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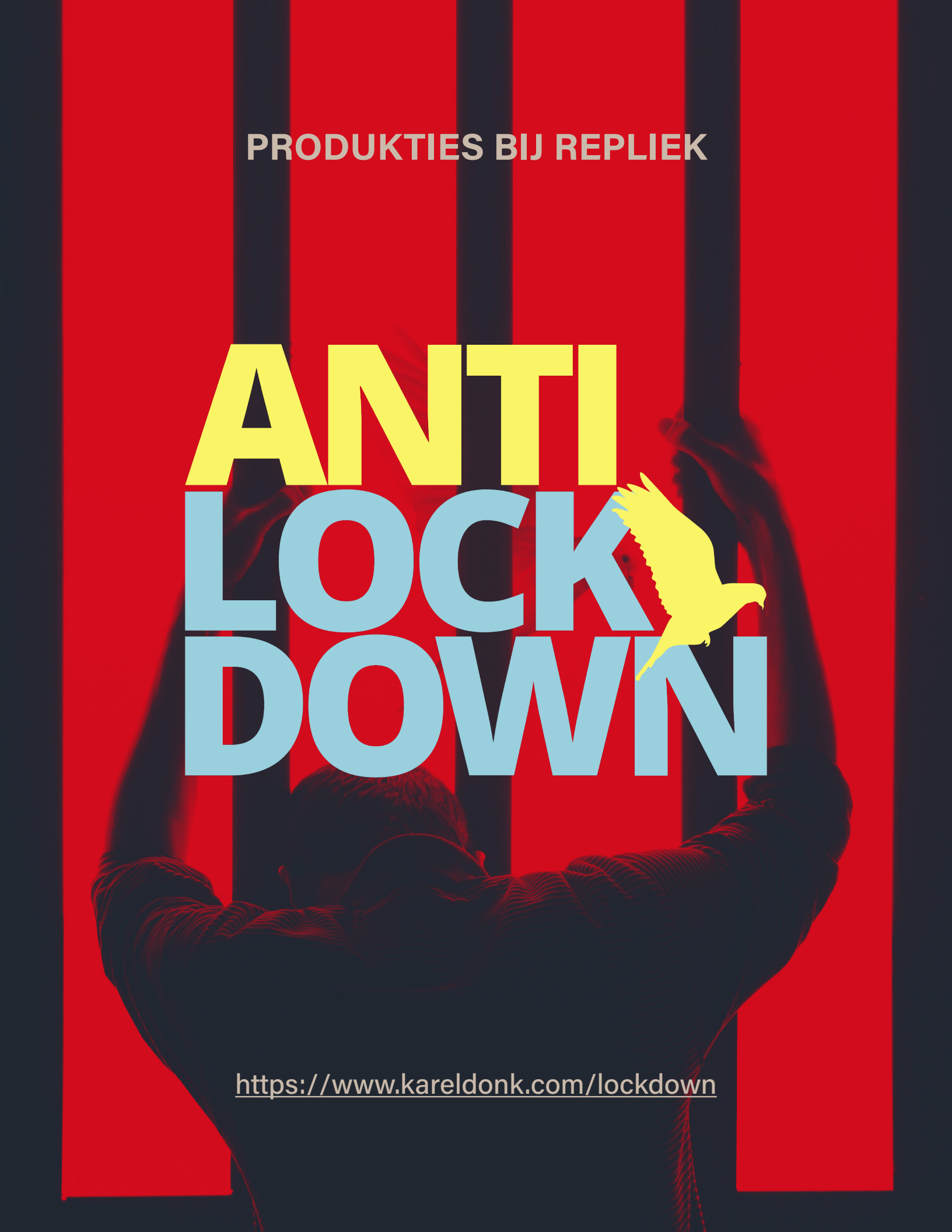

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COMMONWEALTH OF KENTUCKY
BOONE CIRCUIT COURT
DIVISION I
CASE NO. 20-CI-00678

RIDGEWAY PROPERTIES, LLC
dba Beans Café & Bakery **PLAINTIFF**

AND

COMMONWEALTH OF KENTUCKY, **INTERVENING**
***ex rel.* ATTORNEY GENERAL DANIEL CAMERON** **PLAINTIFF**

VS.

HON. ANDREW BESHEAR, GOVERNOR,
COMMONWEALTH OF KENTUCKY, *et al.*, **DEFENDANTS**

JUDGMENT AND ORDER

This matter is before the Court for final adjudication. But it comes thus in a bit of a tangle. Despite its recent vintage, this case has an appellate and procedural history that is both extensive and unusual.[1] The Court conducted an evidentiary hearing on May 17, 2021, and

[1] On July 2, 2020, this Court entered a Temporary Injunction against Governor Beshear and other executive agencies enjoining the enforcement of certain orders issued in the wake of the Governor's declaration of emergency. That same day, the Court also allowed Attorney General Daniel Cameron to intervene as Plaintiff on behalf of the people of the Commonwealth of Kentucky, who sought a wider injunction against all of the Governor's orders as offensive to their constitutional rights. Following this Court's initial Order enjoining enforcement, Governor Beshear and other executive agencies petitioned the Kentucky Court of Appeals for a writ of prohibition to prohibit the grant of such relief. That case was captioned, *Hon. Andrew Beshear, et al., v. Hon. Richard A. Brueggemann, et al*., Ky. Ct. App. No. 2020-CA-834-OA. On July 13, 2020, in an opinion by the Hon. Glenn Acree, the Kentucky Court of Appeals denied the writ. Defendants then filed an original action in the Kentucky Supreme Court, petitioning that it mandate Judge Acree to prohibit this Court from acting, or otherwise for the higher court to directly prohibit this Court from acting. That case was captioned, *Hon. Andrew Beshear, et al., v. Hon. Glenn E. Acree, et al*., Ky. S. Ct. 2020-SC-313-OA.

On July 16, 2020, this Court held an evidentiary hearing on whether further temporary injunctions should issue. At the conclusion of that hearing, this Court stated that it was granting the full relief sought by Plaintiffs and Intervening Plaintiff, *ex rel.* Attorney General Daniel Cameron, and that an order with its findings and conclusions would be entered in due course. In an Order entered July 17, 2020, the Kentucky Supreme Court directed this Court to proceed and issue the findings of fact and conclusions of law it found appropriate. However, the Supreme Court also stayed all injunctions previously imposed in the matter and prohibited the issuance of any new injunctive relief "until the full record of proceedings below is reviewed . . . and [the Kentucky Supreme Court] issues a final order."

On July 20, 2020, this Court entered an Order with findings and conclusions that all of the emergency orders issued by the governor and executive agencies violated the constitutional rights of Kentuckians and that, but for the Kentucky Supreme Court's July 17, 2020 Order, would have been enjoined during the pendency of this action. The Kentucky Supreme Court then considered the matter as on appeal in the case captioned as a writ.

pursuant to an agreed briefing schedule, took all remaining matters under submission on May 25, 2021.

PROCEDURAL AND FACTUAL BACKGROUND

On March 6, 2020, Governor Beshear declared that the 2019 coronavirus[2] constituted an emergency in the Commonwealth, invoking KRS Chapter 39A, and began issuing a string of executive orders. Among these, he ordered the closure of all businesses except for specific pursuits that he deemed essential for life.[3] Through the Cabinet for Health and Family Services ("CHFS"), he ordered the closure of churches and houses of worship.[4] Following his directives, CHFS prohibited individuals from meeting together in certain types of mass gatherings, later allowing meetings only in numbers not exceeding ten persons.[5] The Governor prohibited citizens from peaceably assembling for the purpose of petitioning a redress of these grievances but allowed and even joined assemblies for other causes.[6] He had prohibited travel, with limited exceptions, and decreed those daring to travel across state lines in violation of his order must quarantine for 14 days.[7] He ordered all citizens to remain at home unless engaged in a pursuit deemed by the government to be essential for life.[8] The CHFS ordered hospitals and doctors to cease providing any health care, including surgeries, unless said treatment was deemed emergent

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Additionally, due to dismissals on side of both Plaintiffs and Defendants, this case is no longer captioned as *Kentucky Speedway, Inc., et al., v. Northern Kentucky Independent Health District, et al*.

[2] Known as SARS-COV-2, commonly referred to as "Covid-19."

[3] Ky. Exec. Order No. 2020-246, Gov.'s Resp., p. 4, Available at https://governor.ky.gov/attachments/20200322_Executive-Order_2020-246_Retail.pdf .

[4] *Id.* CHFS Order, Mar. 19, 2020, Gov.'s Resp., p. 4, available at https://governor.ky.gov/attachments/20200319_Order_Mass-Gatherings.pdf .

[5] Order of CFHS Re: Mass Gatherings, available at https://governor.ky.gov/attachments/20200319_Order_Mass-Gatherings.pdf. See also, Gov. Beshear Updates Kentuckians on the Fight to Defeat COVID-19, available at https://kentucky.gov/Pages/Activity-stream.aspx?n=GovernorBeshear&prId=168.

[6] Testimony of Dr. Stack, V.R. 07/16/2020, circa 07:42:00; and Exh. 31 to July 16, 2020 hearing.

[7] Ky. Exec. Order No. 2020-258, Available at https://governor.ky.gov/attachments/20200330_Executive-Order_2020-258_Out-of-State-Travel.pdf ;See also Ky. Exec. Order No. 2020-266. Available at https://governor.ky.gov/attachments/20200402_Executive-Order_2020-266_State-of-Emergency.pdf ; and Ky. Exec. Order No. 2020-315, available at https://governor.ky.gov/attachments/20200506_Executive-Order_2020-315_Travel.pdf.

[8] https://kentucky.gov/Pages/Activity-stream.aspx?n=GovernorBeshear&prId=10.

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(that is, likely to result in serious, irreparable harm if not provided within 24 hours), thereby prohibiting the people from access to procedures such as cancer-screenings, dental care and physical therapy.[9] The Governor ordered everyone in Kentucky to wear masks and threatened fines and penalties for violations.[10]

At first, the Governor indicated the emergency would last for just two weeks[11]—fourteen days to flatten the curve. But fourteen months later, the Governor insists his wielding of broad emergency powers must continue. At the hearing on May 17, 2021, the Commissioner of Public Health and Governor's health advisor, Dr. Steven Stack, testified that he could not specify an incidence rate or any precise conditions that would have to be in place in order to end the state of emergency and remove all the mandates.[12] That, he said, was something only the Governor could answer.[13]

In July 2020, for purposes of CR 65.04, this Court found the Governor's orders constitutionally offensive on grounds that KRS Chapter 39A attempted to delegate functions constitutionally reserved to the legislative branch, and also for violating the inherent and unalienable rights of Kentucky's citizens. In *Beshear v. Acree*, 615 S.W.3d 780 (Ky. 2020),[14] the Kentucky Supreme Court reversed this Court's grant of temporary injunctive relief and held the delegation under KRS Chapter 39A to be constitutional.[15] The Kentucky Supreme Court

[9] See Ky. Exec. Order No. 2020-323, Available at https://governor.ky.gov/attachments/20200323_Directive_Elective-Procedures.pdf.
[10] Ky. Exec. Order No. 2020-586, available at https://governor.ky.gov/attachments/20200709_Executive-Order_State-of-Emergency.pdf.
[11] See Com. ex rel. Resp., p. 2, fn. 3, citing "Gov. Beshear Tightens Restrictions," https://kentucky.gov/Pages/Activity-stream.aspx?n=GovernorBeshear&prId=104, quoting the Governor as stating, "Kentucky—these next two weeks are about us . . . doing everything we can to blunt the curve" (last accessed May 30, 2021).
[12] V.R. 05/17/2021, *circa* 03:28:00; 03:47:00
[13] *Id.*; 04:06:30.
[14] See footnote 1, explaining that although *Acree* commenced as a separate original action on petition for a writ in response to denial of a writ, it also effectively resulted in an appeal of this Court's preliminary orders.
[15] *Id.*, at 805-813.

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further held that the challenged orders were not unconstitutionally arbitrary under §§ 1 and 2 of Kentucky's Constitution,[16] except for an order which had prohibited family members from sitting together on outdoor stadium seating at race-tracks.[17] As to the latter, because the Governor had revised that order to remove the offending prohibition, the Kentucky Supreme Court found it to be moot.[18]

The landscape currently, however, has changed. Now, it is Defendants who seek to invalidate certain portions of KRS Chapter 39A on constitutional grounds. Plaintiff and Intervening Plaintiff assert that the Governor's continuing orders violate those Kentucky Statutes. During the 2021 legislative session, the General Assembly amended KRS Chapter 39A to limit the extent and duration of its legislative delegation to the Governor. The specific legislation at issue includes Senate Bill 1 (2021 RS SB1), Senate Bill 2 (2021 RS SB2), House Bill 1 (2021 RS HB1), and House Joint Resolution 77 (2021 RS HJR 77) (all collectively referred to hereinafter as the "New Legislation" or the "Acts"). The Governor vetoed each of these measures, after which the General Assembly overrode his veto with votes of overwhelming majorities.[19] All of the New Legislation contained severability clauses, and also emergency clauses resulting in the Acts going into effect immediately.

Senate Bill 1 amended Chapter 39A in several ways. Section 2 amends KRS 39A.090 to impose a 30-day limit on the duration of any executive orders or administrative regulations that purport to restrict in-person meetings or social gatherings, or thereby impairs the operation of churches, places of worship, schools, private businesses, local governments, nonprofit

[16] *Id*., at 815-829; the Court specifically addressed the economic rights of Plaintiffs but did not address in its analysis the rights under Section 1 of the citizens at large who are represented by the Commonwealth, *ex rel*. Attorney General Daniel Cameron .
[17] *Id*., at 825.
[18] *Id.*
[19] For example, Senate Bill 1 overrode the Governor's veto by vote of 69-20 in the house, and 29-8 in the Senate; and Senate Bill 2 overrode the Governor's veto in the House 72-22, and 29-8 in the Senate.

organizations, and other political, religious or social gatherings. After 30 days, the rules imposed by executive order will expire unless the General Assembly shall vote to extend it.[20] Section 3 of Senate Bill 1 requires reporting on the use of any public funds in connection with an emergency order.[21] Section 4 limits the delegation that would allow the Governor to suspend statutes or regulations by requiring that he specifically identify the law being suspended, and also conditions any suspension of law on the written approval of the Attorney General.[22]

One of the provisions in Senate Bill 2 requires the Cabinet for Health and Family Services to follow the procedures for promulgating regulations (rather than allowing it to merely issue rules) concerning the exercise of its authority relating to the invasion of infectious or contagious disease.[23] It also imposes a 30-day limit similar to that in Senate Bill 1.

House Bill 1 provides that any business or other organization, be it for-profit or nonprofit, as well as local government, including schools and school districts, "may remain open and fully operational for in-person services," so long as the business or organization adopts a plan that follows *either* the Governor's order or guidance issued by the Center for Disease Control ("CDC").[24] In other words, it allows the organization to choose the least restrictive option.

House Joint Resolution 77 expressed approval of 56 of the executive's orders and regulations, 24 of which it provided shall continue for 90 additional days, and 32 of which it extended for 30 additional days.[25] Otherwise, it provided that "[a]ll COVID-19 related executive orders, administrative regulations, other directives issued by the Governor or pursuant to his authority, or agencies or boards under the Governor's authority, not specifically extended by this

[20] 2021 Ky. Acts ch. 6 § 2.
[21] *Id.*, at § 3.
[22] *Id.*, at § 4.
[23] 2021 Ky. Acts ch. 7 § 4.
[24] 2021 Ky. Acts ch. 3 § 1.
[25] 2021 Ky. Acts ch. 168, §§ 2, 3.

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Act are of no further force or effect as of the effective date of this Act."[26] Among the Governor's orders that the General Assembly expressly did not extend was his decree that all Kentuckians wear a mask.

ARGUMENTS PRESENTED[27]

Based on the New Legislation, Plaintiff and Intervening Plaintiff seek a declaration that all of the Governor's emergency orders in conflict with the Acts are void as a matter of law, and also seek a permanent injunction compelling Defendants to comply. Further, they point to existing data from various states to show that the Governor's mandates have had no appreciable effect on fighting the coronavirus and that there is no justification in fact for the same to continue.

Plaintiff presented testimony from Richard Hayhoe, owner of Ridgeway Properties, LLC, to show he is suffering continuing harm. Plaintiff, as to his business, argues the data shows there to be neither any need nor rational basis for certain measures the Governor continues to order and impose, including the mask mandate, social distancing, capacity limitations, and time limitations for serving customers. Plaintiff also presented testimony from Dr. Molly Rutherford and Stephen E. Petty, P.E., CIH., who testified as an expert as a certified industrial hygienist.

On the other side, Defendants filed a cross-motion for summary judgment asking the Court to declare the New Legislation unconstitutional. Defendants argue that the Governor cannot be in violation of the New Legislation because he obtained an injunction from the Franklin Circuit to enjoin application of those Acts and, thus, the Governor's orders remain in effect. Defendants also insist that, even without the ruling in Franklin Circuit, the Governor

[26] *Id.*, at § 1.

[27] Many arguments were presented and, although not recited, were considered. Some arguments or evidence presented may be recited only in the analysis portion of this Order.

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cannot be limited by the New Legislation. According to Defendants, the result is an unconstitutional encroachment by the legislative branch.[28] Defendants presented testimony of Dr. Steven Stack, the Commissioner of Public Health and Governor's health advisor.

Defendants also argue that the harms alleged by Plaintiffs are either non-existent, moot, or have already been decreed by the Kentucky Supreme Court as insufficient to warrant injunctive relief, and that the same is the law of the case. They further point out that the Governor's emergency orders have undergone numerous revisions and that, under his current stated intention, both the capacity limitations on businesses will be removed, and the mask mandate imposed on all Kentuckians lifted, on June 11, 2021—but not in all settings.

Contra the arguments presented by Defendants, *ex rel*. Attorney General Daniel Cameron, as Intervening Plaintiff on behalf of the people of the Commonwealth, insists that the decision in the Franklin Circuit does not effect this case, that the law of the case from *Acree* does not apply to the relief sought and, consequently, that this Court should not delay to reach the merits of the claims and constitutional questions before it. Intervening Plaintiff argues the General Assembly passed the Acts as part of its legislative powers and, because the same are constitutionally sound, urges this Court to deny Defendants' cross-motion and to order Defendants to comply with the New Legislation.

ANALYSIS

No one in the civil realm, however high their office, is above the law. It was for this principle that English Barons assembled at Runnemede meadow and, on June 15, 1215, forced King John to sign the *Magna Carta*, within which he avowed the Crown would abide thereby in

[28] Defendants' specific arguments on this as to each of the Acts will be more fully addressed in the analysis section of this Order below.

perpetuity.[29] Even after he signed, the Barons refused allegiance until he formally affixed upon it the Seal of England. The great charter of Kentucky is its Constitution. And its guarantees are sealed by an oath, one that applies to all offices in all branches. Before a person may take any office, regardless of whether the person is elected or appointed, the individual, among other avowals, must formally declare:

> I do solemnly swear (or affirm . . .) that I will support the Constitution of the United States and the Constitution of this Commonwealth, and be faithful and true . . . so help me God.[30]

The Constitution places limits on what government may do to (and for) its citizens. All the laws enacted by the General Assembly, and all laws enforced by the executive, are subject to those limits. The result, as John Adams put it, is *a government of laws, not men*. No branch, not even all branches acting in concert, can legitimately change any provision of the Constitution. Only by direct vote or convention **of the people**—whose rights the Constitution exists to protect—can any change occur.[31] The text and meaning of the Constitution is fixed, as its framers make clear in § 26:

> To guard against transgression of the high powers which we have delegated, We Declare that every thing in this Bill of Rights is excepted out of the general powers of government, and shall forever remain inviolate; and all laws contrary thereto, or contrary to this Constitution, shall be void.[32]

Words mean things, and the meaning of the words in our Constitution is clear. The legislature alone enacts the laws. "The legislative power shall be vested in a House of Representatives and a Senate . . . ."[33] The executive carries out the law. "The supreme executive

[29] *See, generally*, *Magna Carta*, § 1 ("We furthermore grant and give to all the freemen of our realm for ourselves and our heirs in perpetuity the liberties written below to have and to hold to them and their heirs from us and our heirs in perpetuity"), quoted from National Archives, Magna Carta Translation, https://www.archives.gov/exhibits/featured-documents/magna-carta/translation.html, last accessed, May 29, 2021.
[30] KY. CONST. § 228.
[31] KY. CONST. §§ 256, 258.
[32] KY. CONST. § 26.
[33] Ky. Const. § 29.

power of the Commonwealth shall be vested in . . . the 'Governor . . .' who "shall take care that the laws are faithfully executed."[34] And the judicial branch adjudicates controversies according to the law.[35] No branch "shall exercise any power properly belonging to either of the others, except in the instances . . . expressly directed or permitted [within the text of the Constitution]."[36]

All parties to this action agree on one point, namely, that the Constitution has been violated. The only dispute, when boiled down, is by which it is being transgressed.

A. Law-of-the-Case and Comity

Under the law-of-the-case doctrine, trial courts are not permitted to reopen questions of law that have been decided by an appellate court in the very same case. "A final decision of [an appellate court], *whether right or wrong,* is the law of the case and is conclusive . . . ."[37] Nevertheless, the law-of-the-case rule is not without exceptions. An exception exists in the "limited situation where the controlling law changes after reversal . . . but prior to a subsequent re-trial."[38] Further, the law-of-the-case doctrine applies to questions of law actually decided, and not *dicta*.[39] And the doctrine applies only to determinations made based upon law and not questions of fact.[40]

In *Acree*, the Kentucky Supreme Court held that the legislature can delegate to the Governor emergency rulemaking authority under 39A.[41] That determination is the law of this case. However, Plaintiff and Intervening Plaintiff seek relief based upon intervening changes in

[34] KY. CONST. §§ 69, 81.
[35] KY. CONST. § 109.
[36] KY. CONST. § 28.
[37] *Ragland v. DiGiuro*, 352 S.W.3d 908, 914–15 (Ky. App. 2010); quoting, *Williamson v. Commonwealth*, 767 S.W.2d 323, 325 (Ky.1989) (emphasis original).
[38] *St. Clair v. Commonwealth*, 451 S.W.3d 597, 612–13 (Ky. 2014); *accord*, *Brown v. Commonwealth*, 313 S.W.3d 577, 610 (Ky. 2010), *Sherley v. Commonwealth*, 889 S.W.2d 794 (Ky. 1994).
[39] *Johnson, True & Guarnieri, LLP*, 538 S.W.3d 901, 918 (Ky. App. 2017).
[40] *Inman v. Inman*, 648 S.W.2d 847, 849 (Ky. 1982).
[41] *Acree*, 615 S.W.3d, at 805-13.

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the law since *Acree* was decided. In short, they contend that, by those changes, the legislature has limited some of the power previously granted. Plaintiff and Intervening Plaintiff insist that if the General Assembly can delegate that power, it can also limit the extent of its delegation or revoke it entirely. Although the Court found the Defendants' arguments concerning the law-of-the-case a difficult question, it is persuaded that it does not apply to the issues remaining for decision. In addition to the reasons recited herein, the Court is persuaded otherwise by the arguments presented in *ex rel*. Attorney General Daniel Cameron's Post Hearing Reply.[42] Although Plaintiff was a party plaintiff at the time *Acree* was decided, the law has nonetheless changed, new facts are presented, and the matter is before this Court for final judgment, not temporary relief.

Plaintiff presents evidence of new facts not offered or considered at the preliminary injunction hearing. Intervening Plaintiff provides factual data not existing in July 2020 and concerning which this Court can take judicial notice. The essential questions here are, first, whether the Acts are constitutional. And, if so, in light of the New Legislation and new facts, whether the Governor may continue to impose emergency orders that exceed the limits expressly set under the new law. Defendants argue that the Court may not address that question, entertain permanent injunctive relief, or address the merits in any manner inconsistent with the result reached in the Franklin Circuit.

[42] See pp. 1-9. However, the Court does correct a statement in the Attorney General's argument on page 9, which states that the decision in *Acree* "in no way precludes another Plaintiff, with different facts, in an altogether different legal landscape, from prevailing on its request for a permanent injunction." The current Plaintiff was in fact a Plaintiff at the time *Acree* was decided. However, this Court did not grant a temporary injunction to the current Plaintiff on the economic grounds presented by it but, rather, on the grounds presented by *ex rel*. Attorney General Cameron on behalf of all Kentucky citizens. In fact, this Court expressly held that Plaintiff did not show likelihood that it would suffer irreparable harm in the same way the other Plaintiffs had and that it was not granting injunctive relief on that basis. Consequently, the discussion in *Acree* concerning irreparable harm does not apply. Furthermore, this is on for final judgment and the elements required for temporary injunctive relief do not apply.

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Defendants also assert that the Court should not resolve this matter because the Franklin Circuit has enjoined enforcement or enjoined the applicability of the New Legislation. Relating to this, the parties have presented arguments as to standing, ripeness and whether there was lack of controversy in Franklin Circuit where, purportedly, the party seeking the injunction is also the person that would be enjoined. But those arguments turn solely on the case in Franklin Circuit. The matter that is or was before the Franklin Circuit is different from the controversies presented here. And this Court does not agree that it should prevent final resolution on the merits in this case. Again, the Court agrees with the position espoused by *ex rel*. Attorney General Cameron that there is no basis for displacing the claims and controversies here.[43] "All courts shall be open, and every person for an injury done him . . . shall have remedy by due course of law, and right and justice administered without . . . denial or delay."[44]

As this Court sees it, Defendants' arguments concerning the Franklin Circuit are more closely related to comity than jurisdiction or ripeness. Under the rules of comity, where two identical actions are brought in separate courts that could result in conflicting judgments with "calamitous results," the court with the latter suit is counseled to defer.[45] However, comity only applies where all the parties are identical, and the cause of action in the first suit is identical with that in the second suit.[46] Here, the parties are not identical. Second, the cause of action differs as to the nature of the controversy. Third, there is evidence presented in this case that has not been presented in the other case, or the evidence otherwise differs. Moreover, there are already different decisions in at least two other circuits involving questions relating somewhat to that

[43] See Com. *ex rel*. Attorney General Daniel Cameron's Resp., p. 13, quoting *Baze v. Commonwealth*, 276 S.W.3d 761, 767 (Ky. 2008), *Bell v. Cabinet for Health & Family Servs., Dep't for Cmty. Based Servs*., 423 S.W.3d 742, 751 (Ky. 2014).
[44] KY. CONST. § 14.
[45] *Delaney v. Alcorn*, 301 Ky. 802, 805-806 (Ky. 1946).
[46] *Riddle v. Howard*, 357 S.W.2d 705, 708 (Ky. 1962).

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presented here. It is not uncommon for decisions among circuits to differ, especially on questions of first impression. And here, the parties are ploughing new ground.

Moreover, there are already conflicting rulings in Franklin and Scott Counties. Ultimately, the conflicting circuit decisions will be resolved on appeal—something that can be expedited as the history in this case demonstrates. Delaying decision here would deprive the litigants in this case from presenting their arguments on the facts and law presented here. Defendants contend that this can be remedied by allowing Plaintiff to file an *amicus* brief with the appellate tribunal in those other cases. But that is not equivalent to having one's own case heard. Nor does that allow for the presentation of evidence by the Plaintiff here.

B. Impact of Governor's Emergency Decrees

Plaintiff presented evidence of the injury it is suffering. Plaintiff, along with Intervening Plaintiff, also presented evidence that there is no scientific basis for many of the Governor's orders at issue. Based upon the data presented, they argue that the measures imposed in Kentucky have had no appreciable effect when compared to other states.

Richard Hayhoe, owner of Beans Café & Bakery, testified[47] that as a result of the capacity restrictions ordered by the Governor, he lost two-thirds of his restaurant's seating capacity. According to Hayhoe, the mandates have put his business in a precarious financial condition. Additionally, the Northern Kentucky Independent Health District cited Plaintiff for violating the Governor's mask mandate, for which Hayhoe was later criminally charged. Hayhoe testified that he was not afforded any opportunity to defend against the allegations. He said that, had he been able to, he would have explained that the person not wearing a mask had a health exemption.

[47] V.R. 05/17/2021, *circa* 10:31:30 a.m.

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After passage of the New Legislation, Hayhoe's business opted to develop a compliance plan based upon CDC guidance in lieu of the Governor's mandates. The former, according to Hayhoe, are less restrictive. Hayhoe testified that he fears enforcement actions may still be brought against him even though as yet, that has not occurred following the passage of the Acts.

1. Analysis of Effectiveness of Various Mandates on Covid-19

Dr. Mary ("Molly") Rutherford testified[48] as an expert in medicine in public health. Although Defendants objected to her qualifications, the Court found her education, background and experience sufficient. Dr. Rutherford obtained her master's degree in public health at John Hopkins University, with a focus on epidemiology. She worked for Dr. Fauci for a total of nine years, the first six at National Institute of Allergy and Infectious Diseases, and the latter three at the National Institute of Health. She co-authored an international, peer reviewed article titled, "*Multi-treatment of Early Ambulatory High Risk SARS/COV-2 Infection*."[49] She testified that she has treated nearly 100 patients for Covid-19 in her family practice. Dr. Rutherford is board certified in addiction medicine, and is the past Chair and a current board member of the American Academy of Family Physicians.

Dr. Rutherford pointed to several published articles during her testimony. One analyzed the effect that government mandates have had on the infection rates, hospitalizations and deaths from Covid-19 by comparing data from countries that imposed strict lockdowns against those that did nothing.[50] Among its conclusions, the study found that "government actions such as border closures, full lockdowns and a high rate of COVID-19 testing, were not associated with

[48] V.R. 05/17/2021, *circa* 10:46:30.
[49] Plaintiff's Exh. 16.
[50] Plaintiff's Exh. 17; Rabail Chaundhry, George Dranitsaris, *et al*., *A country level analysis measuring the impact of government actions, country preparedness and socioeconomic factors on Covid-19 mortality and related health outcomes*, EClinicalMedicine 25 (2020) 100464 (21 Jul. 2020).

statistically significant reductions in the number of critical cases or overall mortality."[51] Similarly, a later study likewise found that the "[s]tringency of measures settled to fight pandemia, including lockdown, did not appear to be linked with the death rate."[52]

Another study opined that, even if cases are reduced in the short-term, interventions actually lead to more deaths overall.[53] According to the researchers' findings, and Dr. Rutherford, the focus should have been only on those determined to be high risk, such as those over 70 years of age. Plaintiff also presented an article that is still in manuscript form that, in effect, challenges claims that government interventions saved any lives.[54] This study concludes that the "United Kingdom's lockdown was both superfluous and ineffective," and that proponents of government interventions employ "circular logic."[55]

Dr. Rutherford stated that, at first, she trusted Dr. Fauci and the CDC even though they were pushing governments to impose measures, such as social distancing, that were not based upon known science. However, Dr. Rutherford testified that in the following months, as a result of their actions, she no longer trusts what they say. It isn't just that the government lockdowns did not help. Rather, she opined, the government's actions have inflicted more harm and death. She testified that there has been an increase in overdose deaths and pointed to specific cases where she contends overdose deaths occurred as a direct consequence of the closure of facilities.

Finally, Dr. Rutherford also testified concerning Covid-19 data comparisons from various states, using it to illustrate the lack of difference between states that imposed harsh lockdowns

[51] *Id*., p. 5.
[52] Plaintiff's Exh. 20: Quentin De Larochelambert, Andy Marc, *et al*., *Covid-19 Mortallity: A Matter of Vulnerability Among Nations Facing Limited Margins of Adaption*, Front. Public Health 8:604339 (19 Nov. 2020).
[53] Plaintiff's Exh. 18: Ken Rice, Ben Wynne, et al., *Effect of school closures on mortality from coronavirus disease 2019: old and new predictions*, BMJ 2020; 371:m3588 (7 Oct. 2020).
[54] Plaintiff's Exh. 21: Stefan Homburg and Christof Kuhbandner, *Comment on Flaxman et al*., Leibniz University Hannover and University of Regensburg (christof.kuhbandner@ur.de).
[55] *Id.*

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from those that did not. In connection with this, Plaintiff presented a document identified as "Exhibit 26" containing a table of data comparisons. At the hearing, Defendants objected to admission of that document on grounds of improper foundation, and lack of identification of origin or sources. Because the testimony had occurred earlier in the day, and the witness had already been excused, the Court indicated that it would rule following a review of the testimony. Having done so, Defendant's objection to Exhibit 26 is sustained.[56] However, the objection applied only to Exhibit 26, not her testimony, or the specific points of data contained therein on which she expressed knowledge.

2. Validity of Social Distancing and Mask Mandates on Covid-19

Stephen E. Petty, P.E., CIH, testified[57] as an expert and was accepted as such without objection. Mr. Petty has served as an expert witness in approximately 400 cases relating to toxic or infectious exposure, personal protective equipment ("PPE"), and as a warning expert. He also served as an epidemiology expert for the plaintiffs in the Monsanto "Roundup" cases, and for those in the Dupont C8 litigation. In connection with his service as an expert, he was deposed nearly 100 times and has provided court testimony in approximately 20 trials. Mr. Petty holds nine U.S. patents, has written a book comprising nearly 1,000 pages on forensics engineering, is a certified industrial hygienist, and a recognized expert with the Occupational Safety and Health Agency. Mr. Petty helped write the rules on risk assessment for the State of Ohio and has trained Ohio's risk assessors.

Mr. Petty explained that the field of his expertise is "to anticipate and recognize and control things that could hurt people, everything from making them sick to killing them."[58] He

[56] On cross-examination, Dr. Rutherford testified that she did not participate in compiling the document, could not provide source citations to identify the source(s) of the data within the document, could not state who performed the calculations contained in the document, and could not identify who chose which states to sample.
[57] V.R. 05/17/2021, *circa* 11:45:40.
[58] *Id.*

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testified that, in this context, he has analyzed the use of masks and social distancing in connection with Covid-19. He testified that both the six-foot-distancing rule, and mask mandates, are wholly ineffective at reducing the spread of this virus. Masks are worthless, he explained, because they are not capable of filtering anything as small as Covid-19 aerosols. In addition, masks are not respirators and lack the limited protections that respirators can provide.

The N-95 respirator, which he states is in the bottom class of what may be classified as a respirator, is rated to filter 95% of all particles that are larger than .3 microns. However, a Covid-19 particle, which is only between .09 to .12 micron, is much smaller. Mr. Petty further explained that an N-95 will not even filter above .3 microns if it is not used in accordance with industry standards. Among the requirements, respirators must be properly fitted to seal along the face, and they also must be timely replaced. Mr. Petty stated that N-95 masks, which he said are often utilized as surgical masks, are "not intended to keep infectious disease from either the surgeon or from the patient infecting each other" but only to catch the "big droplets" from the surgeon's mouth."[59]

According to Mr. Petty, masks have no standards, are not respirators, and do not even qualify as protective equipment. In contrast, respirators have standards, including rules that state respirators may not be worn by persons with facial hair, must be fitted to ensure a seal, and must be timely replaced—or, as in higher end respirators, the cartridges must be replaced to prevent saturation. In addition, standards for respirators also require users to obtain a medical clearance because the breathing restriction can impair lung function or cause other problems for persons having such limitations. Putting those persons in a respirator can harm their well-being.

[59] *Id.*

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Concerning the effectiveness of respirators, Mr. Petty explained that it comes down to "big stuff" versus "small stuff." Big stuff can be taken out by the body's defenses, such as its mucus tissue, where droplets can be caught and eliminated. The small stuff, however—like aerosols—are more dangerous. Masks cannot filter the small stuff. According to Petty, because Covid-19 particles are comprised of aerosols, it is really, really, small stuff. And, as he pointed out, an N-95 is designed to filter larger particles. Even for particles as large as .3 micron, Mr. Petty testified that an N-95's effectiveness is in direct proportion to its seal. In fact, he stated it becomes completely ineffective if 3% or more of the contact area with the face is not sealed.

Mr. Petty testified that masks leak, do not filter out the small stuff, cannot be sealed, are commonly worn by persons with facial hair, and may be contaminated due to repetitive use and the manner of use. He emphatically stated that mask wearing provides no benefit whatsoever, either to the wearer or others.

He explained that the big droplets fall to the ground right away, the smaller droplets will float longer, and aerosols will remain suspended for days or longer if the air is stirred. Mr. Petty testified that the duration of time that particles remain suspended can be determined using "Stoke's Law." Based on it, for particles the size of Covid-19 (.12 to .09 micron) to fall five feet would take between 5 and 58 days in still air. Thus, particles are suspended in the air even from previous days. And so, he asks, "If it takes days for the particles to fall, how in the world does a six-foot rule have any meaning?"[60]

Mr. Petty acknowledged that both OSHA and CDC have recommended that people wear masks. However, he called this "at best dishonest."[61] As an example on this, he pointed to CDC guidance documents where, on page 1, it recommends wearing a mask; but then on page 6,

[60] *Id.*
[61] *Id.*

admits that "masks, do not provide . . . a reliable level of protection from . . . smaller airborne particles."[62] According to Mr. Petty, those agencies have smart individuals who know better. Mr. Petty points out that, even before March 2020, it was known that Covid-19 particles are tiny aerosols. And on this, he states that he insisted that fact early on. He also points to a more recent letter by numerous medical researchers, physicians and experts with Ph.D.s, asking the CDC to address the implications of Covid-19 aerosols. During Dr. Stack's subsequent testimony, he also acknowledged that Covid-19 is spread "by . . . airborne transmission that could be aerosols . . . ."[63]

Finally, Mr. Petty pointed to another recent study by Ben Sheldon of Stanford University out of Palo Alto. According to that study, "both the medical and non-medical face masks are ineffective to block human-to-human transmission of viral and infectious diseases, such as SARS, CoV-2 and COVID-19."[64] The Court finds the opinions expressed by Mr. Petty firmly established in logic. The inescapable conclusion from his testimony is that ordering masks to stop Covid-19 is like putting up chain-link fencing to keep out mosquitos. The six-foot-distancing requirements fare no better.

3. Data Comparisons: Kentucky and Freer States

Plaintiff and Intervening Plaintiff argue the Governor's orders have been shown to be ineffectual and, therefore, cannot justify continued imposition on an emergency basis. They compare Kentucky's data with the data from states that purportedly imposed no mandates, such as South Dakota, or states that imposed far less stringent mandates, such as Tennessee, Texas

[62] *Id.*
[63] V.R. 05/17/2021, *circa* 02:05:45.
[64] V.R. 05/17/2021, *circa* 11:45:40.

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and Florida. At the hearing, and in the Attorney General's Reply, the primary focus was on Florida. The Court can take judicial notice of the published data.[65]

As to the greater freedoms allowed by the Governor in Florida, Dr. Steven Stack agreed that, "at varying times," Florida "had much less stringent requirements" than those imposed in Kentucky.[66] He further acknowledged that Florida "opened up earlier than us, yes, significantly."[67]

The population of Florida is more than four times that of Kentucky, Florida's being 21,538,187 and Kentucky's 4,505,836.[68] In addition, Florida has a higher percentage of its population over age 65 than does Kentucky. In Florida, 20.9% of the people are over age 65, whereas in Kentucky 16.9% are over age 65.[69] Florida had 10,471 Covid-19 cases for every 100,000 people, and Kentucky had 10,197 per 100,000 people.[70] The CDC reports that, in Florida, for every 100,000 people, 167 died with Covid-19 and, in Kentucky, for every 100,000 people, 150 people died with Covid-19.[71] That is a difference of a mere 0.017%, with Kentucky's number being slightly better.

However, Florida's population is older. In fact, an additional 4% of Florida's population are over age 65 compared to Kentucky. When that fact is considered, Florida's success and survival rate is better than Kentucky's. In Florida, deaths of persons with Coivd-19 who were at

[65] See Attorney General's Post Hear'g Reply, pp. 9-12; see also KRE 201(c), and *Doe v. Golden & Walters, PLLC*, 173 S.W.3d 260, 264 (Ky. App. 2005), holding a court can take judicial notice of a fact that is generally known and "[c]apable of accurate and ready determination by resort to sources whose accuracy cannot reasonably be questioned."
[66] V.R. 05/17/2021, *circa* 03:58:38 p.m.
[67] *Id.*
[68] See U.S. Census Bureau data for 2020, available at: https://www.census.gov/quickfacts/fact; see also Att. Gen. Reply, p. 10 for 2019 Census Data.
[69] *Id.*
[70] See CDC Covid Data Tracker, available at: https://covid.cdc.gov/covid-data-tracker/#cases_casesper100k; see also, Att. Gen. Reply, p. 11.
[71] *Id.*

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age 65 and older represent 75.16% of the total persons who died of Covid-19 in that state.[72] Compare that to Kentucky, where persons who died with Covid-19 over the age of 65 represent 87.75% of all Covid-19 deaths.[73] In any event, the data comparison demonstrate there to be no emergency justification for continuing Governor Beshear's orders.

4. Accuracy of CDC Case Counts

Dr. Stack testified as to the different methods by which cases are determined to be positive for Covid-19. He also provided information on the polymerase chain reaction ("PCR") test and that, by government order, the cycle rates used in that testing may not be disclosed. According to Dr. Stack, federal regulation prohibits labs from reporting to the public the number of cycles it took to yield a positive result during the test.[74] This is commonly referred to as "cycle threshold" or "Ct" values.[75] The Ct value is "the number of amplification cycles . . . at which the diagnostic test result of the real-time PCR changes from negative (not detectable) to positive (detectible).[76] According to the guidance, the total number of cycles required to yield a positive result "generally ranges from about 15 to 45 cycles."[77] The guidance provided by Dr. Stack explains that, "[d]iagnostic laboratories should not include Ct values on laboratory reports because it could be out of compliance with laboratory regulations and they should not be used to inform patient management."[78]

[72] Compare CDC Covid Data Tracker, available at https://www.cdc.gov/nchs/nvss/vsrr/covid_weekly/index.htm#SexAndAge, with https://covid.cdc.gov/covid-data-tracker/#cases_casesper100k, and https://www.census.gov/quickfacts/fact.
[73] *Id.*
[74] V.R. 05/17/2021, at 03:50:00 p.m.; and 04:07:00.p.m
[75] See Defendants' Exh. A, at p. 31 of 34; *Ct Values: What They Are and How They Can be Used*; Vers. 1 APHL (Nov. 9, 2020).
[76] *Id.*
[77] *Id.*
[78] *Id*.

In contrast, however, the CDC has recently indicated that Ct values should be limited at, or less than, 28 cycles when cataloguing "breakthrough infections," *i.e.*, infections occurring in persons that have been fully vaccinated for Covid-19. For those cases, the CDC states that "Clinical specimens for sequencing should have an RT-PCR Ct value ≤28."[79] This is, at the very least, a curious difference. The CDC accepts Cycle thresholds for ordinary PCR testing for sequencing even when amplified as high as 45 cycles. But for "breakthrough" cases, states it should be no higher than 28. This invites many questions, such as why Ct values in Covid tests should differ based upon whether or not the individual being tested has been vaccinated; and, why a federal government agency has ordered labs to "not include Ct values on laboratory reports . . . to inform patient management," even though the CDC indicates that PCR Ct values should be ≤28. These are important questions. Case counts have been the poster child for the need to deprive people of their liberty.

C. Constitutionality of the Acts

Defendants point out that, under the New Legislation, the General Assembly did not repeal the delegation it granted under Chapter 39A. Thus, Defendants argue, since the General Assembly has maintained its delegation to the Governor, thereby allowing him to make rules during an emergency, it cannot at the same time manage the Governor in how he goes about it. That, they insist, would be engaging in executive functions by the legislature. According to Defendants, because the New Legislation attempts to do so, it encroaches on the powers granted to the executive branch under the Constitution.

As to House Bill 1, Defendants' challenge is on grounds that it attempts to delegate functions to the CDC. According to Defendants, House Bill 1 makes the CDC the interpretative

[79] See CDC, *COVID-19 vaccine breakthrough case investigation, Information for public health, clinical, and reference laboratories*, available at: https://www.cdc.gov/vaccines/covid-19/downloads/Information-for-laboratories-COVID-vaccine-breakthrough-case-investigation.pdf (last accessed, June 7, 2021).

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or determinative body of what measures should be imposed upon businesses. Defendants complain that House Bill 1 does not specify which of the CDC's 100-plus guidance documents are not to be Kentucky law. Defendants further assert that CDC guidance is conflicting and difficult to navigate. Therefore, Defendants argue, because it makes CDC guidance the regulatory standard, House Bill 1 violates §§ 1 and 2 of Kentucky's Constitution for being impermissibly arbitrary, vague, and unintelligible.

Dr. Stack testified that he, in consult with others in the executive branch, reviews the guidance of the CDC and tailors the emergency orders that are imposed on Kentucky businesses.[80] According to Dr. Stack, CDC guidance would be too difficult for individual businesses to navigate on their own.[81] However, as Plaintiff points out, the emergency orders issued by Defendants also contain references to CDC guidance. Initially Dr. Stack contended that it would be impossible to enforce a company's compliance plan if it was predicated on the CDC guidance.[82] But, on cross-examination, he conceded that enforcement based upon CDC guidelines "should generally be doable."[83]

It is true that the General Assembly may not legitimately delegate functions to the CDC, or make it the interpretive or determinative body for Kentucky law. But House Bill 1 does not delegate legislative function to the CDC. Rather, House Bill 1 uses CDC guidance as a limit on the rule-making authority delegated to the Governor. It caps the extent or scope of rulemaking that the Governor may impose by emergency decree. The Kentucky Supreme Court held that the General Assembly may delegate rulemaking under KRS Chapter 39A. House Bill 1 sets a

[80] V.R. 05/17/2021, *circa* 02:18:00 p.m.
[81] *Id.*
[82] *Id., circa* 02:31:00 – 02:33:00 p.m.
[83] V.R. 05/17/2021, *circa* 03:02:00 p.m.

boundary on that delegation by using CDC guidance as the foul-line. For the reasons Defendants point out, it is not likely much of a limit. But it is a limit nonetheless.

Whereas House Bill 1 limits executive decrees by their scope, or extent of their reach, Senate Bills 1 and 2 limit their duration. Senate Bill 1 still allows the executive to restrict in-person meetings or social gatherings, and to impair attendance at places of worship, schools, businesses, and other organizations under Chapter 39A, but it limits any such orders to 30 days "unless an extension, modification, or termination is approved by the General Assembly."[84] Senate Bill 2, § 22, contains a similar time limitation on administrative regulations. Defendants argue that this violates §§ 36 and 42 of the Kentucky Constitution which mandates that the General Assembly meet for only 30 days in odd years, and 60 days in even years. Further, Defendants point to § 80 of the Constitution, which provides that the Governor "may" call an extraordinary session. According to Defendants, because that provision gives the Governor discretion to call a special session, it implies that, should he decide not to, he has authority to decree whatever rules he deems necessary. This proposition, however, turns the Constitution's strict separation of powers into a meaningless formula.

In support of their proposition, Defendants present historical accounts of Kentucky's 1890-91 Constitutional Convention. Specifically, they quote delegates to show the Convention was called to constrain the General Assembly from meeting too often; that an ongoing legislature makes the people "subject at times to very great abuses;"[85] that without curbing the time during which the General Assembly may legislate, they "might go on for several months and expend the money of the people of Kentucky,"[86] and that the result was "too much legislation."[87] None of

[84] 2021 Ky. Acts ch. 6 § 2.
[85] Defendants' Resp. and Cross-motion, p. 36, quoting Delegate DeHaven, 1890 Debates, at 206.
[86] *Id.*, quoting Delegate Cox, 1890 Debates, 1126-27.
[87] *Id.*

this, however, proves that the people reined-in the legislature only to empower their governor to rule by mere decree in its stead. Indeed, that circumstance would be far worse than the first. The quotes presented by Defendants support the oft repeated quote that "*no one's life, liberty, or property is safe while the legislature is in session*."[88] But the complaint it expresses is not remedied by replacing legislation with executive rulemaking. As is so cleverly illustrated by the old Schoolhouse Rock cartoon, "*I'm Just a Bill*," it's not easy to pass a law. It's not supposed to be. We have a bicameral legislature for a reason.

Defendants contend the Acts violate § 80 of the Constitution "[b]y forcing the Governor to call a special session to extend emergency orders," thereby "effectively [rewriting §§ 36 and 42] to allow the General Assembly to meet for 30 legislative days during odd-numbered years and 60 legislature days in even numbered years, *unless an emergency exists*."[89] The Court disagrees. The Acts do not provide any means for the General Assembly to reconvene itself by virtue of its own legislation. It still requires a call from the Governor, and that call still remains at his discretion. Section 80 of the Constitution provides that the Governor "may, on extraordinary occasions, convene the General Assembly . . . . stating the subjects to be considered, and no other shall be considered." The Acts are consistent with this provision. The following quote attributed to Delegate MacKoy perhaps best makes the point:

> It is to be presumed, I think, when the Legislature is convened in special session, that it is so called in pursuance of some emergency of some public demand that is urgent, and that the Governor, knowing the wishes of the people and understanding fully the emergency, will call the Legislature in special session only when it is absolutely necessary that it shall be done.[90]

[88] Author unknown.
[89] Defendants' Resp. and Cross-motion, p. 37 (italics in original).
[90] *Id*., quoting Delegate MacKoy, 1890 Debates, at 1049.

Before KRS Chapter 39A, if there was "some emergency" and the General Assembly was not then in normal session, the Governor had to call a special session and, as provided in § 80, present "the subjects to be considered" for legislation. Under the New Legislation, if there is "some emergency," the Governor may declare an emergency and act on his own for up to 30 days. After that, the authority delegated expires unless the General Assembly shall approve an extension. This does not square with Defendants' position that executive power is being usurped. As Delegate MacKoy remarked, a special session is "called in pursuance of some emergency . . . that is urgent." If a purported emergency that would extend beyond 30 days is not sufficiently urgent to call a special session, then it is not sufficiently urgent to justify the imposition of indefinite and open-ended rulemaking by executive decree. As John Adams counseled, "*The only maxim of a free government ought to be to trust no man living with power to endanger the public liberty*."[91]

Defendants also attack § 4 of Senate Bill 1 because it requires the Governor to identify with specificity the laws being suspended, and conditions the Governor's emergency power to suspend laws upon the written approval of the Attorney General. According to Defendants, that is constitutionally offensive because it makes the action of the Governor depend upon a lesser constitutional officer. However, § 15 of the Constitution commands that, "No power to suspend laws shall be exercised unless by the General Assembly or its authority." Clearly, if the Governor can suspend laws, he can only do so "by the General Assembly or its authority." In *Acree*, the Kentucky Supreme Court held the General Assembly could delegate that authority. Now the General Assembly has, "by its authority," limited that delegation by the conditions set out in Senate Bill 1.

[91] John Adams, Bill of Rights Institute, https://billofrightsinstitute.org/founders/john-adams, last accessed May 29, 2021.

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Defendants also assert that, if the Governor's emergency orders are not legislative in nature, or do not involve legislative power, then he has the authority under the Constitution to act without regard to any delegation under KRS Chapter 39A. If the Governor's emergency orders were not engaging in legislative power, that would certainly be true. Legislative power is defined in Black's Law Dictionary as, "[t]he power to make laws and to alter them at discretion . . . ."[92] Legislative function means "[t]he duty to determine legislative policy"; "the duty to form and determine future rights and duties."[93] And the definition of legislate includes, "[t]o bring something into or out of existence by making laws; to attempt to control (something) by legislation . . . ."[94]

Cleary, what has been ordered by the Governor's emergency decrees constitute legislation. Dr. Stack's testimony demonstrates that he and others engage in a process of collaboration and review of CDC guidelines and other documents, the purpose of which is to impose rules on persons and businesses in Kentucky, and that in formulating these rules they tailor them to apply uniformly across the Commonwealth.[95] This is formulating policy. He further testified that they have repeatedly amended and revised their orders, thus showing they deem to have the power to make laws and alter them at discretion. Indeed, he described the orders imposed as having a "breathtaking scope."[96]

It is obvious from even a cursory review that the orders issued over the past fifteen months "attempt to control" and seek "to form and determine future rights and duties" of Kentucky citizens. These included ordering the closure of all businesses, except those the Governor deemed essential. He ordered churches closed, prohibited social gatherings, including

[92] BLACK'S LAW DICTIONARY, 7th ed., West Group, p. 911 (St. Paul MN: 1999) (defining "legislative power").
[93] *Id*. (defining "legislative function").
[94] *Id*., at 910 (defining "legislate").
[95] V.R. 05/17/2021, *circa* 02:18:00.
[96] *Id*., at *circa* 03:02:00.

at weddings and funerals, prohibited travel, and through CHFS, even prohibited citizens from receiving scheduled surgeries and access to medical care. And then there is the order that everyone wear a mask. These are, undeniably, attempts to control, set policy, and determine rights and duties of the citizenry. Except in those instances where the federal courts have stepped in, Defendants assert authority to modify or re-impose these orders at their sole discretion. Consider, for example, the recent modification of the mask mandate. It orders persons who did not get vaccinated for Covid-19 to wear masks but lifts that requirement for others. That is setting policy and determining future rights and duties.

At the hearing, Defendants took exception to the Attorney General's characterization of the Governor's actions as a "lockdown," and argued that prohibiting persons from entering those restaurants is not the same as ordering that they be closed. But that doesn't minimize the impact on those who lost their businesses as a result, or those in nursing homes condemned to spend their final hours alone, deprived of the comfort from loved ones (or even any real contact with humanity), or those citizens who the Governor prohibited from celebrating their wedding day with more than ten persons, or those he forced to bury their dead alone, without the consoling presence of family and friends (and who likewise were deprived of paying their final respects), or those persons who were barred from entering church to worship Almighty God during Holy Week, and even Easter Sunday, or those persons who were denied access to health care, including cancer-screenings, or those denied entry into government buildings (which they pay for with their taxes) in order to obtain a necessary license, and who were forced to wait outside for hours in the sweltering heat, or rain, purportedly to keep them from getting sick.

What the people have endured over the past fifteen months—to borrow a phrase from United States District Judge Justin R. Walker—"is something this Court never expected to see

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outside the pages of a dystopian novel."[97] Yet, Defendants contend that the Governor's rule by mere emergency decree must continue indefinitely, and independent of legislative limits. In effect, Defendants seek declaratory judgment that the Constitution provides this broad power so long as he utters the word, "emergency." It does not. For this Court to accept Defendant's position would not be honoring its oath to support the Constitution; it would be tantamount to a *coup d'état* against it.

To succeed on their claims that the New Legislation is unconstitutional, Defendants bear a heavy burden. Statutes enacted by the General Assembly enjoy a "strong presumption of constitutionality."[98] This is especially true here, since Defendants contend that the Acts are unconstitutional on their face. "A facial challenge to a legislative Act is, of course, the most difficult challenge to mount successfully."[99] In order to find legislation unconstitutional, "the violation of the Constitution must be clear, complete and unmistakable."[100] Further, the party "must establish that no set of circumstances exists under which the Act would be valid."[101] For all of the foregoing reasons, this Court finds that Defendants have failed to meet their burden. And for the same reasons, Plaintiff's Motion, and the arguments of the Attorney General, are well taken.

THEREFORE, JUDGMENT IS HEREBY ENTERED in favor of Plaintiff and **DECLARATORY RELIEF** is **GRANTED** in that the Court finds and declares that all actions taken by Defendants, Hon. Andrew Beshear, as Governor, Mr. Eric Friedlander, as acting Secretary of the Cabinet for Health and Family Services, and Dr. Steven Stack, M.D., as

[97] *On Fire Christian Center, Inc., v. Greg Fischer, et al*. 3:20-CV-264-JRW, p. 3 (U.S. Dist. Ct., W. Dist. Ky., Apr. 11, 2020).
[98] *Wynn v. Ibold, Inc*., 969 S.W.2d 695, 696 (Ky. 1998).
[99] *Williams v. Commonwealth*, 213 S.W.3d 671, 681 (Ky. 2006), quoting, *Rust v. Sullivan*, 500 U.S. 173, 183 (1991).
[100] *Williams*, 213 S.W.3d, at 681, quoting *Kentucky Industrial Utility Customers, Inc. v. Kentucky Utilities Company*, 983 S.W.2d 493, 499 (Ky.1998).
[101] *Williams*, 213 S.W.3d, at 681, quoting *Rust*, 500 U.S., at 183.

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Commissioner for the Kentucky Department of Public Health, and all emergency orders imposed by said Defendants, or that are being continued by said Defendants, are unconstitutional, void and without any legal effect, to the extent that the same are in conflict with, or are otherwise contrary to, House Bill 1, Senate Bill 1, Senate Bill 2, and House Joint Resolution 77, as passed in the 2021 session of the General Assembly.

IT IS FURTHER HEREBY ORDERED that Plaintiff's Motion for Permanent Injunction is **GRANTED** and that, effective June 10, 2021, at 5:00 p.m., Defendants, Hon. Andrew Beshear, as Governor, Mr. Eric Friedlander, as acting Secretary of the Cabinet for Health and Family Services, and Dr. Steven Stack, M.D., as commissioner for the Kentucky Department of Public Health, are enjoined from enforcing Plaintiff to comply with any emergency orders imposed by said Defendants, or that are being continued by said Defendants, that are in conflict with, or are otherwise contrary to, House Bill 1, Senate Bill 1, Senate Bill 2, and House Joint Resolution 77, as passed in the 2021 session of the General Assembly.

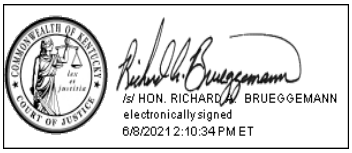
IT IS FURTHER HEREBY ORDERED that Plaintiff's Motion for Class Certification is **DENIED**, in that the result of the Declaratory Judgment has the same effect.

IT IS FURTHER HEREBY ORDERED that Defendants' Cross-Motion for Declaratory Judgment that the General Assembly violated the Constitution in passing House Bill 1, Senate Bill 1, Senate Bill 2, and House Joint Resolution 77, is **DENIED**.

There being no just cause for delay in the entry of this Judgement, this Judgment is final and appealable.

The Clerk shall serve notice of entry hereof in accordance with CR 77.

IT IS SO ORDERED.



JUDGE RICHARD A. BRUEGGEMANN
BOONE CIRCUIT COURT

CC: ALL COUNSEL AND PARTIES OF RECORD.

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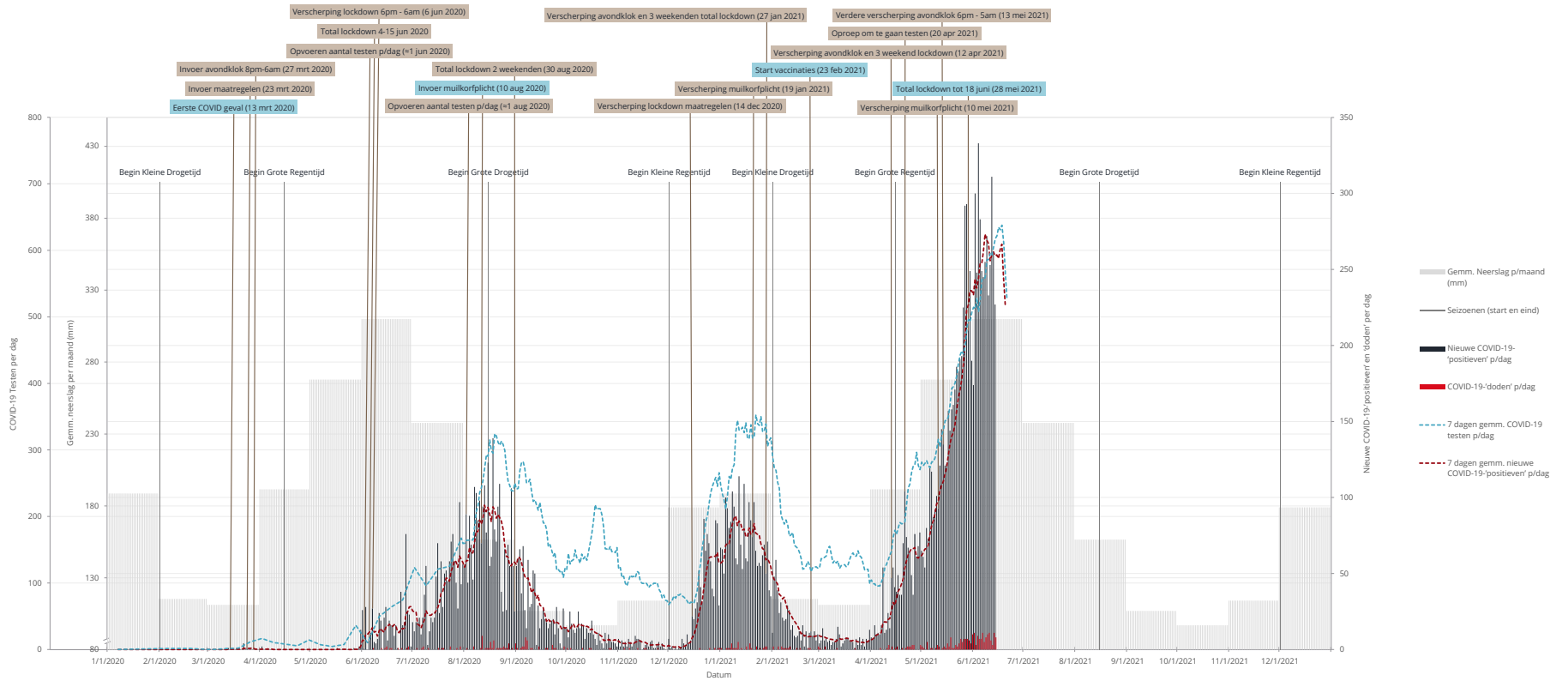
PRODUKTIE 21



Verloop COVID-19-'positieven' en 'doden' in Suriname vergeleken met de seizoenen en maatregelen (per 14 juni 2021)

De aantallen COVID-19-'positieven' en 'doden' zijn afkomstig van de WHO/PAHO en COVID-19.sr. De hoeveelheid neerslag is afkomstig van de Meteorologische Dienst, station Zorg en Hoop 1961-2005.

PRODUKTIE 22

External peer review of the RTPCR test to detect SARS-CoV-2 reveals 10 major scientific flaws at the molecular and methodological level: consequences for false positive results

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* Corresponding author

ABSTRACT

In the publication entitled “Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR” (Eurosurveillance 25(8) 2020) the authors present a diagnostic workflow and RT-qPCR protocol for detection and diagnostics of 2019-nCoV (now known as SARS-CoV-2), which they claim to be validated, as well as being a *robust diagnostic methodology for use in public-health laboratory settings*.

In light of all the consequences resulting from this very publication for societies worldwide, a group of independent researchers performed a point-by-point review of the aforesaid publication in which 1) all components of the presented test design were cross checked, 2) the RT-qPCR protocol-recommendations were assesses w.r.t. good laboratory practice, and 3) parameters examined against relevant scientific literature covering the field.

The published RT-qPCR protocol for detection and diagnostics of 2019-nCoV and the manuscript suffer from numerous technical and scientific errors, including insufficient primer design, a problematic and insufficient RT-qPCR protocol, and the absence of an accurate test validation. Neither the presented test nor the manuscript itself fulfils the requirements for an acceptable scientific publication. Further, serious conflicts of interest of the authors are not mentioned. Finally, the very short timescale between submission and acceptance of the publication (24 hours) signifies that a systematic peer review process was either not performed here, or of problematic poor quality.

We provide compelling evidence of several scientific inadequacies, errors and flaws. Considering the scientific and methodological blemishes presented here, we are confident that the editorial board of Eurosurveillance has no other choice but to retract the publication.

CONCISE REVIEW REPORT

This paper will show numerous serious flaws in the Corman-Drosten paper, the significance of which has led to worldwide misdiagnosis of infections attributed to SARS-CoV-2 and associated with the disease COVID-19. We are confronted with stringent lockdowns which have destroyed many people's lives and livelihoods, limited access to education and these imposed restrictions by governments around the world are a direct attack on people's basic rights and their personal freedoms, resulting in collateral damage for entire economies on a global scale.

There are ten fatal problems with the Corman-Drosten paper which we will outline and explain in greater detail in the following sections.

The first and major issue is that the *novel* Coronavirus SARS-CoV-2 (in the publication named 2019-nCoV and in February 2020 named SARS-CoV-2 by an international consortium of virus experts) is based on *in silico* (theoretical) sequences, supplied by a laboratory in China [1], because at the time neither control material of infectious ("live") or inactivated SARS-CoV-2 nor isolated genomic RNA of the virus was available to the authors. To date no validation has been performed by the authorship based on isolated SARS-CoV-2 viruses or full length RNA thereof.

According to Corman et al.: *"We aimed to develop and deploy robust diagnostic methodology for use in public health laboratory settings without having virus material available."* [1]

The focus here should be placed upon the two stated aims: a) *development* and b) *deployment* of a *diagnostic test for use in public health laboratory settings*. These aims are not achievable without having any actual virus material available (e.g. for determining the infectious viral load). In any case, only a protocol with maximal accuracy can be the mandatory and primary goal in any scenario-outcome of this magnitude. Critical viral load determination is mandatory information, and it is in Christian Drosten's group responsibility to perform these experiments and provide the crucial data.

Nevertheless these *in silico* sequences were used to develop a RT-PCR test methodology to identify the aforesaid virus. This model was based on the assumption that the *novel* virus is very similar to SARS-CoV from 2003 (Hereafter named SARS-CoV-1) as both are beta-coronaviruses.

The PCR test was therefore designed using the genomic sequence of SARS-CoV-1 as a control material for the Sarbeco component; we know this from our personal email-communication with [2] one of the co-authors of the Corman-Drosten paper. This method to model SARS-CoV-2 was described in the Corman-Drosten paper as follows:
"the establishment and validation of a diagnostic workflow for 2019-nCoV screening and specific confirmation, designed in absence of available virus isolates or original patient specimens. Design and validation were enabled by the close genetic relatedness to the 2003 SARS-CoV, and aided by the use of synthetic nucleic acid technology."

In short, a design relying merely on close genetic relatives does not fulfill the aim for a "robust diagnostic test" as cross reactivity and therefore false-positive results will inevitably occur.
Validation was only done in regards to *in silico* (theoretical) sequences and within the laboratory-setting, and not as required for in-vitro diagnostics with isolated genomic viral RNA. This very fact hasn't changed even after 10 months of introduction of the test into routine diagnostics.
There are numerous other severe scientific errors regarding the biomolecular design of the primers, the PCR method, as well as the molecular validation of the PCR products and methods described in the Corman-Drosten paper which are examined in detail in the following chapters. The paper itself already signifies that a large number of false positive results are generated by this test, even under controlled laboratory conditions, making it completely unsuitable as a reliable virus screening method for entire populations in an ongoing pandemic. Given the far-reaching implications, including quarantine measures, lockdowns, curfews and impacts on education etc., this paper must be immediately retracted.

DESIGN AND ERRORS in RT-PCR

The Reverse Transcription-Polymerase Chain Reaction (RT-PCR) is an important biomolecular technology to rapidly detect rare RNA fragments, which are known in advance. In the first step, RNA molecules present in the sample are reverse transcribed to yield cDNA. The cDNA is then amplified in the polymerase chain reaction using a specific primer pair and a thermostable DNA polymerase enzyme. The technology is highly sensitive and its detection limit is theoretically 1 molecule of cDNA. The specificity of the PCR is highly influenced by biomolecular design errors.

What is important when designing an RT-PCR Test and the quantitative RT-qPCR test described in the Corman-Drosten publication?

1. The primers and probes:

   a) the concentration of primers and probes must be of optimal range (100-200 nM)
   b) must be specific to the target-gene you want to amplify
   c) must have an optimal percentage of GC content relative to the total nitrogenous bases (minimum 40%, maximum 60%)
   d) for virus diagnostics at least 3 primer pairs must detect 3 viral genes (preferably as far apart as possible in the viral genome)

2. The temperature at which all reactions take place:

   a) DNA melting temperature (>92°)
   b) DNA amplification temperature (TaqPol specific)
   c) Tm; the annealing temperature (the temperature at which the primers and probes reach the target binding/detachment, not to exceed 2˚C per primer pair).
   Tm heavily depends on GC content of the primers

3. The number of amplification cycles (less than 35; preferably 25-30 cycles); In case of virus detection, >35 cycles only detects signals which do not correlate with infectious virus as determined by isolation in cell culture [reviewed in 2]; if someone is tested by PCR as positive when a threshold of 35 cycles or higher is used (as is the case in most laboratories in Europe & the US), the probability that said person is actually infected is less than 3%, the probability that said result is a false positive is 97%

[reviewed in 3]

4. Molecular biological validations; amplified PCR products must be validated either by running the products in a gel with a DNA ruler, or by direct DNA sequencing

5. Positive and negative controls should be specified to confirm/refute specific virus detection

6. There should be a Standard Operational Procedure (SOP) available, which unequivocally specifies the above parameters, so that all laboratories are able to set up the exact same test conditions. To have a validated universal SOP is essential, because it enables the comparison of data within and between countries.

MINOR CONCERNS WITH THE CORMAN-DROSTEN PAPER

1. In Table 1 of the Corman-Drosten paper, different abbreviations are stated - “nM” is specified, “nm” isn’t. Further in regards to correct nomenclature, nm means “nanometer” therefore nm should read nM here.

2. It is the general consensus to write genetic sequences always in the 5’-3’ direction, including the reverse primers. It is highly unusual to do alignment with reverse complementary writing of the primer sequence as the authors did in figure 2 of the Corman-Drosten paper. Here, in addition, a wobble base is marked as “y” without description of the bases the Y stands for.

3. Two misleading pitfalls in the Corman-Drosten paper are that their Table 1 does not include Tm-values (annealing-temperature values), neither does it show GC-values (number of G and C in the sequences as %-value of total bases).

MAJOR CONCERNS WITH THE CORMAN-DROSTEN PAPER

A) BACKGROUND

The authors introduce the background for their scientific work as: "*The ongoing outbreak of the recently emerged novel coronavirus (2019-nCoV) poses a challenge for public health laboratories as virus isolates are unavailable while there is growing evidence that the outbreak is more widespread than initially thought, and international spread through travelers does already occur".*

According to BBC News [4] and Google Statistics [5] there were 6 deaths world-wide on January 21st 2020 - the day when the manuscript was submitted. Why did the authors assume a challenge for public health laboratories while there was no substantial evidence at that time to indicate that the outbreak was more widespread than initially thought?

As an aim the authors declared to develop and deploy robust diagnostic methodology for use in public health laboratory settings without having virus material available. Further, they acknowledge that "The present study demonstrates the enormous response capacity achieved through coordination of academic and public laboratories in national and European research networks."

B) Methods and Results

1. Primer & Probe Design

1a) Erroneous primer concentrations

Reliable and accurate PCR-test protocols are normally designed using between 100 nM and 200 nM per primer [7]. In the Corman-Drosten paper, we observe unusually high and varying primer concentrations for several primers (table 1). For the RdRp_SARSr-F and RdRp_SARSr-R primer pairs, 600 nM and 800 nM are described, respectively. Similarly, for the N_Sarbeco_F and N_Sarbeco_R primer set, they advise 600 nM and 800 nM, respectively [1]. It should be clear that these concentrations are far too high to be optimal for specific amplifications of target genes. *There exists no specified reason to use these extremely high*

concentrations of primers in this protocol. Rather, these concentrations lead to increased unspecific binding and PCR product amplification.

Table1: Primers and probes (adapted from Corman-Drosten paper; erroneous primer concentrations are highlighted)

Assay/use	Oligonucleotide	Sequence[a]	Concentration[b]
RdRP gene	RdRp_SARSr-F	GTGARATGGTCATGTGTGGCGG	Use 600 nM per reaction
	RdRp_SARSr-P2	FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ	Specific for 2019-nCoV, will not detect SARS-CoV. Use 100 nM per reaction and mix with P1
	RdRP_SARSr-P1	FAM-CCAGGTGGWACRTCATCMGGTGATGC-BBQ	Pan Sarbeco-Probe will detect 2019-nCoV, SARS-CoV and bat-SARS-related CoVs. Use 100 nM per reaction and mix with P2
	RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA	Use 800 nM per reaction
E gene	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Use 400 nm per reaction
	E_Sarbeco_P1	FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ	Use 200 nm per reaction
	E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Use 400 nm per reaction
N gene	N_Sarbeco_F	CACATTGGCACCCGCAATC	Use 600 nm per reaction
	N_Sarbeco_P	FAM-ACTTCCTCAAGGAACAACATTGCCA-BBQ	Use 200 nm per reaction
	N_Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Use 800 nm per reaction

[a] W is A/T; R is G/A; M is A/C; S is G/C. FAM: 6-carboxyfluorescein; BBQ: blackberry quencher.

[b] Optimised concentrations are given in nanomol per litre (nM) based on the final reaction mix, e.g. 1.5 µL of a 10 µM primer stock solution per 25 µL total reaction volume yields a final concentration of 600 nM as indicated in the table.

1b) Unspecified ("Wobbly") primer and probe sequences

To obtain reproducible and comparable results, it is essential to distinctively define the primer pairs. In the Corman-Drosten paper we observed six unspecified positions, indicated by the letters R, W, M and S (Table 2). The letter W means that at this position there can be either an A or a T; R signifies there can be either a G or an A; M indicates that the position may either be an A or a C; the letter S indicates there can be either a G or a C on this position.

This high number of variants not only is unusual, but it also is highly confusing for laboratories. These six unspecified positions could easily result in the design of several different alternative primer sequences which do not relate to SARS-CoV-2 (2 distinct RdRp_SARSr_F primers + 8 distinct RdRp_SARS_P1 probes + 4 distinct RdRp_SARSr_R). *The design variations will inevitably lead to results that are not even SARS-CoV-2 related. Therefore, the confusing unspecific description in the Corman-Drosten paper is not suitable as a Standard Operational Protocol. These unspecified positions should have been designed unequivocally.*

These wobbly sequences have already created a source of concern in the field and resulted in a Letter to the Editor authored by Pillonel *et al.* [8] regarding blatant errors in the described sequences. These errors are self-evident in the Corman *et al.* supplement as well.

Table 2: Primers and probes (adapted from Corman-Drosten paper; unspecified ("Wobbly") nucleotides in the primers are highlighted)

Assay/use	Oligonucleotide	Sequence[a]	Concentration[b]
RdRP gene	RdRp_SARSr-F	GTGARATGGTCATGTGTGGCGG	Use 600 nM per reaction
	RdRp_SARSr-P2	FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ	Specific for 2019-nCoV, will not detect SARS-CoV. Use 100 nM per reaction and mix with P1
	RdRP_SARSr-P1	FAM-CCAGGTGGWACRTCATCMGGTGATGC-BBQ	Pan Sarbeco-Probe will detect 2019-nCoV, SARS-CoV and bat-SARS-related CoVs. Use 100 nM per reaction and mix with P2
	RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA	Use 800 nM per reaction
E gene	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Use 400 nm per reaction
	E_Sarbeco_P1	FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ	Use 200 nm per reaction
	E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Use 400 nm per reaction
N gene	N_Sarbeco_F	CACATTGGCACCCGCAATC	Use 600 nm per reaction
	N_Sarbeco_P	FAM-ACTTCCTCAAGGAACAACATTGCCA-BBQ	Use 200 nm per reaction
	N_Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Use 800 nm per reaction

W is A/T; R is G/A; M is A/C; S is G/C; FAM: 6-carboxyfluorescein; BBQ: blackberry quencher.

[b] Optimised concentrations are given in nanomol per litre (nM) based on the final reaction mix, e.g. 1.5 µL of a 10 µM primer stock solution per 25 µL total reaction volume yields a final concentration of 600 nM as indicated in the table.

The WHO-protocol (Figure 1), which directly derives from the Corman-Drosten paper, concludes that in order to confirm the presence of SARS-CoV-2, two control genes (the E- and the RdRp-genes) must be identified in the assay. It should be noted, that the RdPd-gene has one uncertain position ("wobbly") in the forward-primer (R=G/A), two uncertain positions in the reverse-primer (R=G/A; S=G/C) and it has three uncertain positions in the RdRp-probe (W=A/T; R=G/A; M=A/C). So, two different forward primers, four different reverse primers, and eight distinct probes can be synthesized for the RdPd-gene. Together, there are 64 possible combinations of primers and probes!

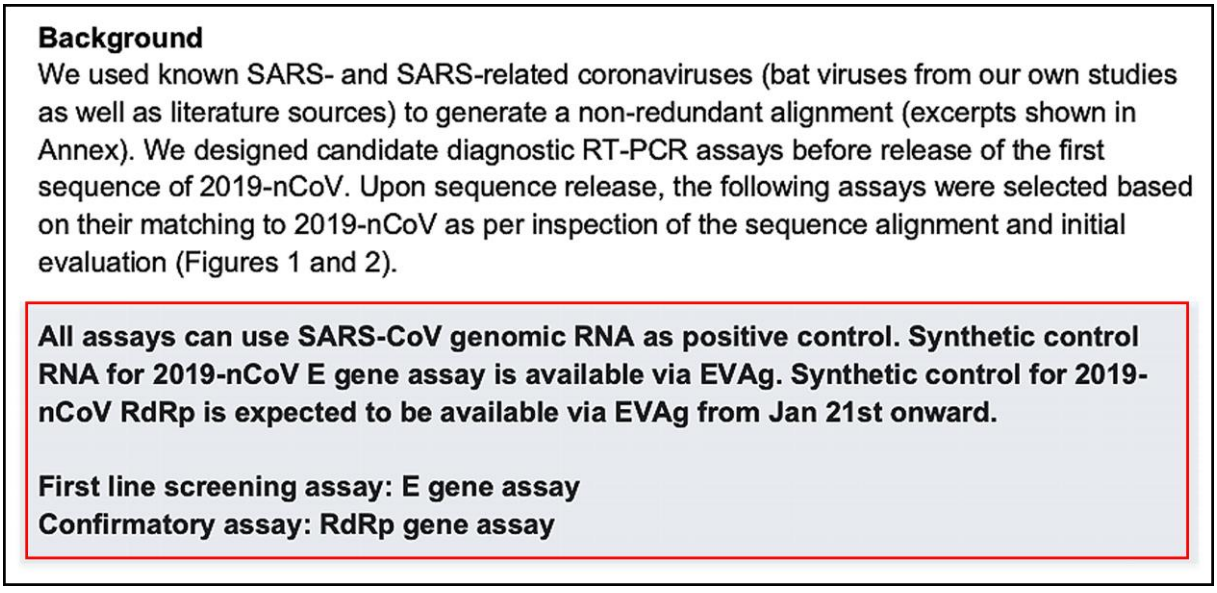
The Corman-Drosten paper further identifies a third gene which, according to the WHO protocol, was not further validated and deemed unnecessary: *"Of note, the N gene assay also performed well but was not subjected to intensive further validation because it was slightly less sensitive."*

This was an unfortunate omission as it would be best to use all three gene PCRs as

confirmatory assays, and this would have resulted in an almost sufficient virus RNA detection diagnostic tool protocol. Three confirmatory assay-steps would at least minimize-out errors & uncertainties at every fold-step in regards to "Wobbly"-spots. (Nonetheless, the protocol would still fall short of any "good laboratory practice", when factoring in all the other design-errors).

As it stands, the N gene assay is regrettably neither proposed in the WHO-recommendation (Figure 1) as a mandatory and crucial third confirmatory step, nor is it emphasized in the Corman-Drosten paper as important optional reassurance "for a routine workflow" (Table 2).

Consequently, in nearly all test procedures worldwide, merely 2 primer-matches were used instead of all three. This oversight renders the entire test-protocol useless with regards to delivering accurate test-results of real significance in an ongoing pandemic.



Background

We used known SARS- and SARS-related coronaviruses (bat viruses from our own studies as well as literature sources) to generate a non-redundant alignment (excerpts shown in Annex). We designed candidate diagnostic RT-PCR assays before release of the first sequence of 2019-nCoV. Upon sequence release, the following assays were selected based on their matching to 2019-nCoV as per inspection of the sequence alignment and initial evaluation (Figures 1 and 2).

All assays can use SARS-CoV genomic RNA as positive control. Synthetic control RNA for 2019-nCoV E gene assay is available via EVAg. Synthetic control for 2019-nCoV RdRp is expected to be available via EVAg from Jan 21st onward.

First line screening assay: E gene assay
Confirmatory assay: RdRp gene assay

Figure 1: The N-Gene confirmatory-assay is neither emphasized as necessary third step in the official WHO Drosten-Corman protocol-recommendation [8] nor is it required as a crucial step for higher test-accuracy in the Eurosurveillance publication.

1c) Erroneous GC-content (discussed in 2c, together with annealing temperature (Tm))

1d) Detection of viral genes

RT-PCR is not recommended for primary diagnostics of infection. This is why the RT-PCR Test

used in clinical routine for detection of COVID-19 is not indicated for COVID-19 diagnosis on a regulatory basis.

"Clinicians need to recognize the enhanced accuracy and speed of the molecular diagnostic techniques for the diagnosis of infections, but also to understand their limitations. Laboratory results should always be interpreted in the context of the clinical presentation of the patient, and appropriate site, quality, and timing of specimen collection are required for reliable test results". [9]

However, it may be used to help the physician's differential diagnosis when he or she has to discriminate between different infections of the lung (Flu, Covid-19 and SARS have very similar symptoms). For a confirmative diagnosis of a specific virus, at least 3 specific primer pairs must be applied to detect 3 virus-specific genes. Preferably, these target genes should be located with the greatest distance possible in the viral genome (opposite ends included). Although the Corman-Drosten paper describes 3 primers, these primers only cover roughly half of the virus' genome. This is another factor that decreases specificity for detection of intact COVID-19 virus RNA and increases the quote of false positive test results.

Therefore, even if we obtain three positive signals (i.e. the three primer pairs give 3 different amplification products) in a sample, this does not prove the presence of a virus. A better primer design would have terminal primers on both ends of the viral genome. This is because the whole viral genome would be covered and three positive signals can better discriminate between a complete (and thus potentially infectious) virus and fragmented viral genomes (without infectious potency). In order to infer anything of significance about the infectivity of the virus, the Orf1 gene, which encodes the essential replicase enzyme of SARS-CoV-1 and SARS-CoV-2 viruses, should have been included as a target (Figure 2). The positioning of the targets in the region of the viral genome that is most heavily and variably transcribed is another weakness of the protocol.

Kim *et al.* demonstrate a highly variable 3' expression of subgenomic RNA in Sars-CoV-2 [23]. These RNAs are actively monitored as signatures for asymptomatic and non-infectious patients [10]. It is highly questionable to screen a population of asymptomatic people with qPCR primers that have 6 base pairs primer-dimer on the 3 prime end of a primer (Figure 3). Apparently the WHO recommends these primers. We tested all the wobble derivatives from

the Corman-Drosten paper with Thermofisher's primer dimer web tool [11]. The RdRp forward primer has 6bp 3prime homology with Sarbeco E Reverse. At high primer concentrations this is enough to create inaccuracies.

Of note: There is a perfect match of one of the N primers to a clinical pathogen (*Pantoea*), found in immuno-compromised patients. The reverse primer hits *Pantoea* as well but not in the same region (Figure 3).

<u>These are severe design errors, since the test cannot discriminate between the whole virus and viral fragments. The test cannot be used as a diagnostic for SARS-CoV-2 viruses.</u>

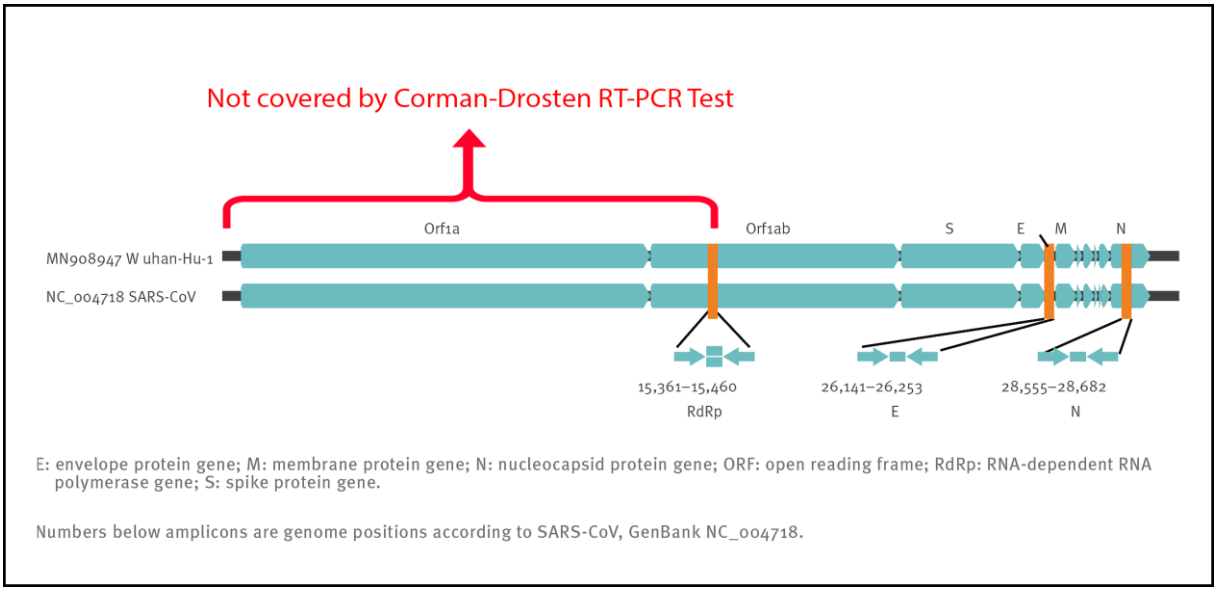


Figure 2: Relative positions of amplicon targets on the SARS-CoV-1 coronavirus and the 2019 novel coronavirus genome. ORF: open reading frame; RdRp: RNA-dependent RNA polymerase. Numbers below amplicon are genome positions according to SARS-CoV-1, NC_004718 [1];

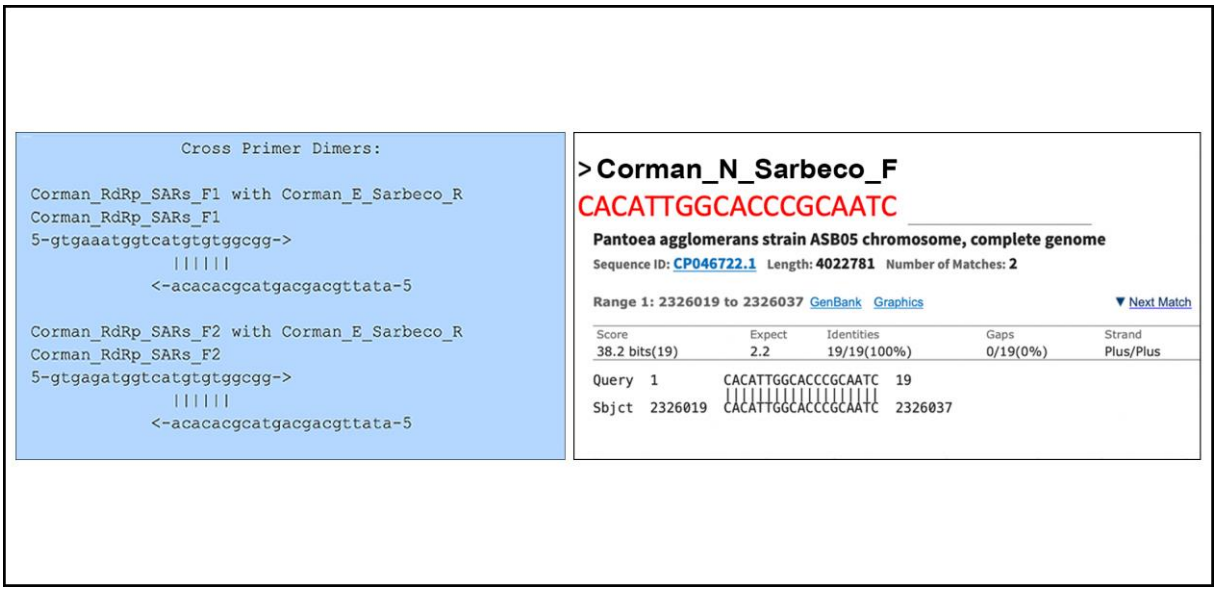


Figure 3: A test with Thermofischer's primer dimer web tool reveals that the RdRp forward primer has a 6bp 3`prime homology with Sarbeco E Reverse (left box). Another test reveals that there is a perfect match for one of the N-primers to a clinical pathogen (*Pantoea*) found in immuno-compromised patients (right box).

2. Reaction temperatures

2a) DNA melting temperature (>92°).

Adequately addressed in the Corman-Drosten paper.

2b) DNA amplification temperature.

Adequately addressed in the Corman-Drosten paper.

2c) Erroneous GC-contents and Tm

The annealing-temperature determines at which temperature the primer attaches/detaches from the target sequence. For an efficient and specific amplification, GC content of primers should meet a minimum of 40% and a maximum of 60% amplification. As indicated in table 3, three of the primers described in the Corman-Drosten paper are not within the normal range for GC-content. Two primers (RdRp_SARSr_F and RdRp_SARSr_R) have unusual and very low GC-values of 28%-31% for all possible variants of wobble bases, whereas primer E_Sarbeco_F has a GC-value of 34.6% (Table 3 and second panel of Table 3).

It should be noted that the GC-content largely determines the binding to its specific target due to its three hydrogen bonds in base pairing. Thus, the lower the GC-content of the primer, the lower its binding-capability to its specific target gene sequence (i.e. the gene to

be detected). This means for a target-sequence to be recognized we have to choose a temperature which is as close as possible to the actual annealing-temperature (best practise-value) for the primer not to detach again, while at the same time specifically selecting the target sequence.

If the Tm-value is very low, as observed for all wobbly-variants of the RdRp reverse primers, the primers can bind non-specifically to several targets, decreasing specificity and increasing potential false positive results.

The annealing temperature (Tm) is a crucial factor for the determination of the specificity /accuracy of the qPCR procedure and essential for evaluating the accuracy of qPCR-protocols. Best-practice recommendation: Both primers (forward and reverse) should have an almost similar value, preferably the identical value.

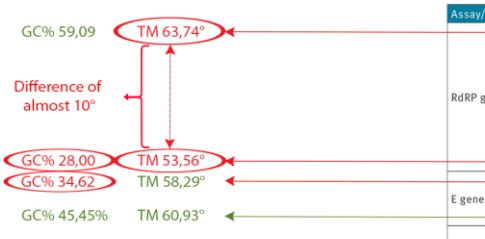
We used the freely available primer design software Primer-BLAST [12, 25] to evaluable the best-practise values for all primers used in the Corman-Drosten paper (Table 3). We attempted to find a Tm-value of 60° C, while similarly seeking the highest possible GC%-value for all primers. A maximal Tm difference of 2° C within primer pairs was considered acceptable. Testing the primer pairs specified in the Corman-Drosten paper, we observed a difference of 10° C with respect to the annealing temperature Tm for primer pair1 (RdRp_SARSr_F and RdRp_SARSr_R). *This is a very serious error and makes the protocol useless as a specific diagnostic tool.*

Additional testing demonstrated that only the primer pair designed to amplify the N-gene (N_Sarbeco_F and N_Sarbeco_R) reached the adequate standard to operate in a diagnostic test, since it has a sufficient GC-content and the Tm difference between the primers (N_Sarbeco_F and N_Sarbeco_R) is 1.85° C (below the crucial maximum of 2° C difference). Importantly, this is the gene which was neither tested in the virus samples (Table 2) nor emphasized as a confirmatory test. In addition to highly variable melting temperatures and degenerate sequences in these primers, there is another factor impacting specificity of the procedure: the dNTPs (0.4uM) are 2x higher than recommended for a highly specific amplification. There is additional magnesium sulphate added to the reaction as well. This procedure combined with a low annealing temperature can create non-specific amplifications. When additional magnesium is required for qPCR, specificity of the assay should be further scrutinized.

The design errors described here are so severe that it is highly unlikely that specific amplification of SARS-CoV-2 genetic material will occur using the protocol of the Corman-Drosten paper.

Table 3: GC-content of the primers and probes (adapted from Corman-Drosten paper; aberrations from optimized GC-contents are highlighted. Second Panel shows a table-listing of all Primer-BLAST best practices values for all primers and probes used in the Corman-Drosten paper by Prof. Dr. Ulrike Kämmerer & her team

Normal ranges for GC%: 40 - 60%; normal ranges for TM: 55-65°; Best-practise for qPCR in our case: 60° for both primers (reverse & forward)



Assay/use	Oligonucleotide	Sequence[a]	Concentration[b]
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	RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA	Use 800 nM per reaction
E gene	E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Use 400 nm per reaction
	E_Sarbeco_P1	FAM-ACACTAGCCATCCTTACTGCGCTTCG-BBQ	Use 200 nm per reaction
	E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Use 400 nm per reaction
N gene	N_Sarbeco_F	CACATTGGCACCCGCAATC	Use 600 nm per reaction
	N_Sarbeco_P	FAM-ACTTCCTCAAGGAACAACATTGCCA-BBQ	Use 200 nm per reaction
	N_Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Use 800 nm per reaction

[a] W is A/T; R is G/A; M is A/C; S is G/C. FAM: 6-carboxyfluorescein; BBQ: blackberry quencher.
[b] Optimised concentrations are given in nanomol per litre (nM) based on the final reaction mix, e.g. 1.5 µL of a 10 µM primer stock solution per 25 µL total reaction volume yields a final concentration of 600 nM as indicated in the table.

		GC	TM	Search in **MN908947** (first full genome from Wuihan, 12.01.2020)						
Primer pairs	**Sequence (5´-3´)**	**Template strand**	**Length**	**Start**	**Stop**	**Tm**	**GC%**	**Self 5' complementarity**	**Self 3' complementarity**	**Product length (bp)**
E_Sarbeco_F	ACAGGTACGTTAATAGTTAATAGCGT	Plus	26	26269	26294	58.29	34.62	8.00	8.00	**113**
E_Sarbeco_R	ATATTGCAGCAGTACGCACACA	Minus	22	26381	26360	60.93	45.45	7.00	1.00	
N-Sarbeco_F	CACATTGGCACCCGCAATC	Plus	19	28706	28724	60.15	57.89	4.00	0.00	**128**
N-Sarbeco_R	GAGGAACGAGAAGAGGCTTG	Minus	20	28833	28814	58.00	55.00	3.00	1.00	
RdRp_SARSr-F	GTGARATGGTCATGTGTGGCGG		22			63.74	59.09	4.00	to be added in next version	
RdRp_SARSr-R	CARATGTTAAASACACTATTAGCATA		25			53.56	28.00	7.00		
If R= G and S= G	GTGAGATGGTCATGTGTGGCGG		22			63.74	59.09	4.00	1.00	
	CAGATGTTAAAGACACTATTAGCATA		26			55.22	30.77	7.00	5.00	not found in the Sequence
If R= G and S= C	GTGAGATGGTCATGTGTGGCGG		22			63.74	59.09	4.00	1.00	
	CAGATGTTAAACACACTATTAGCATA		26			55.68	30.77	7.00	2.00	
If R= A and S= G	GTGAAATGGTCATGTGTGGCGG		22			62.58	54.55	4.00	1.00	
	CAAATGTTAAAGACACTATTAGCATA		26			54.23	26.92	7.00	5.00	
If R= A and S= C	GTGAAATGGTCATGTGTGGCGG		22			62.58	54.55	4.00	1.00	
	CAAATGTTAAACACACTATTAGCATA		26			54.69	26.92	7.00	2.00	
Probes:										
RdRp-SARSr-P2	CAGGTGGAACCTCATCAGGAGATGC		25			64.89	56.00	6.00	5.00	
RdRp-SARSr-P1	CCAGGTGGWACRTCATCMGGTGATGC									
E-Sarbeco-P1	ACACTAGCCATCCTTACTGCGCTTCG		26			66.78	53.85	4.00	2.00	
N-Sarbeco-P	ACTTCCTCAAGGAACAACATTGCCA		25			63.15	44.00	8.00	3.00	

3. The number of amplification cycles

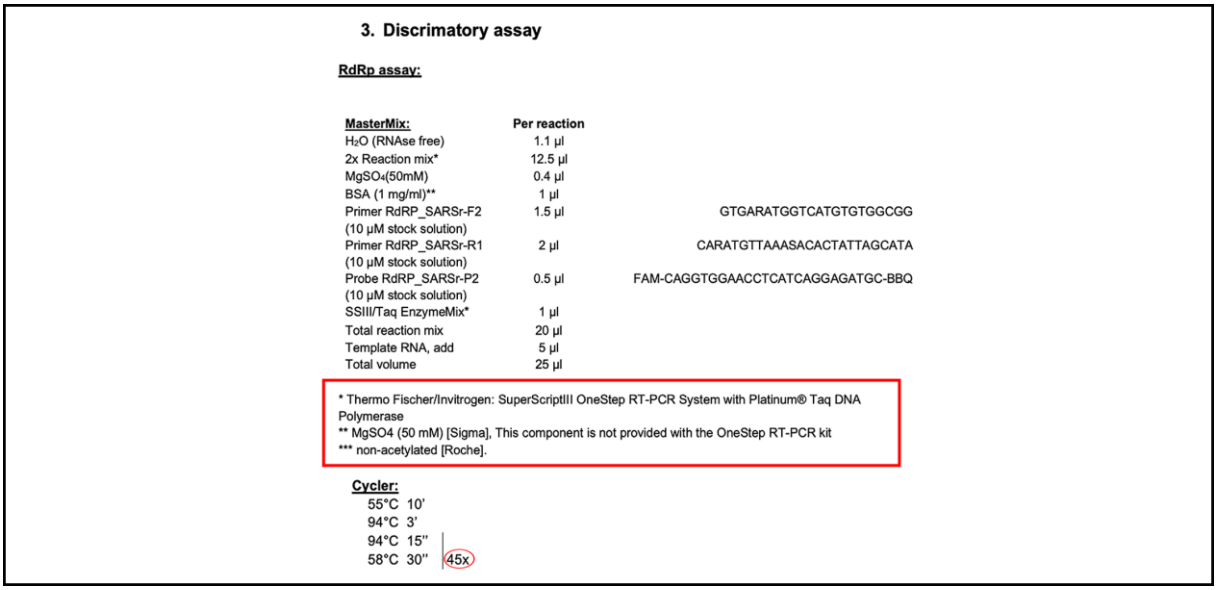
It should be noted that there is no mention anywhere in the Corman-Drosten paper of a test being positive or negative, or indeed what defines a positive or negative result. These types of virological diagnostic tests must be based on a SOP, including a validated and fixed number of PCR cycles (Ct value) after which a sample is deemed positive or negative. The maximum reasonably reliable Ct value is 30 cycles. Above a Ct of 35 cycles, rapidly increasing numbers of false positives must be expected .

PCR data evaluated as positive after a Ct value of 35 cycles are completely unreliable.

Citing Jaafar *et al.* 2020 [3]: *"At Ct = 35, the value we used to report a positive result for PCR, <3% of cultures are positive."* In other words, there was no successful virus isolation of SARS-CoV-2 at those high Ct values.

Further, scientific studies show that only non-infectious (dead) viruses are detected with Ct values of 35 [22].

Between 30 and 35 there is a grey area, where a positive test cannot be established with certainty. This area should be excluded. Of course, one could perform 45 PCR cycles, as recommended in the Corman-Drosten WHO-protocol (Figure 4), but then you also have to define a reasonable Ct-value (which should not exceed 30). But an analytical result with a Ct value of 45 is scientifically and diagnostically absolutely meaningless (a reasonable Ct-value should not exceed 30). All this should be communicated very clearly. *It is a significant mistake that the Corman-Drosten paper does not mention the maximum Ct value at which a sample can be unambiguously considered as a positive or a negative test-result. This important cycle threshold limit is also not specified in any follow-up submissions to date.*



3. Discrimatory assay

RdRp assay:

MasterMix:	Per reaction	
H_2O (RNAse free)	1.1 µl	
2x Reaction mix*	12.5 µl	
$MgSO_4$(50mM)	0.4 µl	
BSA (1 mg/ml)**	1 µl	
Primer RdRP_SARSr-F2 (10 µM stock solution)	1.5 µl	GTGARATGGTCATGTGTGGCGG
Primer RdRP_SARSr-R1 (10 µM stock solution)	2 µl	CARATGTTAAASACACTATTAGCATA
Probe RdRP_SARSr-P2 (10 µM stock solution)	0.5 µl	FAM-CAGGTGGAACCTCATCAGGAGATGC-BBQ
SSIII/Taq EnzymeMix*	1 µl	
Total reaction mix	20 µl	
Template RNA, add	5 µl	
Total volume	25 µl	

* Thermo Fischer/Invitrogen: SuperScriptIII OneStep RT-PCR System with Platinum® Taq DNA Polymerase
** MgSO4 (50 mM) [Sigma], This component is not provided with the OneStep RT-PCR kit
*** non-acetylated [Roche].

Cycler:
55°C 10'
94°C 3'
94°C 15"
58°C 30" 45x

Figure 4: RT-PCR Kit recommendation in the official Corman-Drosten WHO-protocol [8]. Only a "Cycler"-value (cycles) is to be found without corresponding and scientifically reasonable Ct (Cutoff-value). This or any other cycles-value is nowhere to be found in the actual Corman-Drosten paper.

4. Biomolecular validations

To determine whether the amplified products are indeed SARS-CoV-2 genes, biomolecular validation of amplified PCR products is essential. For a diagnostic test, this validation is an absolute must.

Validation of PCR products should be performed by either running the PCR product in a 1% agarose-EtBr gel together with a size indicator (DNA ruler or DNA ladder) so that the size of the product can be estimated. The size must correspond to the calculated size of the amplification product. But it is even better to sequence the amplification product. The latter will give 100% certainty about the identity of the amplification product. Without molecular validation one can not be sure about the identity of the amplified PCR products. Considering the severe design errors described earlier, the amplified PCR products can be anything.

Also not mentioned in the Corman-Drosten paper is the case of small fragments of qPCR (around 100bp): It could be either 1,5% agarose gel or even an acrylamide gel.
The fact that these PCR products have not been validated at molecular level is another striking error of the protocol, making any test based upon it useless as a specific diagnostic tool to identify the SARS-CoV-2 virus.

5. Positive and negative controls to confirm/refute specific virus detection.

The unconfirmed assumption described in the Corman-Drosten paper is that SARS-CoV-2 is the only virus from the SARS-like beta-coronavirus group that currently causes infections in humans. The sequences on which their PCR method is based are *in silico* sequences, supplied by a laboratory in China [23], because at the time of development of the PCR test no control material of infectious ("live") or inactivated SARS-CoV-2 was available to the authors. The PCR test was therefore designed using the sequence of the known SARS-CoV-1 as a control material for the Sarbeco component (Dr. Meijer, co-author Corman-Drosten paper in an email exchange with Dr. Peter Borger) [2].

All individuals testing positive with the RT-PCR test, as described in the Corman-Drosten paper, are assumed to be positive for SARS-CoV-2 infections. There are three severe flaws in their assumption. First, a positive test for the RNA molecules described in the Corman-Drosten paper cannot be equated to "infection with a virus". A positive RT-PCR test merely indicates the presence of viral RNA molecules. As demonstrated under point 1d (above), the Corman-Drosten test was not designed to detect the full-length virus, but only a fragment of the virus. We already concluded that this classifies the test as unsuitable as a diagnostic test for SARS-virus infections.

Secondly and of major relevance, the functionality of the published RT-PCR Test was not demonstrated with the use of a positive control (isolated SARS-CoV-2 RNA) which is an essential scientific gold standard.

Third, the Corman-Drosten paper states:

"To show that the assays can detect other bat-associated SARS-related viruses, we used the E gene assay to test six bat-derived faecal samples available from Drexler et al. [...] und Muth et al. […]. These virus-positive samples stemmed from European rhinolophid bats. Detection of these phylogenetic outliers within the SARS-related CoV clade suggests that all Asian viruses are likely to be detected. This would, theoretically, ensure broad sensitivity even in case of multiple independent acquisitions of variant viruses from an animal reservoir."

This statement demonstrates that the E gene used in RT-PCR test, as described in the Corman-Drosten paper, is not specific to SARS-CoV-2. The E gene primers also detect a broad spectrum of other SARS viruses.

The genome of the coronavirus is the largest of all RNA viruses that infect humans and they all have a very similar molecular structure. Still, SARS-CoV-1 and SARS-CoV-2 have two highly specific genetic fingerprints, which set them apart from the other coronaviruses. First, a unique fingerprint-sequence (KTFPPTEPKKDKKKK) is present in the N-protein of SARS-CoV-1 and SARS-CoV-2 [13,14,15]. Second, both SARS-CoV-1 and SARS-CoV-2 do not contain the HE protein, whereas all other coronaviruses possess this gene [13, 14]. So, in order to specifically detect a SARS-CoV-1 and SARS-CoV-2 PCR product the above region in the N gene should have been chosen as the amplification target. A reliable diagnostic test should focus on this specific region in the N gene as a confirmatory test. The PCR for this N gene was not further validated nor recommended as a test gene by the Drosten-Corman paper, because of

being “not so sensitive” with the SARS-CoV original probe [1].

Furthermore, the absence of the HE gene in both SARS-CoV-1 and SARS-CoV-2 makes this gene the ideal negative control to exclude other coronaviruses. The Corman-Drosten paper does not contain this negative control, nor does it contain any other negative controls. The PCR test in the Corman-Drosten paper therefore contains neither a unique positive control nor a negative control to exclude the presence of other coronaviruses. This is another major design flaw which classifies the test as unsuitable for diagnosis.

6. Standard Operational Procedure (SOP) is not available

There should be a Standard Operational Procedure (SOP) available, which unequivocally specifies the above parameters, so that all laboratories are able to set up the identical same test conditions. To have a validated universal SOP is essential, because it facilitates data comparison within and between countries. It is very important to specify all primer parameters unequivocally. We note that this has not been done. Further, the Ct value to indicate when a sample should be considered positive or negative is not specified. It is also not specified when a sample is considered infected with SARS-CoV viruses. As shown above, the test cannot discern between virus and virus fragments, so the Ct value indicating positivity is crucially important. This Ct value should have been specified in the Standard Operational Procedure (SOP) and put on-line so that all laboratories carrying out this test have exactly the same boundary conditions. It points to flawed science that such an SOP does not exist. The laboratories are thus free to conduct the test as they consider appropriate, resulting in an enormous amount of variation. Laboratories all over Europe are left with a multitude of questions; which primers to order? which nucleotides to fill in the undefined places? which Tm value to choose? How many PCR cycles to run? At what Ct value is the sample positive? And when is it negative? And how many genes to test? Should all genes be tested, or just the E and RpRd gene as shown in Table 2 of the Corman-Drosten paper? Should the N gene be tested as well? And what is their negative control? What is their positive control? The protocol as described is unfortunately very vague and erroneous in its design that one can go in dozens of different directions. There does not appear to be any standardization nor an SOP, so it is not clear how this test can be implemented.

7. Consequences of the errors described under 1-5: false positive results.

The RT-PCR test described in the Corman-Drosten paper contains so many molecular biological design errors (see 1-5) that it is not possible to obtain unambiguous results. It is inevitable that this test will generate a tremendous number of so-called “false positives”. The definition of false positives is a negative sample, which initially scores positive, but which is negative after retesting with the same test. False positives are erroneous positive test-results, i.e. negative samples that test positive. And this is indeed what is found in the Corman-Drosten paper. On page 6 of the manuscript PDF the authors demonstrate, that even under well-controlled laboratory conditions, a considerable percentage of false positives is generated with this test:

“In four individual test reactions, weak initial reactivity was seen however they were negative upon retesting with the same assay. These signals were not associated with any particular virus, and for each virus with which initial positive reactivity occurred, there were other samples that contained the same virus at a higher concentration but did not test positive. Given the results from the extensive technical qualification described above, it was concluded that this initial reactivity was not due to chemical instability of real-time PCR probes and most probably to handling issues caused by the rapid introduction of new diagnostic tests and controls during this evaluation study.” [1]

The first sentence of this excerpt is clear evidence that the PCR test described in the Corman-Drosten paper generates false positives. Even under the well-controlled conditions of the state-of-the-art Charité-laboratory, 4 out of 310 primary-tests are false positives per definition. Four negative samples initially tested positive, then were negative upon retesting. This is the classical example of a false positive. In this case the authors do not identify them as false positives, which is intellectually dishonest.

Another telltale observation in the excerpt above is that the authors explain the false positives away as "handling issues caused by the rapid introduction of new diagnostic tests". Imagine the laboratories that have to introduce the test without all the necessary information normally described in an SOP.

8. The Corman-Drosten paper was not peer-reviewed

Before formal publication in a scholarly journal, scientific and medical articles are traditionally certified by "peer review." In this process, the journal's editors take advice from various experts ("referees") who have assessed the paper and may identify weaknesses in its assumptions, methods, and conclusions. Typically a journal will only publish an article once the editors are satisfied that the authors have addressed referees' concerns and that the data presented supports the conclusions drawn in the paper." This process is as well described for Eurosurveillance [16].

The Corman-Drosten paper was submitted to Eurosurveillance on January 21st 2020 and accepted for publication on January 22nd 2020. On January 23rd 2020 the paper was online. On January 13th 2020 version 1-0 of the protocol was published at the official WHO website [17], updated on January 17th 2020 as document version 2-1 [18], even before the Corman-Drosten paper was published on January 23rd at Eurosurveillance.

Normally, peer review is a time-consuming process since at least two experts from the field have to critically read and comment on the submitted paper. In our opinion, this paper was not peer-reviewed. Twenty-four hours are simply not enough to carry out a thorough peer review. Our conclusion is supported by the fact that a tremendous number of very serious design flaws were found by us, which make the PCR test completely unsuitable as a diagnostic tool to identify the SARS-CoV-2 virus. Any molecular biologist familiar with RT-PCR design would have easily observed the grave errors present in the Corman-Drosten paper before the actual review process. We asked Eurosurveillance on October 26th 2020 to send us a copy of the peer review report. To date, we have not received this report and in a letter dated November 18th 2020, the ECDC as host for Eurosurveillance declined to provide access without providing substantial scientific reasons for their decision. On the contrary, they write that "disclosure would undermine the purpose of scientific investigations." [24].

9. Authors as the editors

A final point is one of major concern. It turns out that two authors of the Corman-Drosten paper, Christian Drosten and Chantal Reusken, are also members of the editorial board of this journal [19]. Hence there is a severe conflict of interest which strengthens suspicions

that the paper was not peer-reviewed. It has the appearance that the rapid publication was possible simply because the authors were also part of the editorial board at Eurosurveillance. This practice is categorized as compromising scientific integrity .

SUMMARY CATALOGUE OF ERRORS FOUND IN THE PAPER

The Corman-Drosten paper contains the following specific errors:

1. There exists no specified reason to use these extremely high concentrations of primers in this protocol. The described concentrations lead to increased nonspecific bindings and PCR product amplifications, making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

2. Six unspecified wobbly positions will introduce an enormous variability in the real world laboratory implementations of this test; the confusing nonspecific description in the Corman-Drosten paper is not suitable as a Standard Operational Protocol making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

3. The test cannot discriminate between the whole virus and viral fragments. Therefore, the test cannot be used as a diagnostic for intact (infectious) viruses, making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus and make inferences about the presence of an infection.

4. A difference of 10° C with respect to the annealing temperature Tm for primer pair1 (RdRp_SARSr_F and RdRp_SARSr_R) also makes the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

5. A severe error is the omission of a Ct value at which a sample is considered positive and negative. This Ct value is also not found in follow-up submissions making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

6. The PCR products have not been validated at the molecular level. This fact makes the protocol useless as a specific diagnostic tool to identify the SARS-CoV-2 virus.

7. The PCR test contains neither a unique positive control to evaluate its specificity for SARS-CoV-2 nor a negative control to exclude the presence of other coronaviruses, making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

8. The test design in the Corman-Drosten paper is so vague and flawed that one can go in dozens of different directions; nothing is standardized and there is no SOP. This highly questions the scientific validity of the test and makes it unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

9. Most likely, the Corman-Drosten paper was not peer-reviewed making the test unsuitable as a specific diagnostic tool to identify the SARS-CoV-2 virus.

10. We find severe conflicts of interest for at least four authors, in addition to the fact that two of the authors of the Corman-Drosten paper (Christian Drosten and Chantal Reusken) are members of the editorial board of Eurosurveillance. A conflict of interest was added on July 29 2020 (Olfert Landt is CEO of TIB-Molbiol; Marco Kaiser is senior researcher at GenExpress and serves as scientific advisor for TIB-Molbiol), that was not declared in the original version (and still is missing in the PubMed version); TIB-Molbiol is the company which was “the first” to produce PCR kits (Light Mix) based on the protocol published in the Corman-Drosten manuscript, and according to their own words, they distributed these PCR-test kits before the publication was even submitted [20]; further, Victor Corman & Christian Drosten failed to mention their second affiliation: the commercial test laboratory “Labor Berlin”. Both are responsible for the virus diagnostics there [21] and the company operates in the realm of real time PCR-testing.

CONCLUSION

In light of our re-examination of the test protocol to identify SARS-CoV-2 described in the Corman-Drosten paper we have identified concerning errors and inherent fallacies which render the SARS-CoV-2 PCR test useless.

The decision as to which test protocols are published and made widely available lies squarely in the hands of Eurosurveillance. A decision to recognise the errors apparent in the Corman-Drosten paper has the benefit to greatly minimise human cost and suffering going forward. Is it not in the best interest of Eurosurveillance to retract this paper? Our conclusion is clear. In the face of all the tremendous PCR-protocol design flaws and errors described here, we conclude: There is not much of a choice left in the framework of scientific integrity and responsibility.

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Author's Affiliations:

1) **Dr. Pieter Borger** (MSc, PhD), Molecular Genetics, W+W Research Associate, Lörrach, Germany,

2) Rajesh Kumar Malhotra (Artist Alias: **Bobby Rajesh Malhotra**), Former 3D Artist / Scientific Visualizations at CeMM - Center for Molecular Medicine of the Austrian Academy of Sciences (2019-2020), University for Applied Arts - Department for Digital Arts Vienna, Austria

3) **Dr. Michael Yeadon** BSs(Hons) Biochem Tox U Surrey, PhD Pharmacology U Surrey. Managing Director, Yeadon Consulting Ltd, former Pfizer Chief Scientist, United Kingdom,

4) **Dr. Clare Craig** MA, (Cantab) BM, BCh (Oxon), FRCPath, United Kingdom

5) **Kevin McKernan**, BS Emory University, Chief Scientific Officer, founder Medical Genomics, engineered the sequencing pipeline at WIBR/MIT for the Human Genome Project, Invented and developed the SOLiD sequencer, awarded patents related to PCR, DNA Isolation and Sequencing, USA

6) **Prof. Dr. Klaus Steger**, Department of Urology, Pediatric Urology and Andrology, Molecular Andrology, Biomedical Research Center of the Justus Liebig University, Giessen, Germany

7) **Dr. Paul McSheehy** (BSc, PhD), Biochemist & Industry Pharmacologist, Loerrach, Germany

8) **Dr. Lidiya Angelova**, MSc in Biology, PhD in Microbiology, Former researcher at the National Institute of Allergy and Infectious Diseases (NIAID), Maryland, USA

9) **Dr. Fabio Franchi**, Former Dirigente Medico (M.D) in an Infectious Disease Ward, specialized in "Infectious Diseases" and "Hygiene and Preventive Medicine", Società Scientifica per il Principio di Precauzione (SSPP), Italy

10) **Dr. med. Thomas Binder**, Internist and Cardiologist (FMH), Switzerland

11) **Prof. Dr. med. Henrik Ullrich**, specialist Diagnostic Radiology, Chief Medical Doctor at the Center for Radiology of Collm Oschatz-Hospital, Germany

12) **Prof. Dr. Makoto Ohashi**, Professor emeritus, PhD in Microbiology and Immunology, Tokushima University, Japan

13) **Dr. Stefano Scoglio**, B.Sc. Ph.D., Microbiologist, Nutritionist, Italy

14) **Dr. Marjolein Doesburg-van Kleffens** (MSc, PhD), specialist in Laboratory Medicine (clinical chemistry), Maasziekenhuis Pantein, Beugen, the Netherlands

15) **Dr. Dorothea Gilbert** (MSc, PhD), PhD Environmental Chemistry and Toxicology. DGI Consulting Services, Oslo, Norway

16) **Dr. Rainer J. Klement**, PhD. Department of Radiation Oncology, Leopoldina Hospital Schweinfurt, Germany

17) **Dr. Ruth Schruefer**, PhD, human genetics/ immunology, Munich, Germany,

18) **Dra. Berber W. Pieksma**, General Practitioner, The Netherlands

19) **Dr. med. Jan Bonte** (GJ), Consultant Neurologist, the Netherlands

20) Dr. Bruno H. Dalle Carbonare (Molecular biologist), IP specialist, BDC Basel, Switzerland

21) **Dr. Kevin P. Corbett**, MSc Nursing (Kings College London) PhD (London South Bank) Social Sciences (Science & Technology Studies) London, England, UK

22) **Prof. Dr. Ulrike Kämmerer**, specialist in Virology / Immunology / Human Biology / Cell Biology, University Hospital Würzburg, Germany

Author's Contributions:

PB: Planned and conducted the analyses and research, conceptualising the manuscript.

RKM: Planned and conducted the research, conceptualising the figures and manuscript.

MY: Conducted the analyses and research.

KMcK: Conducted the analyses and research, conceptualized the manuscript.

KS: Conducted the analyses and research.

PMcS: Proofreading the analyses and research.

LA: Proofreading the analyses and research.

FF: Proofreading the analyses and research.

TB: Proofreading the analyses and research.

HU: Proofreading the analyses and research.

MO: Proofreading the analyses and research.

SS: Proofreading the analyses and research.

MDvK: Proofreading the analyses and research.

DG: Proofreading the analyses and research.

RJK: Proofreading the analyses and research.

RS: Proofreading the analyses and research, and the manuscript.

BWK: Proofreading the analyses and research.

RvV: Proofreading the analyses and research.

JB: Proofreading the analyses and research.

KC: Proofreading the analyses and research.

UK: Planned and conducted the analyses and research, conceptualising the manuscript.

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PERSPECTIVE
INFECTIOUS DISEASES

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Informed consent disclosure to vaccine trial subjects of risk of COVID-19 vaccines worsening clinical disease

Abstract

Aims of the study: Patient comprehension is a critical part of meeting medical ethics standards of informed consent in study designs. The aim of the study was to determine if sufficient literature exists to require clinicians to disclose the specific risk that COVID-19 vaccines could worsen disease upon exposure to challenge or circulating virus.

Methods used to conduct the study: Published literature was reviewed to identify preclinical and clinical evidence that COVID-19 vaccines could worsen disease upon exposure to challenge or circulating virus. Clinical trial protocols for COVID-19 vaccines were reviewed to determine if risks were properly disclosed.

Results of the study: COVID-19 vaccines designed to elicit neutralising antibodies may sensitise vaccine recipients to more severe disease than if they were not vaccinated. Vaccines for SARS, MERS and RSV have never been approved, and the data generated in the development and testing of these vaccines suggest a serious mechanistic concern: that vaccines designed empirically using the traditional approach (consisting of the unmodified or minimally modified coronavirus viral spike to elicit neutralising antibodies), be they composed of protein, viral vector, DNA or RNA and irrespective of delivery method, may worsen COVID-19 disease via antibody-dependent enhancement (ADE). This risk is sufficiently obscured in clinical trial protocols and consent forms for ongoing COVID-19 vaccine trials that adequate patient comprehension of this risk is unlikely to occur, obviating truly informed consent by subjects in these trials.

Conclusions drawn from the study and clinical implications: The specific and significant COVID-19 risk of ADE should have been and should be prominently and independently disclosed to research subjects currently in vaccine trials, as well as those being recruited for the trials and future patients after vaccine approval, in order to meet the medical ethics standard of patient comprehension for informed consent.

1 | THE RISK OF ADE IN COVID-19 VACCINES IS NON-THEORETICAL AND COMPELLING

Vaccine-elicited enhancement of disease was previously observed in human subjects with vaccines for respiratory syncytial virus (RSV), dengue virus and measles.[1] Vaccine-elicited enhancement of disease was also observed with the SARS and MERS viruses and with feline coronavirus, which are closely related to SARS-CoV-2, the causative pathogen of COVID-19 disease. The immune mechanisms of this enhancement have invariably involved antibodies, from direct antibody-dependent enhancement, to immune complex formation by antibodies, albeit accompanied by various coordinated cellular responses, such as Th2 T-cell skewing.[2-7] Notably, both neutralising and non-neutralising antibodies have been implicated. A recent study revealed IgG-mediated acute lung injury in vivo in macaques infected with SARS that correlated with a vaccine-elicited, neutralising antibody response.[8] Inflammation and tissue damage in the lung in this animal model recapitulated the inflammation and tissue damage in the lungs of SARS-infected patients who succumbed to the disease. The time course was also similar, with the worst damage occurring in delayed fashion in synchrony with ramping up of the immune response. Remarkably, neutralising antibodies controlled the virus in the animal, but then would precipitate a severe, tissue-damaging, inflammatory response in the lung. This is a similar profile to immune complex-mediated disease seen with RSV vaccines in the past, wherein vaccinees succumbed to fatal enhanced RSV disease because of the formation of antibody-virus immune complexes that precipitated harmful, inflammatory immune responses. It is also similar to the clinical course of COVID-19 patients, in whom severe COVID-19 disease is associated with the development of anti-SARS-CoV-2 serum antibodies,[9] with titres correlating directly with the severity of disease.[10] Conversely, subjects who recover quickly may have low or no anti-SARS-CoV-2 serum antibodies.[11]

The elicitation of antibodies, specifically neutralising antibodies, is the goal of nearly every current SARS-CoV-2 vaccine candidate. The prior evidence that vaccine-elicited, antibody-dependent enhancement (ADE) of disease is likely to occur to some degree with COVID-19 vaccines is vertically consistent from controlled SARS studies in primates to clinical observations in SARS and COVID-19. Thus, a finite, non-theoretical risk is evident in the medical literature that vaccine candidates composed of the SARS-CoV-2 viral spike and eliciting anti-SARS-CoV-2 antibodies, be they neutralising or not, place vaccinees at higher risk for more severe COVID-19 disease when they encounter circulating viruses. Indeed, studies in mice of prior SARS vaccines revealed this exact phenotype, with four human vaccine candidates eliciting neutralising antibodies and protecting against SARS challenge, but viral re-challenge of thus vaccinated animals resulting

in immunopathologic lung disease.[5] Independently, SARS/MERS vaccine candidates, commonly exhibited ADE associated with high inflammatory morbidity in preclinical models, obstructing their advancement to the clinic.[4,12] SARS ADE of both disease in non-human primates and viral infection of cells in vitro was clearly mapped to specific antibody-targeted SARS viral spike epitopes.[6] This phenomenon was consistent across a variety of vaccine platforms, including DNA, vector primes and virus-like particles (VLP), irrespective of inoculation method (oral, intramuscular, subcutaneous, etc). An unknown variable is how long this tissue damage lasts, possibly resulting in permanent morbidity (eg, diabetes from pancreatic damage[7]).

Current data on COVID-19 vaccines is limited, but does not so far reveal evidence of ADE of disease. Non-human primate studies of Moderna's mRNA-1273 vaccine showed excellent protection, with no detectable immunopathology.[13] Phase 1 trials of several vaccines have not reported any immunopathology in subjects administered the candidate vaccines. However, these subjects were unlikely to have yet encountered circulating virus.[14] Nevertheless, all preclinical studies to date have been performed with the Wuhan or closely related strains of the virus, while a mutant D614G virus is now the most prevalent circulating form. Several observations suggest that this alternative form may be antigenically distinct from the Wuhan derived strain, not so much in composition, but in conformation of the viral spike and exposure of neutralisation epitopes.[15-18] Similarly, Phase 1 and 2 clinical trials of vaccine candidates have only been designed around immunogenicity as an efficacy end point and have not been designed to capture exposure of subjects to circulating virus after vaccination, which is when ADE/immunopathology is designed to occur. Thus, the absence of ADE evidence in COVID-19 vaccine data so far does not absolve investigators from disclosing the risk of enhanced disease to vaccine trial participants, and it remains a realistic, non-theoretical risk to the subjects.

2 | CHALLENGES TO INFORMED CONSENT FOR COVID-19 VACCINE STUDIES

Informed consent procedures for vaccine trials commonly include disclosure of very minor risks such as injection site reactions, rare risks from past, *unrelated* vaccines/viruses, such as Guillain-Barre syndrome for swine flu (interest in which is likely behind the interest in Astra Zeneca's recent vaccine transverse myelitis event) and generic statements about the risk of idiosyncratic systemic adverse events and death. Specific risks to research participants derived from biological mechanism are rarely included, often because of ambiguity about their applicability.[19]

Signed consent forms from the COVID-19 vaccine trials are not publicly available because of privacy concerns. They also vary from clinical site to clinical site, and sample consent forms on which they are based are not required to be disclosed until after the trial is over, if at all. However, these consent forms are usually very similar in content to the "Risks to participants" section of the trial protocols, which have been released publicly by Pfizer, Moderna and Johnson & Johnson for their COVID-19 vaccine trials ([20] & Supplement). As these three vaccines are representative of the diversity of vaccines being tested, it is very likely that the consent form inferred from these protocols is similar or identical to those from any and all of the vaccine trials currently underway. All three protocols mention the risk of disease enhancement by the vaccine, but all three list this risk last or next to last in the list of risks, after risks from the Ad26-Cov2 vector, adenovirus vectors in general, risks of vaccination in general, risks for pregnancy and birth control (which are said to be "unknown"), risks of blood draws and risks from collection of nasal swab samples (for the Johnson and Johnson vaccine), after allergy, fainting, local site injection reaction, general systemic adverse reactions and laboratory abnormalities for the Moderna vaccine and after local site injection reactions and general systemic adverse events for the Pfizer vaccine. In addition, both Moderna and Johnson and Johnson term the risk of vaccine-elicited disease enhancement as "theoretical." Finally, in citing the risk, Pfizer and Moderna note prior evidence of vaccine-elicited disease enhancement with RSV and dengue, as well as feline coronavirus (Pfizer) and measles (Moderna), however, SARS and MERS are not mentioned. Johnson and Johnson discusses SARS and MERS, but make an unusual scientific argument that vaccine-elicited disease enhancement is because of non-neutralising antibodies and Th2-skewed cellular responses and that Ad26 vaccination does not exhibit this profile.Blank consent forms for AstraZeneca and Johnson and Johnson are also available online at https://restoringtrials.org/2020/09/18/covid19trialprotocoland-studydocs/, and while the AstraZeneca form clearly discloses the specific risk of ADE, the disclosure is listed last among risks only in an attached information sheet. In all, the evidence from the Pfizer, Moderna and Johnson & Johnson protocols for their COVID-19 vaccine trials and the sample consent forms, when contrasted with the evidence for antibody-dependent enhancement of disease presented by this report and widely available to any skilled practitioner in the field, establishes that patient comprehension of the specific risk that receiving the COVID-19 vaccine could convert a subject from someone who experiences mild disease to someone who experiences severe disease, lasting morbidity or even death is unlikely to be achieved by the informed consent procedures planned for these clinical trials.

Medical ethics standards required that, given the extent of evidence in the medical literature reviewed above, the risk of ADE should be clearly and emphatically distinguished in the informed consent from risks observed *rarely* as well as the more obvious risk of lack of efficacy, which is unrelated to the specific risk of ADE. Based on the published literature, it should have been obvious to any skilled medical practitioner in 2019 that there is a significant risk to vaccine research subjects that they may experience severe disease once vaccinated, while they might only have experienced a mild, self-limited disease if not vaccinated. The consent should also clearly distinguish the specific risk of worsened COVID-19 disease from generic statements about risk of death and generic risk of lack of efficacy of the vaccine.

3 | CONCLUSION

Given the strong evidence that ADE is a non-theoretical and compelling risk for COVID-19 vaccines and the "laundry list" nature of informed consents, disclosure of the specific risk of worsened COVID-19 disease from vaccination calls for a specific, separate, informed consent form and demonstration of patient comprehension in order to meet medical ethics standards. The informed consent process for ongoing COVID-19 vaccine trials does not appear to meet this standard. While the COVID-19 global health emergency justifies accelerated vaccine trials of candidates with known liabilities, such an acceleration is not inconsistent with additional attention paid to heightened informed consent procedures specific to COVID-19 vaccine risks.

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AUTHOR CONTRIBUTIONS

TC and RV conceived this commentary. TC wrote the manuscript. RV edited and approved the manuscript.

DATA AVAILABILITY STATEMENT

All data referenced in this report have been published in peer-reviewed literature or are available on the World Wide Web/Internet at the URL's indicated in the References section. Therefore, all data referenced in this report are publicly available in widely available data repositories.

Timothy Cardozo[1]
Ronald Veazey[2]

[1]*Department of Biochemistry and Molecular Pharmacology, NYU Langone Health, New York, NY, USA*
[2]*Division of Comparative Pathology, Department of Pathology and Laboratory Medicine, Tulane University School of Medicine, Tulane National Primate Research Center, Covington, LA, USA*

Correspondence
Timothy Cardozo, Department of Biochemistry and Molecular Pharmacology, NYU Langone Health, 550 First Avenue, MSB 222, New York, NY 10016, USA.
Email: cardot01@nyumc.org

ORCID

Timothy Cardozo https://orcid.org/0000-0002-0643-4497

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