels described in system function AAD's assessment. Function Display-Brake-Light is an INF 4 (Rule 2) since there is no expectation that it is used to trigger a safety action due to the short response time required to execute an emergency braking. Function Detect-Obstacles is an AT 1 designed to autonomously initiate emergency braking upon detecting an obstacle on the road (Rule 2). The parent function AEB remains an AT 1.

EMERGENCY BRAKE ASSIST (EBA)

Function EBA relies on the braking action initiated by the vehicle driver to activate emergency braking assistance. The function is thus an RFT 3b (Rule 2) as it cannot start the additional braking action without expressed concurrence for the action by the driver, the independent actor. In addition, failure of the EBA function does not prevent completion of the emergency braking by the vehicle driver who initiated the action as the EBA function is only an assisting function. It is not designed to replace the manual braking action. Further decomposing function EBA into subfunctions shows that function Display-Brake-Light qualifies for an INF 4, Rule 2. The remaining subfunctions retain the RFT 3b SCC level from the parent function (Rule 3).

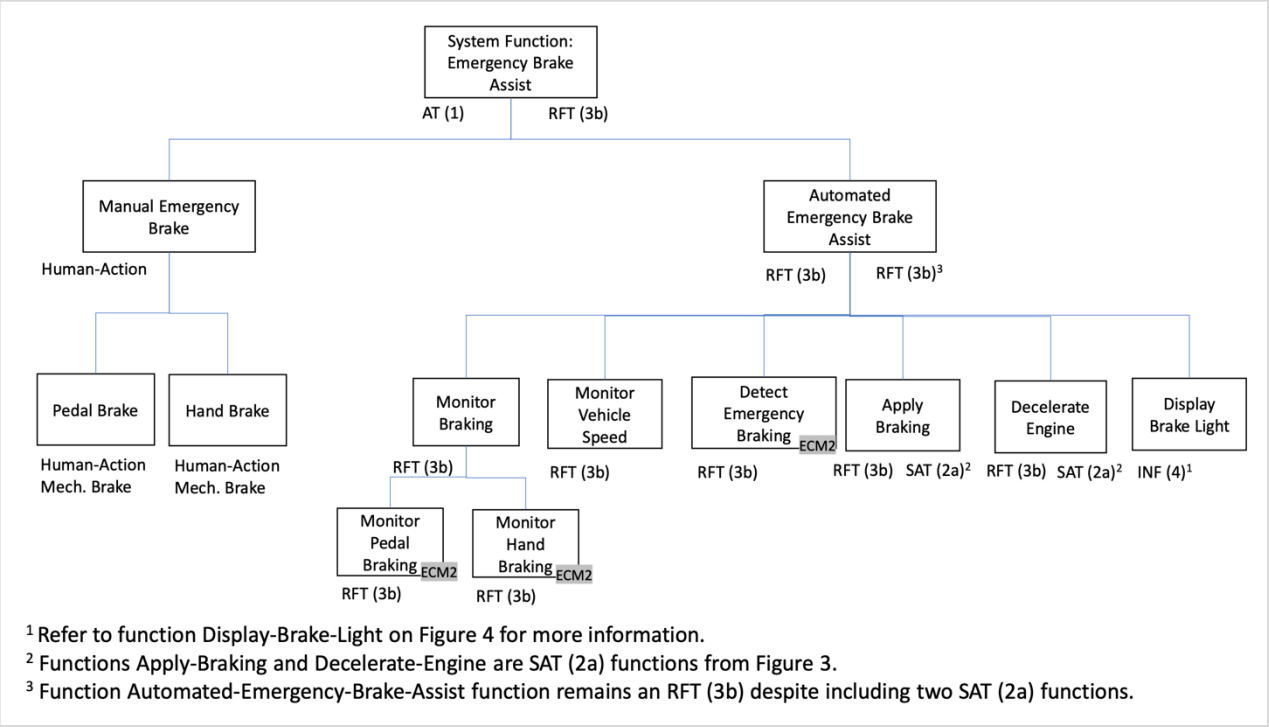

Figure 6: Decomposing Safety-Significant System Function Emergency-Brake Assist

While function Apply-Braking is assigned SAT 2b in Figure 5, it should be noted that it is assigned an RFT 3b here, Figure 6. Applying Rule 5, the SCC level of function Apply-Braking is adjusted as an SAT 2b. We reassess the SCC level of the parent function Automated-Emergency-Brake-Assist once the SCC levels of all its subfunctions have been determined as an RFT 3 due to all the redundant user actions available (Rule 2).

Table 1 presents a mapping of the three SSFs to SCC levels. The map captures 1) the relationship between individual SSFs and the software subfunctions allocated to the components of the system, 2) the degree of control autonomy of the software subfunctions supporting the individual SSFs based on the system architecture, 3) the degree of software control autonomy of the SSFs. There is one column for each SSSF. Below the SSF names are the assigned SCCs. Beneath the assigned SSF SCCs are the allocated software component functions and assigned SCCs. Software component functions supporting multiple SSSFs have multiple assigned SCCs. The rollup of the assigned SCCs to the highest degree of control category for the software component functions is to the right of the table. This SSF-SCC Map provides complete traceability from the SCC levels assigned to the software functions to the SCCs assigned to the SSFs. This traceability simplifies the adjustment of the SCC assignments when an SSF is removed or added.

CONCLUSION

The importance of software system safety as a subdiscipline of system safety continues to grow as software control replaces traditional hardware control in safety-critical systems. The recent high-profile failure of the Boeing 737 MAX systems is a reminder of the software risk in safety-critical systems. The MIL-STD-882E Standard provides a method for determining the software criticality and risk of SSFs. This method relies on the estimation of the degree of control autonomy software has over hazardous system functions. Correct assessment of the SCC level of hazardous system functions is essential for optimizing the safety property of a system developed under budget, schedule, and resource constraints. Presently, little information is available on systematically performing an SCC assessment. Our paper fills this knowledge gap. We presented a functional method for assessing the SCC of the SSFs. For illustration, we provided a detailed description of how to determine the SCC of the brake-assist system functions of an automobile.

Table 1: SSSF – SSC Map

		SSSF			
		AAD	AEB	EBA	
Comp.	**Function**	2	1	3	**SCC**
ACCRA	Monitor ACC Radar A	3a			3a
ACCR	Monitor ACC Radar B	3a			3a
VSS	Retrieve Vehicle Speed	3a	3a		3a
ECM3	Analyze Vehicle Speed	2b	2a		2b
ECM2	Compute Req'd Speed Change	2a			2a
ECM4	Command Brake	2a	1	3b	1
ECM2	Command Engine	2a	1	3b	1
ECM3	Control Engine	2a	1	3b	1
D-ECM	Send Alert	2b			2b
AMBER	Monitor AEB Radar A		3a		3a
AMBER	Monitor AEB Radar B		3a		3a
ECM2	Detect Obstacle		1		1
ECM2	Signal Brake Light		4	4	4
ECM2	Monitor Pedal Braking			3b	3b
ECM2	Monitor Manual Braking			3b	3b
ECM2	Detect Emergency Braking			3b	3b

AUTHORSHIP CONTRIBUTIONS

Vu Tran conceived the presented idea and wrote the paper. Vu Tran and Long Tran co-developed the method. Viet Tran reviewed the literature. Long Tran and Viet Tran co-developed the automobile example. All authors reviewed the paper and contributed to the final manuscript.

COMPETING INTERESTS

All authors declare they have no potential competing interests.

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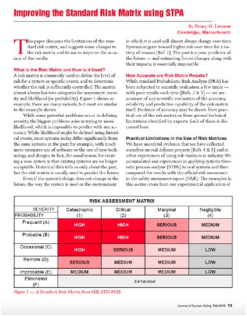
From the JSS Archives

Effective April 2022, JSS announced that it was transitioning to a Gold Open Access publishing model, and we launched our new website at jsystemsafety.com.

To date we have published eight years (2014-2022) of our back issues to the new website. We ultimately plan to republish the entire 57 year archive! This page highlights a few of the many articles currently available in our archives.


Improving the Standard Risk Matrix using STPA

RISK ASSESSMENT MATRIX

SEVERITY / PROBABILITY	Catastrophic (1)	Critical (2)	Marginal (3)	Negligible (4)
Frequent (A)	HIGH	HIGH	SERIOUS	MEDIUM
Probable (B)	HIGH	HIGH	SERIOUS	MEDIUM
Occasional (C)	HIGH	SERIOUS	MEDIUM	LOW
Remote (D)	SERIOUS	MEDIUM	MEDIUM	LOW
Improbable (E)	MEDIUM	MEDIUM	MEDIUM	LOW
Eliminated (F)	Eliminated			

Improving the Standard Risk Matrix using STPA

Nancy Leveson

This paper discusses the limitations of the standard risk matrix and suggests changes to the risk matrix and its use to improve the accuracy of the results.


System Safety in Organizational Safety Decision Making

System Safety in Organizational Safety Decision Making

Malcolm Jones

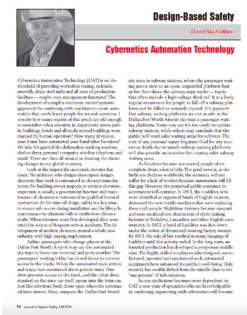
One of this issue's authors explores the structure and nuances of organizational decision making for system safety.


Notes on Society History

Notes on Society History

Rex B. Gordon

The official ISSS historian has produced a series on historical notes on the history of the society, its members, and the system safety concept.


Design-Based Safety

Cybernetics Automation Technology

Design-Based Safety

David MacCollum

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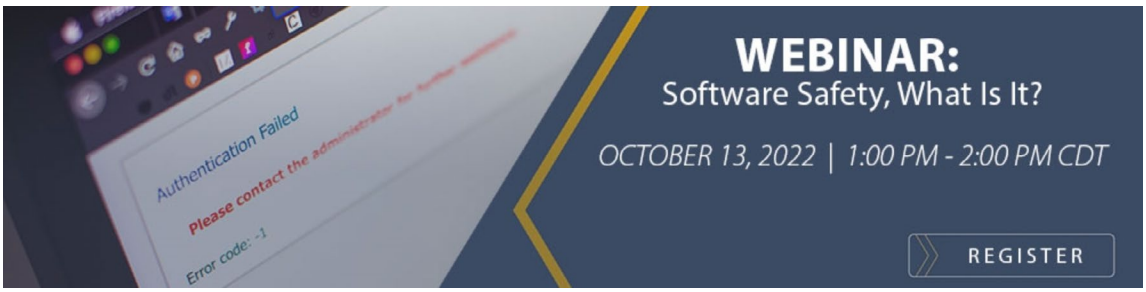
Mark Your Calendar

International Air Safety Summit 2022
Nov. 7-9, 2022
Omni Atlanta Hotel, Atlanta, GA
https://flightsafety.org/event/international-air-safetysummit-2022/

69th Annual Reliability and Maintainability Symposium (RAMS)
Jan. 23-26, 2023
The Florida Hotel and Conference Center, Orlando, Florida
https://rams.org

Safety-Critical Systems Symposium
Feb. 7-9, 2023
York, U.K. and online
https://scsc.uk/e898



Activities

Through its local chapters, committees, executive council, publications and meetings, the Society provides many opportunities for interested members to participate in a va-riety of activities compatible with Society objectives. In addition to the basic operating committees, Society activities include several noteworthy publications and events.

Publications

- Journal of System Safety is the official Society journal. Published three times a year, JSS is a peer-reviewd scholarly journal that keeps members informed of the latest developments in the field of system safety.
- Chapter newsletters are published periodically to disseminate news of chapter activities and items of interest to chapter members.
- Proceedings of Society-sponsored conferences and symposia are made available to members at a special discount.

Meetings — Conferences — Symposia

- International System Safety Conferences are sponsored annually. These conferences have proven to be a very popular and effective means for highlighting the latest techniques, applications and social/legal aspects of system safety.
- Mini-symposia are sponsored by local chapters to provide an in-depth exploration of a specific system safety-related topic.
- Chapter dinner meetings, field trips and panel discussions are held at intervals throughout the year.
- The Society is a co-sponsor of various system safety-related symposia and conferences.

Membership in the Society is open to all persons having an interest in or currently involved in work related to system safety or an allied discipline. Professional member-ship grades are available for those able to demonstrate sufficient qualifications, experi-ence and training. Annual dues are $150 (USD), while student memberships are free. Society members and subscribers are located in all areas of the United States and many countries around the world:

Australia
Austria
Cameroon
Canada
Chile
China
France
Germany
Greece
Israel
Italy
Japan
Netherlands
Nigeria
Norway
Russia
Saudi Arabia
Singapore
South Aftrica
Spain
Sweden
Switzerland
United Kingdom
(England, Northern Ireland, Scotland and Wales)
United Arab Emirates
United States of America

Requests for membership applications, subscription orders, requests for Conference Proceedings and other matters related to membership and services should be addressed to the International System Safety Society, 1000 Westgate Dr., Suite 252, Saint Paul, MN 55114, or contactsystemsafety@system-safety.org. Visit our Website at http://www.system-safety.org.

The **International System Safety Society** is a non-profit organization of professionals dedicated to the safety of systems, products and services through the effective implementation of the system safety concept. Under this concept, appropriate technical and managerial skills are applied so that a systematic, forward-looking hazard identification and control function becomes an integral part of a project, program or activity at the planning phase and continues through the design, production, testing, use and disposal phases.

The Society's Objectives

- To advance the art and science of system safety
- To promote a meaningful management and technological understanding of system safety
- To disseminate advances in knowledge to all interested groups and individuals
- To further the development of the professionals engaged in system safety
- To improve public understanding of the system safety discipline
- To improve the communication of system safety principles to all levels of management, engineering and other professional groups

International System Safety Society

Professionals Dedicated to the Safety of Systems, Products and Services

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Society Website: https://www.system-safety.org
Journal Website: https://www.jsystemsafety.com