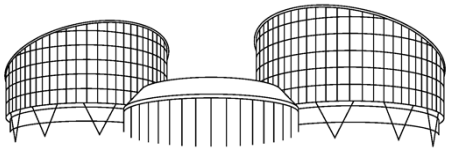

EUROPEAN COURT OF HUMAN RIGHTS
COUR EUROPÉENNE DES DROITS DE L'HOMME

THIRD SECTION

CASE OF TRASKUNOVA v. RUSSIA

(Application no. 21648/11)

JUDGMENT

Art 2 (substantive and procedural) • Positive obligations • Death of participant in clinical trial of new medicinal product after deficient implementation of regulatory framework and non-compliance with guarantees ensuring informed consent • Heightened protection required for participation of mentally ill persons in clinical trials, with particularly strong safeguards • Inadequate judicial response

STRASBOURG

30 August 2022

This judgment will become final in the circumstances set out in Article 44 § 2 of the Convention. It may be subject to editorial revision.

In the case of Traskunova v. Russia,

The European Court of Human Rights (Third Section), sitting as a Chamber composed of:

Georges Ravarani, *President,*
Georgios A. Serghides,
Darian Pavli,
Peeter Roosma,
Andreas Zünd,
Frédéric Krenc,
Mikhail Lobov, *judges,*
and Olga Chernishova, *Deputy Section Registrar,*

Having regard to:

the application (no. 21648/11) against the Russian Federation lodged with the Court under Article 34 of the Convention for the Protection of Human Rights and Fundamental Freedoms ("the Convention") by a Russian national, Ms Nonna Vladimirovna Traskunova ("the applicant"), on 17 March 2011;

the decision to give notice to the Russian Government ("the Government") of the complaint under Article 2 of the Convention and to declare the remainder of the application inadmissible;

the decision to grant priority to the above application;

the parties' observations;

Having deliberated in private on 21 June 2022,

Delivers the following judgment, which was adopted on that date:

INTRODUCTION

1. In the present case the applicant's daughter died while she was participating in a clinical trial of a new medicinal product intended for the treatment of schizophrenia, a mental illness from which she had suffered for many years. The applicant alleges breach of the State's positive obligations under Article 2.

THE FACTS

2. The applicant, who was born in 1925, died on 31 August 2018. Mr Vladimir Yuryevich Traskunov, her grandson and Ms A.T.'s son (see paragraph 5 below), expressed his wish to pursue the present application on the applicant's behalf. The applicant was represented by Mr V. Lapinskiy, a lawyer practising in St Petersburg.

3. The Government were initially represented by Mr M. Galperin, Representative of the Russian Federation to the European Court of Human Rights, and later by his successor in that office, Mr M. Vinogradov.

4. The facts of the case, as submitted by the parties, may be summarised as follows.

5. The applicant was the mother of Ms A.T., born in 1947, now deceased. In 1964 Ms A.T. was diagnosed with schizophrenia. Schizophrenia is an illness or group of illnesses affecting language, planning, emotion, perceptions and movement. "Positive symptoms" often accompany acute psychotic episodes (including delusions, hallucinations, disordered or fragmented thinking and catatonic movements). "Negative symptoms", associated with long-term illness, include feelings of emotional numbness, difficulty in communicating with others, lack of motivation and inability to care about or cope with everyday tasks.

6. According to Ms A.T.'s medical file, her mental illness had been progressing, and she had had treatment for that condition at various psychiatric hospitals, to which she had been admitted on numerous occasions, and as an outpatient until her death. At all times she retained her legal capacity.

I. BACKGROUND INFORMATION

A. The first clinical trial

7. On 25 February 2004 the Ethics Committee at the Federal Body for the Quality Control of Medicinal Products ("the Ethics Committee") approved a clinical trial of a new drug called asenapine; in comparison with olanzapine, in accordance with protocol no. 25517.

8. According to the patient information leaflet ("the patient leaflet"), that research was the third phase of the trial. The number of participants was expected to be 1,200 worldwide, including 200 enrolled in Russia. The trial was designed as a double-blind test, and the participants' allocation to one of the two test groups was random.

9. The patient leaflet explained that participants had been selected as they had a mental illness, with such symptoms as hallucinations, delusions, disordered thinking and difficulty in communicating with others. The purpose of the trial was to test the safety and efficacy of asenapine in comparison with olanzapine, the latter being widely applied for the treatment of schizophrenia and similar conditions, when used for a period not exceeding one year. Participants needed to undergo various medical examinations to determine their eligibility for the trial. In particular, they were required to have a comprehensive health check-up, blood tests and an electrocardiogram. Participation in the trial was subject to patients being in satisfactory health.

10. The patient leaflet included information about the procedures for following up on participants' health and gathering data about the effects of the drug. Regular visits to the doctor who was leading the study were envisaged. In particular, a participant was to see the doctor once a week during the first month of the trial, once a fortnight during the second month, and eventually once a month. During the visits, the doctor would monitor

vital signs, check motor function, and ask questions concerning possible side effects. Measurement of the electrical activity of the heart (an ECG) would be performed at six of the visits, and general blood tests carried out at ten of them.

11. As regards the risks involved in connection with the trial and possible side effects, the patient leaflet contained a warning that the side effects of all experimental medicinal products were unforeseeable and that comprehensive information about the effects on humans of the product being tested was not yet available. With reference to previous clinical tests, the leaflet stated that the most common side effects of asenapine had been sleepiness, headaches and insomnia. The side effects of olanzapine had been constipation, sleepiness, weight gain, dizziness, and agitation. It could also cause neuroleptic syndrome, which condition can lead to a lethal outcome if not treated at its early stages, and tardive dyskinesia.

12. Another risk of asenapine included a potential aggravation of a participant's mental illness. The doctor in charge was required to estimate the degree of that risk in respect of each participant. If the degree of risk was unacceptable from the medical point of view, the doctor would inform the person concerned either before or during the trial. That risk was considerably lower if a participant remained in a hospital.

13. Any participant experiencing side effects would have the dose changed by the doctor. If significant side effects persisted for a long time, the doctor in charge could exclude the participant concerned from the trial. Participants could discontinue treatment at any time on their own initiative.

14. The period of the trial was limited to one year. If during that time new information became available that was capable of affecting a participant's wish to continue treatment, the doctor would inform the participant of that information and ask the person concerned to confirm their intention to continue the trial. Participants would only learn which of the two drugs they had been taking when the analysis of the data collected during the trial had been completed.

B. The second clinical trial

15. On 22 March 2005 the Ethics Committee approved another clinical trial of asenapine in comparison with olanzapine for long-term treatment, in accordance with protocol no. 25520.

16. The patient leaflet in respect of that study stated that the trial aimed to give "an opportunity to continue treatment to the patients who had successfully participated in the previous trial (in accordance with protocol no. 25517) for no less than one year". The new trial was planned for "no less than one year". It could be discontinued if necessary for administrative reasons or for reasons of safety.

17. The patient leaflet also stated that participants would receive the same product as in the previous trial. Information about which drug (asenapine or olanzapine) had been taken by each participant would remain secret until the relevant information about the previous trial had been disclosed.

18. It contained no new information concerning the risks involved for participants.

19. The section on procedures contained information about the required regular visits and check-ups by the doctor. Patients were to see the doctor every month during the trial, an ECG would be performed every six months and general blood tests taken every three months. Admission to the trial depended on the general state of health of the people who agreed to participate.

II. Ms A.T.'S PARTICIPATION IN THE CLINICAL TRIALS

20. On 24 May 2004 the Department for State Control of Medicinal Products, Goods and Devices at the Ministry of Health of Russia allowed eighteen hospitals in various regions of the country to conduct clinical trials of asenapine. The list included Municipal Psychiatric Hospital no. 3 in St Petersburg ("the psychiatric hospital"), to which Ms A.T. was attached.

21. On 19 December 2004 Ms A.T. visited her psychiatrist in that hospital, who invited her to take part in the clinical trial of a new drug.

22. On the same day, she signed a consent form for the trial, in accordance with protocol no. 25517 (see paragraph 7 above). The patient leaflet (see paragraphs 8-14 above) was an integral part of the consent form. The text of the consent form read as follows:

> "I hereby confirm that I have read [the patient leaflet] and have discussed the information therein with my doctor. I have had an opportunity to ask the questions which concern me and have received answers to those questions ... I realise that I do not lose my statutory rights of a participant in a clinical trial.
>
> ...
>
> I freely agree to participate in this trial. I understand that I can end my participation without providing reasons for doing so at any time. I also confirm my readiness to follow all of the doctor's instructions. I will inform the doctor about all the relevant side effects and other medicines I am taking."

23. The form also contained a statement signed by the doctor responsible for the trial. The statement read as follows:

> "I hereby confirm that I have spoken to the patient ... in detail about the nature and procedures of this trial. I also confirm that the patient ... fully understands the risks and benefits in connection with his or her participation in it."

24. Ms A.T. started taking the experimental product on 27 December 2004. As it later turned out, it was asenapine that she was taking. According to the available medical documents, the following side effects were shown in

her case: the progression of her schizophrenia, agitation, insomnia, and weight gain.

25. On 18 May 2005 Ms A.T. was taken by ambulance to the psychiatric hospital as her mental illness had worsened. She remained at the hospital for treatment afterwards.

26. On 26 December 2005, while still at the hospital, Ms A.T. signed a consent form to participate in the further clinical trial of asenapine, in accordance with protocol no. 25520 (see paragraph 15 above). The consent form, of which the patient leaflet (see paragraphs 16-19 above) was an integral part, had the same wording as the one she had signed on 19 December 2004 (see paragraphs 22-23 above).

27. On 10 April 2006 Ms A.T. suffered cardiac and respiratory arrest. After attempts at resuscitation, she was transferred to the intensive care unit. She remained in a coma until her death on 14 April 2006.

28. According to an autopsy report of 17 April 2006, Ms A.T. had had third-degree general atherosclerosis and cardiosclerosis, and she had died as a result of acute cardiovascular insufficiency caused by that disease, the subsequent development of pneumonia, cerebral oedema and brain herniation.

III. INQUIRY INTO Ms A.T.'S DEATH

A. Inquiry by the St Petersburg Healthcare Committee

29. On 26 May 2006 the applicant applied to the Healthcare Committee of the St Petersburg Government ("the Healthcare Committee") in order to establish the circumstances of her daughter's death and to identify those responsible.

30. On 20 September 2006 the Healthcare Committee's expert clinical commission, having examined the case, found that the clinical trials of asenapine had been conducted in compliance with all the required conditions: the Good Clinical Practice procedures had been followed; Ms A.T. had had indications for the drug to be prescribed; she had consented freely to her participation in the trials; and during the trials there had been no health complications or any other grounds for her exclusion therefrom. The commission found no direct causal link between her death and the taking of asenapine.

31. The commission expressed the view that Ms A.T. might have fallen into a coma because of a pulmonary embolism. As she had been taking hepatotoxic (that is, able to affect the liver) neuroleptics for many years, that could have affected her physical state. Such factors, together with vascular sclerosis, could lead to changes in the blood's ability to clot. According to the experts, the pneumonia which had arisen during the coma could also have

been a result of the pulmonary embolism. The commission concluded that there had been no failings in Ms A.T.'s treatment at the psychiatric hospital.

B. Preliminary police inquiry

1. Opening of the inquiry

32. On 15 May 2006 the applicant wrote to the prosecutor's office of the Primorskiy District of St Petersburg, in an attempt to have criminal proceedings instituted to investigate the circumstances of her daughter's death.

33. A pre-investigation inquiry was commenced in connection with the applicant's complaint. In the context of that inquiry, a number of persons were interviewed, including Mr P., who had been Ms A.T.'s psychiatrist who had invited her to participate in, and had monitored her during, both clinical trials.

34. In one of the interviews Mr P. stated, among other things, that on the basis of the findings of the autopsy report which stated that Ms A.T.'s cardiovascular disease had been at an advanced stage (see paragraph 28 above), it was very likely that she had already had it at the time when she had started participating in the first trial, since such a disease could not have appeared and progressed so significantly within the period when the two clinical trials in question had taken place.

2. Medical expert report of 12 January 2007

35. On 28 December 2006 the prosecutor ordered an expert examination. The question to be addressed by the experts read as follows: "to establish whether 'asenapine' could provoke a heart attack with thrombosis and death".

36. In a report of 12 January 2007, a commission of five experts identified certain shortcomings surrounding the applicant's daughter's participation in the clinical trials of asenapine. In particular, the experts noted that asenapine belonged to a group of drugs that could have a cardiotoxic effect, and that it was essential to keep under observation heart and liver function and blood pressure, however no information regarding any such observation could be found in Ms A.T.'s medical file. The only ECG report available to the experts was dated 10 April 2006, that is when Ms A.T. had already fallen into a coma. Moreover, in the period before her death she had been seen by doctors every third or fourth day instead of the daily check-ups required when a new medicine was being tested.

37. The experts noted that the first clinical trial had revealed various negative side effects in Ms A.T.'s case, such as aggravation of her schizophrenia, insomnia, agitation, anxiety and weight gain. The clinical picture, in conjunction with the cardiotoxic effect of asenapine, could therefore have constituted grounds to exclude the applicant's daughter from

further participation in the trial. The experts also noted that Ms A.T.'s medical documents lacked information about any checks of her cardiovascular system during the second clinical trial of asenapine.

38. The experts attested that Ms A.T.'s coma on 10 April 2006 had been caused by several factors: pneumonia, which had been overlooked by the doctors; the taking of asenapine, which had had a cardiotoxic effect; and a latent cardiovascular disease. They concluded that there was therefore an indirect causal link between her death and the taking of asenapine.

3. Medical expert reports of 10 April and 30 December 2009

39. On 26 March 2009 the investigator asked for a new expert examination in the case. The experts were invited to answer, in particular, the question of whether the treatment strategy for Ms A.T. during the clinical trials of asenapine and when trying to resuscitate her had been correct; and whether there was a causal link between the actions of the psychiatric hospital's personnel – the shortcomings in the course of the two clinical trials identified in the expert report of 12 January 2007 – and her death.

40. In a report of 10 April 2009, a commission composed of four experts again confirmed that there had been various shortcomings as regards Ms A.T.'s participation in the clinical trials of asenapine. In particular, they referred to the lack of general monitoring of the state of her health; a lack of monitoring of her heart and liver function; engaging Ms A.T. for a new trial of asenapine, which was not advised given the possible cardiotoxic effect of the product and the side effects she had experienced during the first trial (aggravation of her schizophrenia, insomnia, agitation, anxiety and weight gain); and the failure to detect her pneumonia in a timely manner. The experts pointed out that no information about Ms A.T. having any physical or laboratory examinations (pulse, blood pressure, temperature, blood and urine tests, and so forth) could be found in her medical file.

41. The experts expressed the opinion that there was a causal link between those shortcomings and Ms A.T.'s death, but that the link was indirect as they could have contributed to the worsening of her cardiovascular and respiratory diseases, with the possibility of an adverse outcome. They also stated that the applicant's daughter's intensive care treatment in the period between 10 and 14 April 2006 had been correct.

42. On 30 December 2009, at the investigator's request, an additional expert report supplementing that of 10 April 2009 was prepared. The questions remained the same, but the commission this time included five experts. They were also provided with some additional material, such as the brochures for the clinical trial of asenapine and the trial report. The additional material mentioned that an order had been inserted in Ms A.T.'s medical file relating to her hospitalisation in May 2005 (see paragraph 25 above), to remedy violations of certain licence requirements. The points of criticism in

the order had included, for example, the fact that of all the required specialists, the patient had been seen only by a gynaecologist. Actual measurements of her blood pressure, temperature, blood and urine test results had also not been found anywhere in the medical files. The conclusions of the additional study were similar to those of the report of 10 April 2009 (see paragraph 41 above).

4. Refusal to open a criminal case

43. On 31 December 2009, after several refusals to open a criminal case and subsequent remittals of the case for additional pre-investigation inquiry, ordered either by a prosecutor or the domestic courts, the investigator in charge yet again refused to institute criminal proceedings for the lack of elements of a crime being present in the relevant doctors' actions.

44. Relying on the statements of the applicant and the relevant health professionals, as well as the expert reports, the investigator pointed out that both the applicant and her daughter had known that the latter had been taking part in clinical trials of a new medicine; and that Ms A.T. had given her express informed consent thereto, as confirmed by her signature on the consent forms of 19 December 2004 and 26 December 2005. The investigator further referred to the expert reports in so far as they pointed to the absence of a direct causal link between Ms A.T.'s death and the shortcomings in the provision of medical services to her which had been identified by the experts. He also relied on the experts' findings stating that the applicant's daughter's intensive care treatment in the period between 10 and 14 April 2006 had been correct. The investigator further mentioned Ms A.T.'s participation in an earlier clinical trial (which does not form part of the present application), stating that "no shortcomings on the part of the doctor in charge had been detected", but remained silent as regards Ms A.T.'s participation in the two clinical trials that had taken place from December 2004 until Ms A.T.'s death on 14 April 2006.

45. The applicant challenged the decision of 31 December 2009 before a court. On 13 August and 5 October 2010 the national courts, at two levels of jurisdiction, dismissed her complaint.

RELEVANT LEGAL FRAMEWORK

I. DOMESTIC LAW

46. Federal Law no. 86-FZ of 22 June 1998 on medicinal products (*Федеральный закон от 22 июня 1998 г. № 86-ФЗ «О лекарственных средствах»*), as in force at the relevant time, provided in section 38 that a clinical trial of a medicine should be performed on the basis of a decision by

a federal executive agency competent to carry out State control and monitoring in that sphere.

47. Section 39 established a procedure to be followed when setting up a clinical trial, and envisaged, in particular, that a clinical trial of medicines could be interrupted if a danger to the participants' lives was detected in the course of such a trial.

48. Section 40 set forth the rights of the participants of the trial. It provided, in particular, that participation should be free and that a participant had the right to refuse further participation in the trial at any stage.

49. For the further application of the above-mentioned legal measure, by Decree no. 266 dated 19 June 2003, the Russian Ministry of Health established the Rules of Clinical Practice in the Russian Federation (*Правила клинической практики в Российской Федерации*).

50. The Rules, as in force at the relevant time, established requirements for the planning, conducting, documenting, and monitoring of clinical trials; were designed to guarantee the protection of the rights, safety and healthcare of those participating in trials; and were compulsory for all parties involved in clinical trials in Russia (rule 1.2).

51. A person enrolled in a trial had to give his or her written consent to participating in it, and that participation was required to be free. A participant had to be informed, *inter alia*, about the tested drug, the nature of the research, and about the expected efficacy, safety and risks for participants. A participant could, at any stage, refuse to participate in the trial (rules 3.1-3.3).

52. A written consent form was to be approved by the Ethics Committee prior to the start of any clinical trial. Information about the trial had to be delivered to potential participants in clear and understandable terms. A potential participant had to be given enough time to make a decision about whether or not to participate in a trial and had to be given access to detailed information about it (rules 4.1-4.9).

53. The doctor heading a study was responsible for ensuring medical assistance in the context of a trial. In particular, such a doctor and/or the relevant healthcare institution was required to provide a participant with necessary medical assistance if any negative effects were revealed during a clinical trial. The doctor heading the study and/or the relevant healthcare institution bore an obligation to inform a participant about the necessity of treating illnesses detected during a clinical trial (rules 5.1-5.3).

54. The doctor responsible for a trial had to recruit participants who could be involved in the clinical trial of a medicinal product on the basis of medical indications (rule 7.13). The doctor heading a study could stop the clinical trial if any danger to the health of participants was identified during the trial (rule 7.15).

II. COUNCIL OF EUROPE MATERIALS

55. The Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine of 1997, also known as the Convention on Human Rights and Biomedicine or the Oviedo Convention (Council of Europe Treaty Series No. 164), is the only binding international treaty in the field, which is ratified by 29 States and signed by 7 others. The Russian Federation has not signed or ratified the Oviedo Convention. Its relevant provisions read as follows:

Article 1 – Purpose and object

"Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine.

Each Party shall take in its internal law the necessary measures to give effect to the provisions of this Convention.

..."

Chapter II – Consent
Article 5 – General rule

"An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it.

This person shall beforehand be given appropriate information as to the purpose and nature of the intervention as well as on its consequences and risks.

The person concerned may freely withdraw consent at any time.

..."

Chapter V – Scientific research
Article 15 – General rule

"Scientific research in the field of biology and medicine shall be carried out freely, subject to the provisions of this Convention and the other legal provisions ensuring the protection of the human being."

Article 16 – Protection of persons undergoing research

"Research on a person may only be undertaken if all the following conditions are met:

i. there is no alternative of comparable effectiveness to research on humans;

ii. the risks which may be incurred by that person are not disproportionate to the potential benefits of the research;

iii. the research project has been approved by the competent body after independent examination of its scientific merit, including assessment of the importance of the aim of the research, and multidisciplinary review of its ethical acceptability;

iv. the persons undergoing research have been informed of their rights and the safeguards prescribed by law for their protection;

v. the necessary consent as provided for under Article 5 has been given expressly, specifically and is documented. Such consent may be freely withdrawn at any time."

THE LAW

I. PRELIMINARY ISSUE

56. The Government contested the standing of Mr Traskunov, who was the applicant's grandson and Ms A.T.'s son (see paragraph 2 above), to pursue the present application on the applicant's behalf. They pointed out that he could have lodged an application with the applicant but had chosen not to do so. He had never lodged any complaints or requests in connection with his mother's death at the domestic level. The Government furthermore pointed out that although the applicant had died on 31 August 2018, the applicant's representative had informed the Court thereof only on 30 January 2020, that is a year and a half later. They argued that the application did not raise any issue of general interest and therefore it should be struck out pursuant to Article 37 § 1 of the Convection.

57. The Court normally permits the next of kin to pursue an application, provided that they have a legitimate interest, where the original applicant died after lodging the application with the Court (see *Adzhigitova and Others v. Russia*, nos. 40165/07 and 2593/08, § 149, 22 June 2021, with further references). Also, human rights cases before the Court generally have a moral dimension and persons near to an applicant may thus have a legitimate interest in ensuring that justice is done, even after the applicant's death (see *Todorov and Others v. Bulgaria*, nos. 50705/11 and 6 others, § 126, 13 July 2021, with further references).

58. The Court does not see any special circumstances in the present case so as to depart from its established case-law, and is prepared to accept that the applicant's grandson can pursue the application initially brought by the applicant. Consequently, the Government's objection must be dismissed (see *Novaković v. Croatia*, no. 73544/14, § 34, 17 December 2020, and *Hristozov and Others v. Bulgaria*, nos. 47039/11 and 358/12, §§ 68-75, ECHR 2012 (extracts)).

59. For practical reasons, Ms Traskunova will continue to be called "the applicant" in this judgment, although Mr Traskunov is now to be regarded as such (see *Dalban v. Romania* [GC], no. 28114/95, § 1, ECHR 1999-VI).

II. ALLEGED VIOLATION OF ARTICLE 2 OF THE CONVENTION

60. The applicant complained that health professionals had acted in violation of the relevant regulations for clinical trials and in breach of their duty to ensure her daughter's safety in such clinical trials, which had brought about her death, and that she had not received an adequate judicial response in that connection. She relied on Article 2 of the Convention, which, in its relevant part, reads as follows:

> "1. Everyone's right to life shall be protected by law ..."

A. Admissibility

61. The Court notes that the application is neither manifestly ill-founded nor inadmissible on any other grounds listed in Article 35 of the Convention. It must therefore be declared admissible.

B. Merits

1. Submissions by the parties

62. The applicant argued that the doctors in the present case had acted in violation of the applicable regulations and had breached their obligation to ensure Ms A.T.'s safety in clinical trials. They had put her life at risk by their failure to carry out a comprehensive medical examination of her state of health prior to admitting her to participate in the medical trials, to duly monitor her condition throughout the trials, and to discontinue the trials as soon as side effects had appeared.

63. More specifically, Ms A.T. had been involved in the clinical trials without giving her informed consent. In that connection, the applicant expressed doubts regarding the authenticity of Ms A.T.'s signature on the consent form. She also argued that even assuming that it had indeed been Ms A.T. who had signed the consent form, she had only consented to participate in the first clinical trial (the one that had ended in 2005), and she had not given her consent to participate in the following clinical trial.

64. Moreover, the applicant's daughter had participated in one clinical trial following another without a necessary break. With reference to the relevant medical evidence (see paragraphs 37 and 40 above), the applicant argued that Ms A.T. should not have been admitted to the second trial given her progressing generalised sclerosis with lesion of the heart and brain vessels, which disease had eventually led to her death. She stressed that Ms A.T.'s medical file contained no information that the necessary examination of her health as required by the relevant regulations relating to the clinical trials had ever been performed. She also argued that the health professionals had not detected Ms A.T.'s pneumonia in time, with the result that she had not received adequate treatment.

65. The applicant further challenged as unobjective the checks that had been carried out into the circumstances of Ms A.T.'s death, and argued that by refusing to institute criminal proceedings, the authorities had breached their procedural obligation under Article 2 of the Convention.

66. The Government argued that the circumstances of the present case did not reveal any failure on their part to comply with their obligations under Article 2 of the Convention. They pointed out, in particular, that Ms A.T. had given her consent to her participation in the relevant clinical trials by signing the consent form each time, of which the patient information leaflet had been an integral part. Those documents had provided full information regarding the clinical trials and also indicated that written consent was to be given only after participants had obtained full information and had received replies to all the questions they might have. In particular, the documents had stated that asenapine was a new medicine and that there was no complete information as regards its potential effects on a human; at the same time, the known side effects had been clearly listed. By signing the relevant documents, Ms A.T. had confirmed that she had been apprised of the information in question. In addition, she had been informed that her participation in the trials was voluntary and that it was open to her to withdraw at any moment. The Government stressed that Ms A.T. had retained her legal capacity at all times and therefore had been fully able to give her consent to participation in the trials. They also argued that the authenticity of Ms A.T.'s signature on both consent forms had been confirmed by experts during the preliminary checks into the circumstances of her death.

67. The Government furthermore submitted, without however producing any medical documents, that, prior to her participation in the clinical trials, the applicant's daughter had undergone a medical examination which had not revealed any health issues or counter-indications to her participation in the clinical trials. Also, throughout the entire period of both clinical trials her physical health condition had remained stable, and she had not made any complaints. After Ms A.T.'s health condition had rapidly deteriorated on 10 April 2006, she had immediately been resuscitated, stabilised and transferred to an intensive care unit, where she had died four days later despite the health professionals' efforts. A number of medical forensic examinations carried out had not established any direct causal link between the fact that Ms A.T. had been taking asenapine and her death. A preliminary inquiry carried out in connection with the incident had not established elements of criminal offences in the actions of the health professionals who had been monitoring Ms A.T. during her participation in the clinical trials.

2. The Court's assessment

68. The applicant's complaint relating to the State's obligations under Article 2 of the Convention has two limbs: substantive and procedural. The

Court will address them in turn (see, for a similar approach, *Sarishvili-Bolkvadze v. Georgia*, no. 58240/08, § 66, 19 July 2018).

(a) The substantive aspect

(i) General principles

69. The Court reiterates that in the context of healthcare, the States' substantive positive obligations relating to medical treatment are limited to a duty to regulate, that is to say, a duty to put in place an effective regulatory framework compelling hospitals, whether private or public, to adopt appropriate measures for the protection of patients' lives. The Court has, moreover, emphasised that the States' obligation to regulate must be understood in a broader sense which includes the duty to ensure the effective functioning of that regulatory framework. The regulatory duties thus encompass necessary measures to ensure implementation, including supervision and enforcement (see *Lopes de Sousa Fernandes v. Portugal* [GC], no. 56080/13, §§ 186 and 189, 19 December 2017 and *Sarishvili-Bolkvadze,* cited above, § 74; see also, for the summary of the applicable principles regarding effective functioning of relevant framework in the broader context of unintentional taking of life, *Smiljanić v. Croatia*, no. 35983/14, § 66, 25 March 2021).

70. The Court has also emphasised that it is important for individuals facing risks to their health to have access to information enabling them to assess those risks. It has held in particular that States are bound to adopt the necessary regulatory measures to ensure that doctors consider the foreseeable impact of a planned medical procedure on their patients' physical integrity and to inform patients of these consequences beforehand in such a way that the latter are able to give informed consent (see *Ioniță v. Romania*, no. 81270/12, § 84, 10 January 2017, in the context of the Article 2 complaint; and *Csoma v. Romania*, no. 8759/05, § 42, 15 January 2013; and *Botoyan v. Armenia*, no. 5766/17, § 93, 8 February 2022, in the context of the Article 8 complaint).

(ii) Application of those principles in the present case

71. In the present case, the applicant's daughter, Ms A.T., was invited to take part, and participated, in two consecutive clinical trials of an experimental medicine in the period from December 2004 to April 2006. While participating in the second clinical trial, she fell into a coma on 10 April and died on 14 April 2006. Three expert reports eventually revealed that Ms A.T. had had an undetected cardiovascular disease and that the taking of the experimental medicine in question, which had a cardiotoxic effect, could have aggravated her condition and thus could have indirectly led to her death (see paragraphs 38, 40-41 and 42 above).

72. The Court observes at the outset that the circumstances of the present case go beyond the scope of a mere medical negligence. What is at stake in the case at hand is Ms A.T. 's safety during clinical trials of a new medicine approved by the authorities. In that connection, the Court reiterates that it is in the nature of experimental medicinal products that their quality, efficacy and safety are open to doubt (see *Hristozov and Others*, cited above, § 120, in the context of the complaint under Article 8). There can be no doubt that clinical trials of such products entail inherent risks to their participants' health and lives, and are, as such, a form of dangerous activity which must engage States' positive obligation to adopt and implement measures designed to ensure the safety of those involved in such trials. The Court reiterates in this connection that situations which may engage States' positive obligations are not exhaustive, and it has found that the positive obligation under Article 2 must be construed as applying in the context of any activity, whether public or not, in which the right to life may be at stake (see *Vardosanidze v. Georgia*, no. 43881/10, § 53, 7 May 2020).

73. In the particular context of dangerous activities, the Court has placed special emphasis on regulations geared to the special features of the activity in question, particularly with regard to the level of the potential risk to human lives. They must govern the licensing, setting up, operation, security and supervision of the activity and must make it compulsory for all those concerned to take practical measures to ensure the effective protection of citizens whose lives might be endangered by the inherent risks (see, as a recent authority, *Smiljanić*, cited above, § 67, with further references). Whenever a State undertakes or organises dangerous activities, or authorises them, it must ensure through a system of rules and through sufficient control that the risk is reduced to a reasonable minimum. If nevertheless damage arises, it will only amount to a breach of the State's positive obligations if it was due to insufficient regulations or insufficient control, but not if the damage was caused through the negligent conduct of an individual or the concatenation of unfortunate events (see *Stoyanovi v. Bulgaria*, no. 42980/04, § 61, 9 November 2010).

74. The key question in the present case is thus whether, when engaging the applicant's daughter in clinical trials of a new medicinal product, the authorities fulfilled their positive obligation to ensure, through a system of rules and through sufficient control, that the risk to her life was reduced to a reasonable minimum (see paragraph 73 above).

75. The Court observes that the regulatory framework applicable in the respondent State at the relevant time is not as such in issue in the present case. It notes, in particular, that safeguards and procedures to be followed when organising and carrying out a clinical trial were established in a relevant legal measure and their practical implementation was established in a relevant by-law (see paragraphs 46-54 above). The Court does not discern any

deficiencies in this respect that could entail a violation of the State's positive obligations under Article 2 of the Convention.

76. The practical implementation of that legal framework in the present case is, however, open to doubt. The Court notes, firstly, that the relevant protocols required that a comprehensive medical check-up of participants be carried out prior to their admission to the trial, and that such admission was subject to participants being in satisfactory health (see paragraphs 9 and 19 above). As the experts eventually pointed out, in the absence of any relevant information in Ms A.T.'s medical file, it does not appear that any such examination was carried out before she was admitted to the clinical trials (see paragraph 36 above). Moreover, the expert reports consistently attest to the lack of any information regarding monitoring of Ms A.T.'s state of health throughout the whole period of both clinical trials (see paragraphs 36-37, 40 and 42 above). Indeed, it appears that the first electrocardiogram was taken only after the applicant's daughter had fallen into coma (see paragraph 36 above). It is also relevant that after the first clinical trial the applicant's daughter displayed symptoms which argued against her participation in the second clinical trial. Nevertheless, she was invited to take part therein without the state of her health being duly examined (see paragraphs 37 and 40 above).

77. It is not for the Court to speculate whether Ms A.T.'s cardiovascular disease, which she had most likely already had before the first clinical trial (see paragraph 34 above), could have been detected if she had undergone a comprehensive medical examination before she was admitted to participate in the trials, and if the state of her health had been duly monitored during the trials. However, bearing in mind what was at stake for Ms A.T., the Court finds it unacceptable that she was admitted to, and continued to participate in, the clinical trials in breach of the rules and safeguards created by the domestic system itself (compare *Csoma*, cited above, § 57).

78. Secondly, the Court takes issue with Ms A.T.'s consent to her participation in the clinical trials. It is true that prior to each of the two trials she signed a consent form, of which a patient leaflet listing possible risks was an integral part (see paragraphs 22 and 26 above); and that, at least formally, she was competent to do so since she retained her legal capacity at all times (see paragraph 6 above). The Court is thus prepared to accept that the applicant's daughter can be regarded as having been duly informed about general health risks inherent in the trials. At the same time, the above-mentioned expert findings make it clear that the health professionals in charge of the clinical trials remained unaware of Ms A.T.'s actual state of health, including her cardiovascular disease, as a result of their failure to perform the most basic medical check-ups (see paragraph 76 above). Ms A.T. therefore did not receive full information which would have enabled her to assess potential risks in her particular situation, and to make an informed choice regarding her participation in either of the two clinical trials (see paragraph 70 above).

79. The Court furthermore notes that Ms A.T. suffered from a serious mental illness for many years. It considers that, in view of their vulnerability, it is important that mentally ill patients enjoy a heightened protection and that their participation in clinical trials be accompanied by particularly strong safeguards, with due account given to the particularities of their mental condition and its evolution over time. It is essential, in particular, that such patients' decision-making capacity be objectively established in order to remove the risk that they have given their consent without a full understanding of what was involved (compare *Arskaya v. Ukraine*, no. 45076/05, §§ 87-90, 5 December 2013). The facts of the case reveal that Ms A.T.'s mental illness worsened during the first clinical trial (see paragraphs 24-25 above). It is noteworthy in this connection that a mental illness such as the one which the applicant's daughter suffered from could manifest itself, among other things by disordered thinking and difficulties in communicating with others (see paragraphs 5 and 9 above). Yet there is no evidence in the case file that, when inviting her to take part in the second clinical trial and accepting her consent thereto, the doctors in charge duly assessed whether the applicant's daughter was indeed able to take rational decisions regarding her continued participation in the trial.

80. Bearing in mind the above shortcomings, Ms A.T.'s vulnerability, and the serious consequences of those decisions for her, the Court finds that the practical implementation of the existing framework was deficient and that the existing guarantees ensuring the informed consent of participants of clinical trials were not complied with in the present case, with the result that there has been a breach the State's substantive positive obligations under Article 2 of the Convention.

(b) The procedural aspect

(i) General principles

81. The procedural obligation of Article 2 in the context of health care requires States to set up an effective and independent judicial system so that the cause of death of patients in the care of the medical profession, whether in the public or the private sector, can be determined and those responsible made accountable. In some exceptional situations, where the fault attributable to the healthcare providers went beyond a mere error or medical negligence, the Court has considered that compliance with the procedural obligation must include recourse to criminal law. In all other cases where the infringement of the right to life or to personal integrity is not caused intentionally, the procedural obligation imposed by Article 2 does not necessarily require the provision of a criminal-law remedy (see *Lopes de Sousa Fernandes*, cited above, §§ 214-15). That obligation will be satisfied if the legal system affords victims a remedy in the civil courts, either alone or in conjunction with a remedy in the criminal courts, enabling any responsibility of the doctors

concerned to be established and any appropriate civil redress to be obtained. Disciplinary measures may also be envisaged (see, among many other authorities, *Ioniță*, cited above, § 73).

(ii) Application of those principles in the present case

82. The Court observes that the applicant's attempts to have disciplinary proceedings instituted against those responsible were unsuccessful as the Healthcare Committee established no defects in the conduct of the clinical trials and the treatment of her daughter (see paragraphs 29-31 above).

83. The applicant also sought to have criminal proceedings initiated in connection with her daughter's death. After several rounds of pre-investigation inquiry, her request was ultimately refused. In the latest decision, the investigator in charge essentially referred to Ms A.T.'s written consent to both clinical trials; the fact that no defects had been identified in her intensive care treatment after she had fallen into a coma, or in a certain clinical trial in which she had participated earlier; and the experts' findings about the absence of a direct causal link between her participation in the two clinical trials under examination and her death (see paragraph 44 above). That decision was later upheld by the domestic courts (see paragraph 45 above).

84. The Court notes that the national authorities did not clarify the relevance of an earlier clinical trial in the context of the applicant's complaint, which related to the two trials that had taken place in the period from December 2004 to April 2006. They furthermore left without any consideration the experts' conclusions regarding the apparent lack of a comprehensive medical examination of Ms A.T. prior to, or monitoring of her health during, either of the two clinical trials at hand, which was indicative of the breach of the relevant legal framework which was in place. They also made no assessment of the experts' findings in so far as they pointed to counter-indications to Ms A.T.'s participation in the second clinical trial.

85. It is not the Court's role to determine whether the law-enforcement authorities correctly applied the domestic criminal law, or indeed whether the doctors in charge should have been held criminally liable in the present case; what is in issue is not individual criminal-law liability, but the State's responsibility under the Convention. In that connection, the Court considers that for the assessment of the case it was relevant to examine whether the clinical trials in question had been carried out in compliance with the relevant legal framework, and in particular had respected the safeguards in place (compare *Ioniță*, cited above, § 88). In the absence of any such assessment by the authorities, the remedy in question cannot be said to have been effective in the circumstances of the present case.

86. Lastly, the Court notes that the applicant has never brought a civil claim against the relevant healthcare professionals or the institution. The Government did not contend that she could have effectively pursued her

relevant complaint outside the framework of criminal and disciplinary proceedings (compare *Bilbija and Blažević v. Croatia*, no. 62870/13, § 104, 12 January 2016). It is thus unclear whether any such avenue was available to her and, if so, whether it would have achieved the result sought by Article 2 of the Convention by establishing the circumstances surrounding the death of the applicant's daughter, holding those responsible accountable and providing appropriate redress to the applicant (see *Movsesyan v. Armenia*, no. 27524/09, § 74, 16 November 2017, and *Botoyan*, cited above, § 94). It is furthermore unclear, in the absence of any submissions on this point from the Government, whether a civil-law remedy would have pursued the same objective as the criminal-law remedy, or, in other words, whether it would have added any essential elements that were unavailable through the use of the criminal-law remedy (compare and contrast *Dumpe v. Latvia* (dec.), no. 71506/13, §§ 61 and 70-77, 16 October 2018, and *Milić v. Serbia* (dec.), no. 62876/15, §§ 59-60, 21 May 2019).

(c) Conclusion

87. The foregoing considerations are sufficient to enable the Court to conclude that the respondent State has failed to comply with its substantive and procedural obligations under Article 2 of the Convention. In particular, it has not ensured an effective implementation and functioning of the legal framework with a view to protecting the right to life of the applicant's daughter – a mentally ill and thus vulnerable individual – in the context of clinical trials of experimental medicinal products, and it has not provided an adequate judicial response to the applicant in that connection.

88. There has accordingly been a violation of Article 2 of the Convention.

III. APPLICATION OF ARTICLE 41 OF THE CONVENTION

89. Article 41 of the Convention provides:

> "If the Court finds that there has been a violation of the Convention or the Protocols thereto, and if the internal law of the High Contracting Party concerned allows only partial reparation to be made, the Court shall, if necessary, afford just satisfaction to the injured party."

A. Damage

90. The applicant claimed 25,000 euros (EUR) in respect of non-pecuniary damage.

91. The Government submitted that if the Court were to find a violation in the present case, Article 41 of the Convention should be applied in compliance with the Court's well-established case-law.

92. The Court awards the applicant EUR 20,000 in respect of non-pecuniary damage, plus any tax that may be chargeable.

B. Costs and expenses

93. The applicant also claimed 10,753 Russian roubles (approximately EUR 270) for the costs and expenses incurred before the Court.

94. The Government made no particular submissions on this point.

95. According to the Court's case-law, an applicant is entitled to the reimbursement of costs and expenses only in so far as it has been shown that these were actually and necessarily incurred and are reasonable as to quantum. In the present case, regard being had to the documents in its possession and the above criteria, the Court considers it reasonable to grant the applicant's relevant claim in full. It thus awards the sum of EUR 270 for the proceedings before the Court, plus any tax that may be chargeable to the applicant.

C. Default interest

96. The Court considers it appropriate that the default interest rate should be based on the marginal lending rate of the European Central Bank, to which should be added three percentage points.

FOR THESE REASONS, THE COURT, UNANIMOUSLY,

1. *Declares* the application admissible;

2. *Holds* that there has been a violation of Article 2 of the Convention;

3. *Holds*
   (a) that the respondent State is to pay the applicant, within three months from the date on which the judgment becomes final in accordance with Article 44 § 2 of the Convention, the following amounts, to be converted into the currency of the respondent State at the rate applicable at the date of settlement:
      (i) EUR 20,000 (twenty thousand euros), plus any tax that may be chargeable, in respect of non-pecuniary damage;
      (ii) EUR 270 (two hundred and seventy euros), plus any tax that may be chargeable to the applicant, in respect of costs and expenses;
   (b) that from the expiry of the above-mentioned three months until settlement simple interest shall be payable on the above amounts at a rate equal to the marginal lending rate of the European Central Bank during the default period plus three percentage points;

4. *Dismisses* the remainder of the applicant's claim for just satisfaction.

Done in English, and notified in writing on 30 August 2022, pursuant to Rule 77 §§ 2 and 3 of the Rules of Court.

Olga Chernishova	Georges Ravarani
Deputy Registrar	President

In accordance with Article 45 § 2 of the Convention and Rule 74 § 2 of the Rules of Court, the separate opinion of Judge Serghides is annexed to this judgment.

G.R.
O.C.

CONCURRING OPINION OF JUDGE SERGHIDES

1. The present judgment finds that the respondent State failed to comply with its substantive and procedural obligations under Article 2 of the Convention to protect the life of the applicant's daughter, who was suffering from schizophrenia and eventually died (see paragraph 87 and point 2 of the operative part of the judgment).

2. The purpose of this concurring opinion is to venture deeper into the conceptual and operational frameworks of positive obligations in relation to the principle of effectiveness, in order to show the origin of positive obligations, in the Court's case-law, and the extent to which they protect the right to life under Article 2. Most importantly, it argues that one cannot deal with positive obligations without examining them in the context of the principle of effectiveness, to which the judgment makes no reference.

3. In my view, "[t]he relationship between positive obligations and the principle of effectiveness can be said to resemble the affinity between offspring and their forebears"[1]. The principle of effectiveness is both a significant method of interpretation and a norm of international law inherent in each Convention provision, including Article 2[2]. As a method of interpretation, the said principle requires that Convention provisions and the rights secured therein be interpreted in a practical and effective manner and be given "their fullest wight and effect consistent with their text and object"[3]. As a norm of international law, the said principle maintains that international legal rules, including Convention provisions, must be effective and treated as such. The doctrine of positive obligations springs from the principle of effectiveness[4], being a sub-capacity thereof, and, as such, it is both a sub-method of interpretation and a sub-norm of international law. There is an intimate interrelationship between the two capacities and sub-capacities of the principle of effectiveness and it is also mutually enriching[5]. In my view, the principle of effectiveness and the doctrine of positive obligations have the same DNA and that is why I submit that the degree and extent of protection of a right, either directly through the principle or indirectly through the doctrine of positive obligations, should be the same; thus, a full and broad

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[1] See my concurring opinion in *Güzelyurtlu and Others v. Cyprus and Turkey* [GC], no. 36925/07, 29 January 2019, at § 7 of the opinion.

[2] See on the dual capacity of the principle of effectiveness in Georgios A. Serghides, *The Principle of Effectiveness and its Overarching Role in the Interpretation and Application of the ECHR: The Norm of all Norms and the Method of All Methods,* Strasbourg, 2022, pp. 33-144.

[3] See proposed Article 72 by Sir Humphrey Waldock, special rapporteur of the first draft of what became the Vienna Convention on the Law of Treaties; J. Merrills, *The Development of International Law by the European Court of Human Rights,* 2nd edn., Manchester, 1996; Serghides, *op. cit.*, pp. 97-98.

[4] Serghides, *op. cit.*, pp. 329-334, 583-584.

[5] *Ibid.,* pp. 126-129, 326-329, 584.

protection, as the applicant has indeed been offered by the Court in the present case.

4. As rightly pointed out by the former President of the Court, Linos-Alexander Sicilianos, "as a whole the case-law of the Court in respect of positive obligations under the substantive limb of Article 2 constitutes an important development in the field of prevention of human rights violations"[6]. Indeed, the doctrine of positive obligations of member States constitutes one of the most significant developments in the fields of human rights protection and one of the best demonstrations of the application of the doctrine that the Convention is a living instrument that has to be adapted and interpreted according to present-day conditions[7].

5. Though finding a violation of either the substantive or procedural limbs would be sufficient for a breach of Article 2 in the present case, the judgment rightly examines and finds a violation of both the substantive and procedural limbs of that Article. This is in order to ensure the full, complete and effective protection of the life of the applicant's daughter and to prevent any perforation of or leakage from the protective shield of that right, and, at the same time, demonstrating the overall or holistic responsibility of the respondent State to practically and effectively protect the right of the applicant's daughter.

6. Although, as has been said above, the judgment rightly deals with and finds a non-fulfilment of positive obligations, both substantively and procedurally, and also correctly reiterates that these obligations are not exhaustive (see paragraph 72), it regrettably, however, omits to refer directly to the principle of effectiveness as an overarching and ubiquitous Convention principle and as the foundation stone, source or matrix of positive obligations. Such a direct reference to the principle of effectiveness by the Court would ensure that it does not divert its attention away from the need to protect the core of the right or from the central issues surrounding it or stemming from

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[6] See Linos-Alexander Sicilianos, "Out of harm's way: positive obligations under Article 2 of the European Convention on Human Rights", Lawrence Early, Anna Austin, Clare Ovey and Olga Chernishova (eds), *The Right to Life under Article 2 of the European Convention on Human Rights: Twenty Years of Legal Developments since McCann v. the United Kingdom: In Honour of Michael O'Boyle,* Oisterwijk, 2016, 29, at p. 44.

[7] Interestingly, it was in 1978, in *Tyrer v. the United Kingdom* (25 April 1978, Series A no. 26), a judgment prohibiting judicial corporal punishment, that the Court held for the first time that the Convention was a living instrument to be interpreted in the light of present-day conditions; and ever since, this has been repeatedly applied in the case-law of the Court. It is to be noted, however, that the doctrine of positive obligations was first enunciated by the Court, about 10 years before the first explicit reference to the living instrument doctrine, namely in 1968 in the "*Belgian linguistic case*" (*Case "relating to certain aspects of the laws on the use of languages in education in Belgium"* (merits), 23 July 1968, Series A no. 6). If one considers that the establishment and development of positive obligations in the case-law of the Court is an example of the application of the living instrument doctrine, then one could interestingly remark that positive obligations had appeared first, and many years before the living instrument doctrine was crystallised by the Court. See Serghides, *op. cit.*, pp. 594-595.

it, such as that of positive obligations. This would also help the Court to be constantly mindful of the *raison d'être* of the Convention and indeed of its mission, namely the practical and effective protection of human rights[8] and of why it is dealing with positive obligations. It is not, in my humble view, sufficient to say, as the judgment confines itself to saying (see paragraphs 73, 81, 85 and 87), that the substantive and procedural obligations should be fulfilled effectively, without explaining, at the same time, that this should be so in order for the right in question to be practical and effective, as required by the principle of effectiveness.

7. The vulnerability of the applicant's daughter, who is suffering from schizophrenia, is an even more significant element to consider when dealing with the practical and effective interpretation, application and safeguarding of her rights. As such, it is imperative to make a direct reference to the principle of effectiveness. A direct reference to this principle was thus made in my opinion in *Savran v. Denmark*[9], regarding an impugned violation of the Article 3 right of a person who was suffering from schizophrenia and who was eventually expelled to another country with the risk of a deterioration in his mental condition. In that case, contrary to the decision of the majority, concluding that there had been no violation of Article 3, I based my partly concurring and partly dissenting opinion on the principle of effectiveness, which assisted me in finding a violation of that provision. Fortunately, in the present case, the Court not only acknowledged the seriousness of schizophrenia as a mental condition which might lead to death, but also found a violation of Article 2, rendering the respondent State responsible for not fulfilling its positive obligation to protect the life of the applicant's daughter. But for the death of the applicant's daughter, however, it is uncertain whether the Court in the present case would have come to the same conclusion and have found a violation of Article 2, unless it had focussed its examination on the principle of effectiveness.

[8] See also § 6 of my concurring opinion in *Mihalache v. Romania* [GC], no. 54012/10, 8 July 2019.
[9] [GC], no. 57467/15, 7 December 2021.