

## ISDB 2021 Newsletter

Message from the President of ISDB, Dr. Dick Bijl

Dear friends,

We are happy to send you the third newsletter of ISDB this year. We have again several contributions by our members with focus also on COVID-19. I hope you will enjoy it.

Alan Cassels continues to interview members of ISDB and in this issue you will find an interview with Etzel Gysling of Pharma Kritik Switzerland, one of the oldest members of ISDB.

Regarding the General Assembly the Committee decided to organise a digital meeting in September/October 2022. Our friends from the Belgian Center for Pharmacotherapeutic Information (BCFI/CBIF) have offered to help with the implementation of that meeting. The Committee is working on the program and we will inform you on the progress. In that meeting there is also time for the election for the new ISDB Committee.

BCFI pays attention to the role of rational pharmacotherapy which is one of the core elements of ISDB.

*Continued on page 2*



Dick Bijl, Chairman of ISDB

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## Message from the President, continued

Rational pharmacotherapy relates to the prescribing of proper drugs by finding the best balance of efficacy, safety and cost. Properly conducted randomized double-blind trials with a control group taking placebo or standard treatment should be the key basis when deciding drug treatment-options for Covid-19. As BCFI states correctly the regulating authorities in the European Union and the United States have given marketing authorizations to vaccines and antiviral drugs without sharing the study data with public. For doctors, pharmacists and also for patients it is therefore impossible to decide what forms the scientific basis of this improvements. Finally, I again ask the members to alert us to articles they have published that might be of interest to other members and people outside ISDB.

Dick Bijl

## Transparency of Regulatory Data Across the EMA, Health Canada, and US FDA

Link [here](#).

**Letter to ICMJE Supported by ISDB: “The ICMJE will not consider results data contained in assessment reports published by HTAs, medicine regulators, medical device regulators, or other regulatory agencies to be prior publication.”**

Dear Editors,

A research article published in the BMJ Open by Dr Leeza Osipenko showed that [over 80% of NICE](#)

[appraisals contain redacted data](#), including data on clinical trial outcomes that are of importance to patients, clinicians and researchers. HTAs in other countries also [routinely redact clinical trial outcome data](#).

A significant portion of these data are redacted as being “**academic in confidence**” (as opposed to “commercially confidential information”) based on widespread concern among researchers that disclosure of trial data in a public HTA report could prevent them from later publishing the outcomes of the trial in a peer-reviewed journal.

Several medical journals, including the BMJ, have informed us that researchers’ fears in this regard are unfounded, and that trial data contained within reports published by HTAs and regulatory agencies (including EMA and FDA assessment reports) does not constitute ‘prior publication’ and would not compromise researchers’ ability to later publish trial outcomes in peer-reviewed journals. However, not all journals share this position.

**We are currently advocating with HTAs to discontinue their “academic in confidence” redactions so that patients, clinicians, and researchers can access all clinically relevant elements of HTA reports.**

**In this context, it would be extremely helpful for ICMJE to highlight, clarify and support journals’ existing position by formally issuing the following statement:**

**“The ICMJE will not consider results data contained in assessment reports published by HTAs, medicines regulators, medical device regulators, or other regulatory agencies to be prior publication.”**

By eliminating the putative rationale for “academic in confidence” redactions, such a statement by ICMJE

would put an end to the current misguided redaction practices of HTAs.

Please do not hesitate to contact us if you require additional information, or if you would like to discuss this issue further with us.

Can you please let us know by when you expect to reach a decision on this issue?

Thank you for your time, we look forward to hearing from you,

Dick Bijl, on behalf of ISDB

## New Book: Pandemic Chaos (Edited by Dr. Dick Bijl)



Pandemic Chaos closely examines the Dutch government’s Covid-19 policies by an esteemed group of writers including physicians, medical specialists, psychologists, philosophers, health scientist, a mathematician, an economist, a political scientist, an educator, a researcher of the future and a lawyer. The book even contains a contribution from the pharmaceutical industry. The authors, 17 in total, are all experts in the field they are examining and most of them are professors.

During the Corona crisis, the Dutch government took measures that increasingly restricted the freedom of movement of citizens. Lockdowns,

travel restrictions, face masks, closed shops and closed schools were supposed to help contain the pandemic.

In the economic, social, psychological, pedagogical, legal, ethical and medical fields, great sacrifices were required. As scientific knowledge about the virus increased the government pinned all hopes on an effective vaccine. But how scientifically substantiated were the measures taken? The book was wildly popular and went into its sixth edition only three weeks after its publication. It is now being translated into English.

Congratulations Dick!

## Interview with Dr. Etzel Gysling **pharma-kritik**

Pharma-Kritik, Switzerland [www.infomed.org](http://www.infomed.org)



Dr. Etzel Gysling lives in Wil, near Zurich in Switzerland

### **What is your background and how did you come to work for Pharma-Kritik?”**

In the 1970's I lived in Sherbrooke, Quebec, Canada and worked as an assistant professor and with a joint appointment in internal medicine and pharmacology. There I was exposed to the Medical Letter (from the US) and the Drugs and Therapeutics Bulletins (from the UK). I decided that when I moved back to Switzerland I

should start my own therapeutics bulletin, even though my friends in clinical pharmacology told me, “you can try but you won't succeed.”

Dr. Gysling has proven them wrong. He has been the head of Pharma-Kritik since 1979 and the lead editor that produces independent drug bulletins mostly for his audience of Swiss clinicians. Has a very small team, mostly medical doctors some who are in active practice and others in academic institutions. His journal used to produce a medical letter of about eight pages and today puts out six issues per year.

### **Pharma-Kritik has been going now for 40 years, which is a huge accomplishment. What do you attribute your publication's success and longevity to?**

He tells me it was different in the past. For the first ten years most doctors that he communicated with were in single practices, yet that has changed a lot. Those physicians needed an independent source of drug information and subscribed to his journal, and that money from the subscriptions provided sufficient funding to keep it going. His journal accepts no money from any sponsors, and has no advertising, so as to not be beholden to government or industry. They currently they have about 3,000 subscribers. He's very proud of his loyal following even though when asked what sort of impact he has had, he admits that his group is well respected by the community but noted that “I still hesitate to say everyone follows what we say.”

### **What are some of the major therapeutic areas have you tackled most successfully?**

Many years ago, Pharma-Kritik produced a booklet of 100 important drugs, which contained the majority of treatments used by the typical Swiss general practitioner. This guide was recently turned into an app and is available from their website in German yet the English version is still in development. Covering all areas of general practice it is a concise guide to the most commonly used drugs.

This guide has proved quite popular and he has already completed the 3rd edition last year which people are still asking for. One activity that is in progress is an attempt to disseminate information for consumers and patients. His group has produced a series of package leaflets for the public—available in eight languages—but they are currently working out a way to get them better known. Quoting the sentiments of our late friend and colleague, Andrew Herxheimer, Dr. Gysling said “we always have to get nearer the general public. Professionals are important but we also need to come to the patients.”

### **Do you think your organization is making a positive difference in prescribing in Switzerland?**

Currently there is lots of competition for independent therapeutics Bulletins and there are three of them alone in Germany. Having said that he admits that “people who have used it, tell us that it influences the prescribing practices of our doctors.” In the early days Dr. Gysling had many teaching opportunities which gave him a lot of contact with general practitioners and when the internet started in the 1990s his group made special courses for doctors.

### **Is it difficult to maintain a newsletter that is independent from the pharmaceutical industry?**

In the earlier years—the first 20 years we had considerable trouble with the pharma—threats that they would sue us, but we managed somehow to calm them down. We were never taken to court. As of late, the Swiss pharmaceutical industry has become rather quiet—as they concentrate more and more on producing high cost specialty drugs, where most of their profits are focused. These days there is almost no reaction to his therapeutic letter from the pharmaceutical companies.

### **What does the future look like for PharmaKritik and are you planning any new initiatives in the future?**

In their next issue they are looking at



## Interview with Dr. Etzel Gysling, continued

four different areas including caffeine, some new drugs for Multiple Sclerosis, and anxiolytics, drugs for anxiety. He is also looking at the issue of doping in sports, as general practitioners in Switzerland often have to deal with body builders who tend to use many kinds of drugs in the pursuit of the perfect muscled body. He considers it an important topic. "I personally think that anabolic steroids are most abused in the private area, people want to bulk up their muscles." He said he had some help from a sports medicine specialist in completing that letter.

**Do you have any advice you could share with ISDB and any secrets of your success?**

We are in a good position here. We are on good terms with our neighbours, including the Italians, Germans, and French, where we collaborate and exchange information. All this is good to contribute to the future of our work.

## Celebrating World Evidence-based Healthcare Day, October 21, 2021

Blog post from David Phizackerley, Deputy Editor, Drug and Therapeutics Bulletin: From info-desert to info-democracy: the role of independent drug bulletins. Link [here](#).

## ISDB General Assembly

BCFI has agreed to host the General Assembly, which will be done virtually in September or October 2022 yet an exact date has yet to be decided. We will record the sessions and make them available via YouTube. The ISDB committee is seeking out appropriate speakers for a range of topics, and

suggestions are welcome. Possible topics include:

- The interface between journalism and appropriate use of medicines in the context of Covid and public health.
- Transparency, Clinical trials, information gathered for Covid.
- New Research requirements and research methods for regulatory approval.
- Future of public financing of CME.
- Topics of interest for countries in the South.

## MEMBER NEWS

### December Issue of "La Revue Prescrire"



Published in French, includes the updated list of medicines to avoid. Link [here](#).

### Therapeutics Initiative Discusses Informed, Intentional Non-adherence

## Therapeutics Initiative

Link [here](#).

### Public Citizen's exposé on Pfizer's Power published, October 19, 2021



Link [here](#).

Also translated into Spanish: El Poder de Pfizer, publicado en Boletín Farmacos: Ética y Derecho: 2021; 24(4), Link [here](#).

## COVID-19: On the Oral Antivirals Molnupiravir and PF-07321332+Ritonavir: No Published Studies at the Moment



Currently there are insufficient data to properly assess the efficacy and safety of molnupiravir and PF-07321332+ritonavir. Results of these products are preliminary (based on preprints and media releases) and will likely vary after final results have been published, yet this is what we know as of December 2021.

The oral antiviral drugs against COVID-19 molnupiravir and the combination PF-07321332 + ritonavir received much media but what do we know at the moment?

- The European Medicines Agency (EMA) refers for each of the two antivirals to a randomized, placebo-controlled study in non-hospitalized patients with mild to moderately severe COVID-19 and risk of developing severe COVID-19, whose interim results show a beneficial effect on hospitalization or death. **The results of these studies are not available in detail and have neither been peer-reviewed nor published.**

#### •Molnupiravir (Lagevrio®)

- The active metabolite of molnupiravir, N-hydroxycytidine-triphosphate, is incorporated into the viral RNA and thus inhibits virus replication.

- The MOVE-OUT study (phase 2/3 study) of molnupiravir was reported in a company press release which was revised from an early press release

reporting a 50% reduction in the risk of “hospitalization or death” compared to placebo. This latest release reported a 30% relative risk reduction—which was an absolute 3.0% risk reduction (9.7% risk of hospitalization or death in the placebo group (68/699) versus 6.8% (48/709) in the molnupiravir group.

-This [company press release](#) studied molnupiravir in hospitalized patients (MOVE-IN study) and it was stopped early in the spring of because a clinical benefit in this patient population is considered unlikely.

-Molnupiravir is not currently **licensed in the European Union**. The European Medicines Agency (EMA) is [currently evaluating](#) an application for marketing authorization, for use in non-hospitalized patients with mild to moderate COVID-10 and risk of developing severe COVID-19. In late November, 2021, the EMA issued “[advice](#)” to support Member States which would decide to use molnupiravir before the marketing authorization is granted. The EMA published a provisional [summary of product characteristics](#) although the study data will have to be adjusted in light of the final data.

#### •PF-07321332 + ritonavir (Paxlovid®)

-PF-07321332 is a SARS-CoV-2 protease inhibitor and thus inhibits virus replication. Ritonavir (also a protease inhibitor, but not active against SARS-CoV-2) is added in a low dose to slow down the metabolism of PF-07321332.

-This combination is not currently **licensed in the European Union** and there is no evaluation of an application for marketing authorization at this moment (situation on 06/12/21). The EMA [notified on 19/11](#) that it is preparing “advice” to support Member States that would decide to use the combination before the marketing authorization is granted.

-For PF-07321332 + ritonavir is being studied in the EPIC-HR study as reported in this [media release](#).

#### BCFI comments

Oral antiviral drugs have advantages over monoclonal antibodies - which are administered intravenously – as they can be used more widely in outpatient practice. At present, the data to make a proper assessment of the efficacy and safety of molnupiravir and the combination PF-07321332+ritonavir are lacking. The authors of the BMJ editorial “[Safety and efficacy of antivirals against SARS-CoV-2. We need evidence not optimism](#)” (28/10/21)<sup>1</sup> advocate licensing and deploying antiviral drugs against COVID-19 on the basis of evidence, and not on the basis of optimism. The authors also point out that the cost of these products has not been made public and also refer to past experience with HIV where the use of antivirals in monotherapy has led to development of resistance. The editor in chief of the BMJ also points in an editorial [Covid 19: Why we need a global pandemic treaty \(02/12/21\)](#)<sup>2</sup> at the worrying fixation on expensive antiviral drugs for which there is currently insufficient evidence of efficacy.

The BCFI emphasizes that in the urgent search for drugs against COVID-19, the principles of rational pharmacotherapy should not be forgotten (see also the statement of the International Society of Drug Bulletins, organization to which the BCFI is also affiliated: “[COVID-19 and the quest for drugs and vaccines: Statement from the International Society of Drug Bulletins](#)” (04/04/2020)).

#### Specific resources

1.Sidebottom DB, Smith DD en Gill D. Safety and efficacy of antivirals against SARS-CoV-2. Editorial. BMJ 2021;375:n2611. Doi: <https://doi.org/10.1136/bmj.n2611> (28/10/21)

2.Godlee F (editor in chief). Covid 19: Why we need a global pandemic treaty. Editor's Choice. BMJ 2021;375:n2963. Doi: <https://doi.org/10.1136/bmj.n2963> (02/12/21)