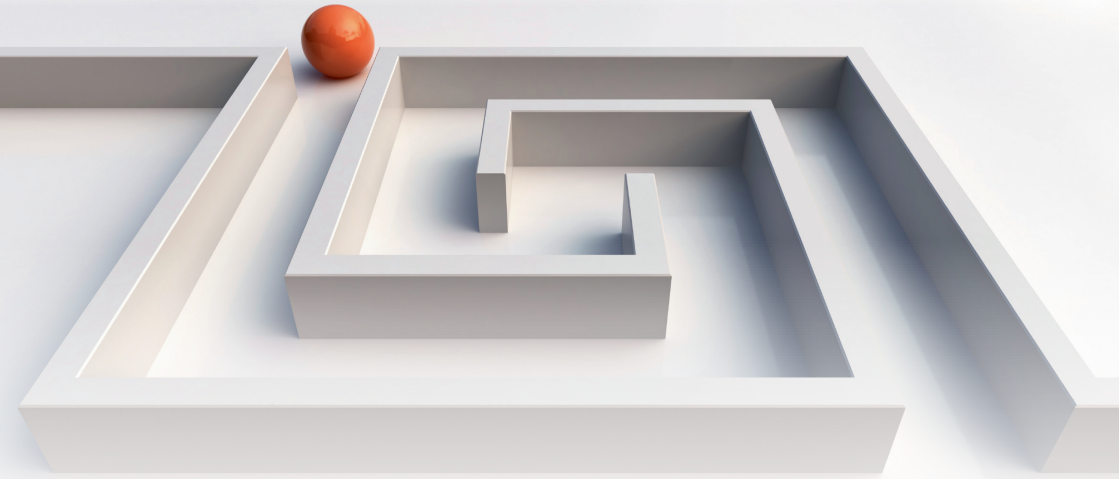
THE ORPHACOL SAGA

How a small pharmaceutical laboratory stood up for its rights against the European Commission to obtain marketing authorisation for an orphan medicine

A 1,000-DAY BATTLE IN THE LABYRINTH OF POST-LISBON COMITOLOGY.



An extract from

« COMITOLOGY: HIJACKING EUROPEAN POWER? »

by Daniel Guéguen
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A kind of murky trench warfare

As we approach the end of «*Comitology: Hijacking European Power?*», it should be clear that primary legislation makes up 4% of the EU acquis, whereas secondary legislation (Regulatory Procedure with Scrutiny, delegated acts, implementing acts) represents 96%. Curiously, all lobbying cases analysed in university courses or during European affairs trainings are based on primary legislation, as if secondary legislation, which regulates technical and administrative issues, was only of minor interest to academics and professionals.

Indeed, for primary legislation, the three Institutions act out their roles in an 'open air theatre', where they have the help of their working groups, committees and experts. The media takes an interest, lobbyists are active; everyone becomes a player on the EU scene. One could call this 'classical lobbying', or even 'diplomatic lobbying'.

For secondary legislation however, nothing of the kind. Miles away from news and media, adopted via obscure procedures; there is no transparency or diplomacy here. Lobbying secondary legislation is a struggle between a challenger – generally a company, sometimes an SME – defending a file (perhaps marginal at first glance, but often essential for the company) against a clear opponent – generally the European Commission, or more specifically, a Unit within one of its twenty-seven Directorates-General.

Here, we are in a kind of murky trench warfare. To illustrate how this battle unfolds from start to finish, there is no better example than the Orphacol file. More a thriller than a lobbying case, it has all the ingredients of an 'EU psychodrama'.

Orphacol is the tale of a 1,000-day battle between the European Commission's Directorate-General for Health and Consumers (DG SANCO) and CTRS, a small pharmaceutical laboratory. In this tale, we encounter two judgments of the EU Court of Justice; a media saga where, for the first time, specific civil servants are named and shamed; an American competitor controlled by the Seventh-day Adventist Church; and finally, after three years of effort, an incredible outcome where CTRS emerges victorious with the unanimous support of all twenty-eight Member States.

A product resulting from clinical research by the Assistance Publique des Hôpitaux de Paris

Orphacol was originally the result of a transatlantic collaboration between Cincinnati Hospital in the USA and the Kremlin-Bicêtre Hospital in France – two institutions of very high reputation. At the beginning of the 1990s, the two medical research centres began developing an active substance – cholic acid – capable of curing a liver enzyme deficiency in young children on a lasting basis.

Before Orphacol, the only treatment for these very young patients (three to nine months old) was a liver transplant. Without a transplant, the illness is fatal. Thanks to Orphacol, a patient will survive by taking a capsule every day for the rest of his or her life. The number of patients was extremely low (estimated at less than a hundred in the whole of Europe) but the controlled delivery of this treatment produced 100% positive results. No contraindication, relapses or liver transplants were observed. Three young women treated with Orphacol gave birth to seven children, all in perfect health.

In 2007, with a record of around fifteen years of treatment, the Assistance publique des hôpitaux de Paris (the umbrella body for public hospitals in the Paris area) decided, on the basis of a public-private partnership, to select a private company to make the most of the research and bring the product onto the market. CTRS, a small laboratory specialised in orphan medicines, was chosen. For your information, CTRS – founded by a team of doctors, pharmacists and biologists – had a turnover of € 5 million in 2013. That is right: € 5 million, not € 5 billion! CTRS is a very small company.

Once selected by this Parisian body, CTRS now had to submit an application for marketing authorisation (MA) to the European Medicines Agency (EMA) in London via a centralised EU procedure (compulsory for orphan medicines), which begins with the issuing of a scientific opinion.

DG SANCO disputes the EMA's positive opinion from the outset

In October 2009, the EMA sent the application for marketing authorisation to its specialised committee – the Committee for Medicinal Products for Human Use (CHMP). Composed of highly qualified experts from every Member State, the body issued in December 2010 a unanimously positive opinion in favour of marketing authorisation for Orphacol. The medicine was qualified by experts in the CHMP as a "life-saving treatment". In 2010, the EMA also ranked Orphacol among thirteen products of major interest for public health.

In the majority of cases, a positive EMA opinion leads almost automatically to the drawing up by the Commission of a draft decision granting marketing authorisation for the product in question.

For Orphacol however, this classical scenario went out the window. Even though the EMA's opinion was unanimous, DG SANCO was not satisfied.

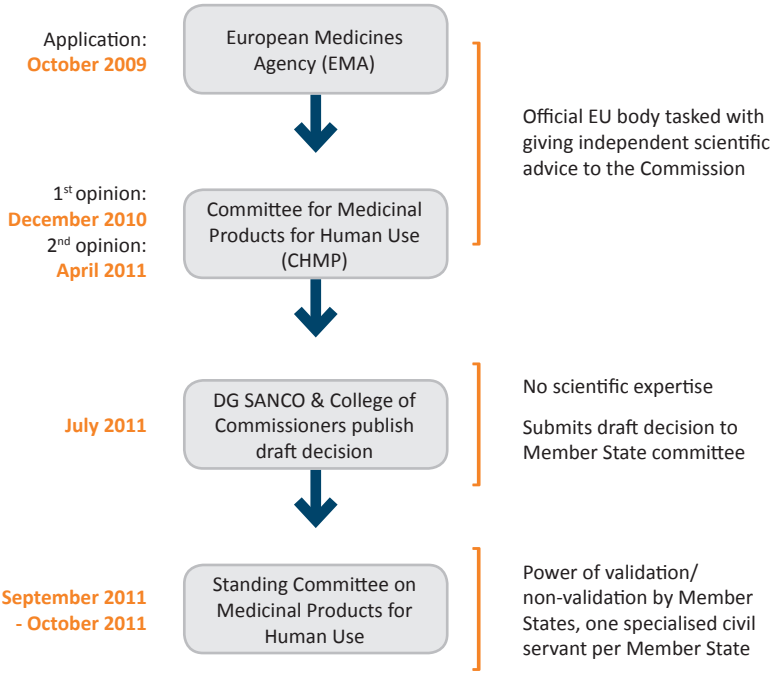
In defiance of the experts' opinion, it judged that Orphacol had not been subjected to any clinical tests and therefore was not entitled to an MA. In response, CTRS stated that the issue of clinical tests was irrelevant, since there had been "Well-Established Use" of the medicine since 1993 without any complications.

It also added that the carrying out of clinical tests would mean dividing the patients (twenty-one at the time) into two groups, with the first receiving a placebo and the second continuing to be treated with Orphacol. As a consequence, the first group would be condemned either to undergo a liver transplant or die. Truly surreal!

CTRS's arguments fell on deaf ears. At the beginning of 2011, following various exchanges between the Commission and the EMA, of which CTRS was not informed, DG SANCO (possessing no scientific expertise, which is what the EMA is there for!) asked the Agency to re-evaluate its conclusions and issue a new opinion. **In April 2011, this second opinion, an identical twin of the first, was – once again – adopted unanimously by the EMA, confirming the latter's wish to see marketing authorisation granted to this miracle medicine.**

Statistics published by the EMA are revealing. In the past four years, only 7% of its opinions have been subject to re-examination, all of which were requested by the applicant itself. Practically never by DG SANCO!

Marketing Authorisation for Orphacol: The Preliminary Steps



Why such determination to block Orphacol from the beginning?

As I pointed out above, a positive – let alone unanimous – opinion of the European Medicines Agency leads, in practice, almost automatically to the granting of marketing authorisation by the European Commission.

From the beginning, Orphacol was a case apart. Not only was the EMA asked to give a second opinion, but even the issuing of two unanimous opinions in favour of Orphacol was not enough to change DG SANCO's mind. **Far from following the EMA's conclusions, on 7 July 2011 DG SANCO, and then the College of Commissioners, published a draft decision (in this case, an "Implementing Decision") refusing marketing authorisation for Orphacol. This was unheard of!**

The draft anti-Orphacol decision, which deliberately ignored the two EMA opinions, was then submitted in the middle of the summer period for the approval of the Member States via a simple written procedure. In other words, the Commission would not have to hold an actual meeting of the Standing Committee on Medicinal Products for Human Use. Composed of one specialised civil servant per Member State, the role of this Committee is either to approve or reject draft implementing acts of the Commission. In Brussels language, we call this a **'comitology committee'**.

It would make sense to use the written procedure whenever the Commission is simply giving effect to the opinion of EMA experts. However, when the Commission decides to ignore two unanimously positive opinions of scientists, resorting to the written procedure seems, at the very least, audacious. It was as if DG SANCO was trying to avoid alerting the Member States and keep them in the dark about the refusal to authorise Orphacol.

Two Member States, however, opposed the use of the written procedure. This forced the Commission to convene a meeting of the Standing Committee.

Why such determination to block Orphacol from the very start? After a 1,000-day battle, there is still no clear answer to this question. At the very least, we have some clues: most notably, the presence of a mysterious American competitor, a company called Asklepion Pharmaceuticals.

As CTRS would find out later, this company had been in contact with DG SANCO since January 2011, providing arguments that were subsequently used by the Commission in its draft decision of 7 July 2011.

Around the same time, CTRS learned that Asklepion Pharmaceuticals is financially controlled by the Seventh-day Adventist Church – information that, incidentally, was completely public.

There is no doubt that the odds were stacked against Orphacol from day one, given the many obstacles that would be laid in its path. What is also certain is that DG SANCO officials in charge of the file, or any high-ranking figures within the Commission, would have been wrong to think for one second that CTRS, this small lab, would lie down and accept a decision it considered so unfair, unethical and scientifically unfounded.

CTRS and Asklepion Pharmaceuticals: Two companies competing for one exclusive MA

Under EU Regulation 726/2004 (authorisation of human and veterinary medicines), a marketing authorisation for orphan medicines provides for a 'ten-year exclusivity' rule, which is intended to encourage innovation and development of new medicines for rare diseases. As CTRS and Asklepion Pharmaceuticals were both competing for the MA, only one of the two companies would be able to obtain it and therefore benefit from an exclusive right to market the product throughout the EU for a period of ten years.

The Commission submits a draft decision rejecting MA for Orphacol to the Member States under the new post-Lisbon comitology

The Lisbon Treaty is the distant successor to the draft Constitutional Treaty rejected by the French and Dutch via referenda in 2005. The masterminds of Lisbon (mainly Sarkozy and Merkel) viewed it as a 'simplifying treaty'. However, the Treaty was cursed with bad luck from day one, confronted with opposition from Member States and victim of another Irish 'no' vote. Lisbon combined a lack of political vision with extreme complexity in the EU decision-making process.

The latter was especially the case for 'implementing acts', which are technical and administrative measures; sometimes general, sometimes individual. These are, in principle, minor measures, but they do have important economic repercussions for affected stakeholders.

This was certainly true for CTRS, which had taken the risk of developing this medicine with patients currently undergoing treatment. However, in addition to the obvious economic consequences, CTRS regarded DG SANCO's (and by extension, the Commission's) refusal to grant MA as an affront to their medical probity and to the very integrity of their company.

Before the Lisbon Treaty, the procedures for adopting implementing acts were already complicated. However, nothing compares to the post-Lisbon system which involves two committees: an Examination Committee at first instance and an Appeal Committee.

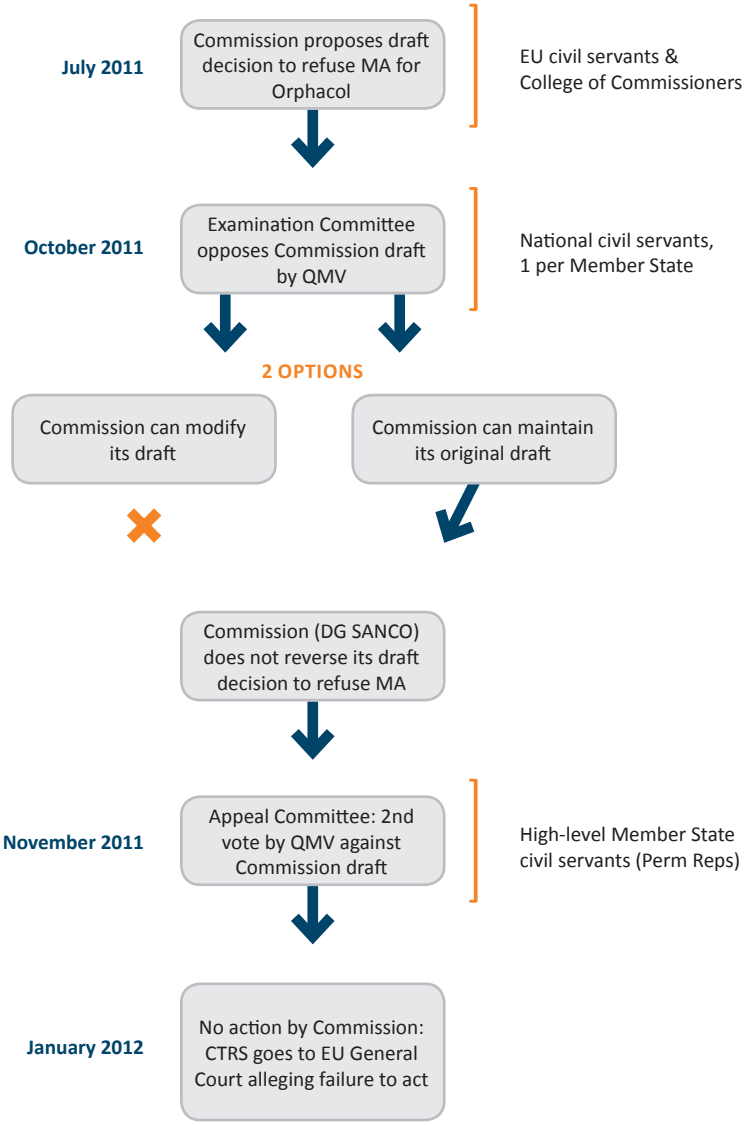
The Commission's draft decision refusing MA for Orphacol was submitted to the Standing Committee on Medicinal Products for Human Use. As I mentioned before, this is an Examination Committee made up of one specialised civil servant per Member State. The Committee is chaired by a Commission official – in this case, Patricia Brunko, who was then Head of Unit D.5 "Medicinal Products – Authorisations, European Medicines Agency" within DG SANCO. The Committee could either approve the draft decision by qualified majority or oppose it.

The problem in this instance was that the Committee was chaired by a civil servant openly hostile to the medicine. In addition, with twenty-seven Member States, it is already difficult enough to achieve a qualified majority in favour. Obtaining a qualified majority against is clearly even more difficult, since it is never easy to oppose the Commission.

Finding itself in a transitional regime between pre-Lisbon comitology and the new post-Lisbon system, Orphacol had another disadvantage to contend with. Under the new system, a simple majority of Member States (14 out of 27) is enough to block the adoption of a draft Commission implementing act.

However, this rule did not apply to Orphacol, which was still partially subject to the rules of the former management committees, where a qualified majority is needed to block adoption. As we will see later on, this exception had important consequences for Orphacol since it led to a second action before the EU Court of Justice.

Orphacol and the new post-Lisbon comitology



The Examination Committee met for the first time on 13 September 2011, where the draft anti-Orphacol decision was considered to be technically unsatisfactory. Undoubtedly conscious of the weaknesses in its draft, the Commission put forward a second version of the proposal in the same meeting. In doing so, it did not respect the 14-day period for prior submission to the Member States, thus ruling out any possibility of a vote.

A second meeting, chaired again by Ms Brunko, was held on 13 October 2011. It ended with a vote which revealed a qualified majority of Member States against the Commission's draft; in other words, in favour of MA for Orphacol.

In this situation, Article 3 paragraph 4 of Regulation 182/2011 (which sets down the rules for comitology procedures) requires that "[t]he chair shall endeavour to find solutions which command the widest possible support within the committee." Here, there is no obligation to achieve a particular result; the Commission simply has to make efforts to achieve the result, which was not the case.

In principle, DG SANCO should have initiated consultations, or at least a dialogue, in order to take account of the wishes of the majority of Member States. However, this did not happen.

On the contrary, DG SANCO retained its text and submitted it on 8 November 2011 to the Appeal Committee, composed – like the Examination Committee – of national civil servants, but of a higher rank. The Chair was also occupied by a higher-ranking Commission official: Mr Martin Seychell, Deputy Director General of DG SANCO.

The result of the Appeal Committee vote completely confirmed the vote of the Examination Committee. The Member States gave the Commission a second 'red card', effectively voting by qualified majority in favour of granting MA for Orphacol.

The Member States vote twice by qualified majority against the Commission

What is a qualified majority vote (QMV)?

Each EU Member State has a 'weighted vote' linked partly to its population, e.g. :

- Germany, France, United Kingdom & Italy have **29 votes** each
- Malta has : **3 votes**

To obtain a QMV, the majority must represent:

- 255 votes out of 345
- 14 Member States out of 27

The voting results for Orphacol:

	For the Commission draft (against Orphacol)	Against the Commission draft (for Orphacol)	Abstentions
1st vote (Examination Committee)	**79**	**266** (>255)	0
2nd vote (Appeal Committee)	**64**	**281** (>255)	0

Twice disavowed by the Member States, DG SANCO simply digs in its heels! CTRS has no other option but to go to the EU Courts

Three days after the Appeal Committee's qualified majority vote confirming Member State support for Orphacol, CTRS wrote to DG SANCO asking them to comply with the Member States' position by granting MA. **A few weeks later, on 5 December 2011, the Commissioner in charge of health matters, Mr John Dalli, replied stating that the Commission would not grant MA to Orphacol.**

In the face of this persistent refusal which was ignoring two negative Member State votes, CTRS had no option but to launch an action on 12 January 2012 before the EU Court of Justice – more precisely, before the General Court which is the court of first instance for actions launched by private companies.

For its representation, CTRS chose Bristows, a British law firm where lawyer Marie Manley leads a department specialised in comitology files. Working with fierceness, devotion and skill, Marie and her team would be immersed in this file every single day until the adoption of the final decision on 12 September 2013.

CTRS and Bristows based their action on two claims:

- Principally, **an action for failure to act**, alleging that the Commission had infringed EU Regulation 726/2004 which requires the Commission to adopt a decision on an authorisation within 15 days of the end of the comitology procedure;
- As a subsidiary plea, **an action for annulment**. CTRS claimed that the Commission did not respect the two negative votes of the Examination and Appeal Committees, and that the refusal to grant authorisation was based on fundamental errors of assessment.

The first concrete outcome was on 8 February 2012, when CTRS obtained the benefit of the "expedited procedure" (i.e. urgency procedure) for its case. This meant they could expect a judgment from the Court towards the end of 2012.

CTRS decides to combine the expertise of a law firm with the expertise of a lobbying firm specialised in comitology

On 10 April 2012, I met Dr. Antoine Ferry, President of CTRS, and his associate Bernard Deschamps for the first time in their small offices in the Parisian area of Boulogne-Billancourt. Dr. Ferry and Mr. Deschamps are both highly experienced medical scientists.

In 2002, Mr. Deschamps created CTRS (Cell Therapies Research & Services), a laboratory specialised in orphan medicines. A year later, Antoine Ferry joined the business as its CEO and joint shareholder.

A few weeks before our meeting, Dr. Ferry bought a copy of my book Comitology: Hijacking European Power? online – the very book you are reading right now. As he turned the pages, he began to realise the true context of his case and felt

intuitively that Bristow's purely legal action should be complemented with a lobbying campaign in Brussels.

I myself have always been convinced of the effectiveness of an alliance between a specialised law firm and a lobbying consultancy. The first takes care of the law, making sure that every word of every letter is legally sound. The second, while not a legal expert, understands how the law is applied in practice. It masters the procedure of the file and knows the key players. The respective roles are clear.

In parallel with Bristows's action, it was up to us to meet with the Permanent Representations of the twenty-seven Member States, explain the file to them and create a positive image for Orphacol. Over the coming months, I would have only one face-to-face meeting with Bristows, but thanks to CTRS we would be in constant contact, with one side always conscious of the synergy created by the other side's action.

A sudden turn of events:

While the General Court analyses the Orphacol case, the Commission puts forward a new draft decision refusing MA. The comitology committee is convened to discuss it on 8 May 2012, a public holiday!

At the General Court, the expedited procedure got underway. In March and April 2012, three Member States (the Czech Republic, the United Kingdom and France) decided to intervene in support of CTRS's action: now there were four complainants. We would learn later on that, on 20 April, Asklepion Pharmaceuticals – the American competitor – asked the General Court for permission to intervene in support of the Commission. The Court refused this request.

On 23 April came a dramatic twist. On the eve of the public hearing in Luxembourg, the Commission informed the General Court that it had just drawn up a new draft decision refusing MA for Orphacol and that it planned to convene the Standing Committee on Medicinal Products for Human Use straight away – the same Examination Committee that had rejected the Commission's anti-Orphacol draft!

Bypassing the on-going deliberations of the General Court and openly defying the Member States, DG SANCO had come back once again with the same draft.

Was it really the same text? The answer is yes, because again it refused to grant marketing authorisation for Orphacol. Admittedly, DG SANCO had beefed up its proposal a bit (the draft was now four pages longer), changed one or two sentences and switched a few paragraphs around, but in substance, it was the same text.

The Standing Committee now had to meet to discuss and vote on the new draft. The meeting was chaired once again by Patricia Brunko who (with the agreement of her superiors, I would imagine) decided to hold the meeting on 8 May – a public holiday in a number of European countries.

Many claimed that choosing this date did not, in itself, distort the result. This is possible, but what is certain is that holding the meeting on a public holiday made things more complicated and put extra pressure on how the discussions took place. We know, for example, that one Member State had to insist on the validity of its voting mandate, which the Commission chair initially seemed to dispute. Whatever happened, the result of the vote turned out to be distressing for a number of reasons:

- A huge portion of Member States opposed the Commission's draft for a third time (the 'nos' counted for 232 votes and only 57 votes were in favour, with an abstention of 29 votes).
- Because of Spain's absence from the meeting (for a reason that remains unknown) and Italy's decision to switch from 'no' to 'abstention' (which is counted as a 'yes' in this procedure) due to a change of minister, the Member States could not reach a qualified majority. This time, they fell short by 23 votes (out of 345)!
- The Commission could now adopt its anti-Orphacol decision, there being no qualified majority against the draft.
- The Commission benefited from a transitional procedure which, as I indicated before, requires a qualified majority of Member States to block a Commission draft. Under the current system, a simple majority (14 out of 27) would have been enough to force the Commission either to negotiate with Member States or go to the Appeal Committee.

As a result, the Commission's decision refusing MA for Orphacol was adopted on 25 May 2012. CTRS was unable to market its medicine throughout the European Union, but it could – for the moment, at least – continue treating patients in France.

The adoption of the decision refusing MA for Orphacol means the General Court can no longer adjudicate. CTRS is forced to launch a new action

CTRS's action against the Commission (following the two negative Member State votes in the Examination and Appeal Committees and DG SANCO's refusal to grant MA) suddenly found itself negated by the unexpected adoption of the second draft decision refusing MA for Orphacol.

On 4 July 2012, the General Court – now in a situation where any judgment would be pointless – therefore had no choice but to declare CTRS's action inadmissible. Nonetheless, the judges did order the Commission to bear the costs of CTRS and its lawyers and other expenses (in fact, this issue has not yet been resolved, seemingly due to ill will on the part of the Commission).

CTRS immediately filed a new action before the General Court on 10 July 2012. The case was assigned to the same three judges, who then granted "priority treatment" (but not the urgency procedure) to the new action. Priority treatment is rarely awarded. It differs from the urgency procedure in that the timeframe, while accelerated, is less precise.

Over the course of September and October 2012, the Czech Republic, Denmark, France, Austria and the United Kingdom all requested permission to intervene in support of CTRS. Poland, on the other hand, asked to intervene in support of the Commission. All of these requests were granted by the Court. There were now eight parties in the proceedings: the claimant – CTRS – supported by five Member States and the defendant – the European Commission – supported by Poland.

The second action was structured differently from the first. It was an action for annulment of the Commission Decision, based on two different angles:

- **A procedural argument:** CTRS claimed that the Commission infringed the comitology procedures by re-submitting a draft decision that was in substance identical to the one twice rejected by the Examination and Appeal Committees;
- **An argument on the merits:** CTRS alleged that the decision adopted by the Commission on 25 May 2012 refusing MA for Orphacol contained fundamental errors of assessment.

500 days after the case began, lobbying and communication reinforce the legal dimension

When I took up the Orphacol file, my first priority was to assess the state of play. I followed the wise words of Georg Brodach, former Vice-President of ABB, to the letter (also quoted in my book Reshaping European Lobbying):

"Whenever I take up a case, I analyse the stakeholders, the balance of powers and the opportunities for alliance. Then I look for a high-level figure within my network who could give me a comprehensive, objective and neutral view on the file - for example, the EU ambassador of a non-member country. In the Commission, I don't look at the level of hierarchy. I look for someone I can talk to in full confidence and who can tell me if there is more here than meets the eye."

It only took a few days for the most informed observers of the Orphacol file to express their disbelief. The general view was that nobody had ever seen anything like this. What motivated DG SANCO to show such hostility? Why was the stubbornness of low-level civil servants condoned by the hierarchy of DG SANCO (and by extension of the whole Commission)? How is it possible that the Commission could twice disregard the opposition of the Member States? Why did this happen? How could this happen?

The initial counter-attack came from the press. First, from Europolitics: on 14 May 2012, it published a long article entitled "Commission's rejection of medicine results in imbroglio". Two days later, again in Europolitics, I personally wrote an 'Open Forum' entitled: "Concerns over the EU legal order – How far can the Commission go in interpreting Community procedures?"; a week later, I penned another article in Euractiv on 22 May: "The European Legal Order: who is the boss in Brussels?".

These articles in the European press – read by most civil servants, MEPs and lobbyists – brought the Orphacol case out of the shadows and into the light. **Over the course of June and July 2012, a whole series of events would put Orphacol at the heart of EU news:**

- On 21 June 2012, thanks to the determination of MEP Gilles Pargneaux, the Environment, Public Health and Food Safety Committee (ENVI) of the European Parliament asked DG SANCO to answer some questions at a public hearing. Ms Paola Testori-Coggi, the Director General invited to the hearing, was represented by Ms Brunko, the relevant Head of Unit. As Europolitics reported: "Pargneaux says he has 'evidence that the Commission contacted the competitor directly'... Patricia Brunko firmly rejected this allegation and

said the executive 'never heard the competitor' but 'contacted it to learn the timeframe of the request'". CTRS claimed that these statements were erroneous, since in January 2011 Ms Brunko had received a letter from Asklepion Pharmaceuticals presenting arguments that were later used in the Commission's draft.

- On 18 July 2012, Austria got the Orphacol file onto the COREPER I agenda. COREPER is the level immediately below the Council of Ministers, and is made up of the Permanent Representatives (i.e. Ambassadors) of the EU Member States – in this case, the Deputy Permanent Representatives (i.e. Deputy Ambassadors), due to the technical nature of the issue. At the meeting, Austria presented a non-paper outlining how it believed the Commission had infringed the comitology procedure and expressing its concerns about the precedent this might create. Eleven Member States took part in the discussion, bringing the Orphacol file firmly into the 'political' arena.

September 2012 and beyond: months of intense activity by CTRS in Brussels

For Antoine Ferry, the first day of visits to Brussels began on 1 September 2012. It kicked off with a 9 a.m. meeting with civil servants from the Secretariat of the Council of Ministers. This meeting was not straightforward for Dr. Ferry. He feared that becoming entangled in the web of the Council's administration could create a backlash for his file. In reality, this was not the case – quite the contrary, in fact. Our interlocutors welcomed us warmly and the discussion was constructive. In particular, they gave us the impression that they were fully up to speed on the file, which was unexpected. They encouraged us to meet with the Permanent Representations (Perm Reps) of the Member States in Brussels and told us they would remain available in future to exchange information.

Antoine Ferry and I began a very long series of visits to the Perm Reps, particularly to those that were supporting CTRS at the General Court, and also to Poland who was supporting the Commission. As for the other Perm Reps, we met as many as possible.

Before the visits began, we made sure to identify the key players precisely. In general, three per Perm Rep: the health attaché, the legal attaché and the Deputy Permanent Representative, and sometimes the Permanent Representative as well. The three (sometimes four) officials met us together or separately, depending on their availability.

Every meeting was split into two separate parts: Dr. Ferry would present the scientific and medical arguments regarding the medicine, then I would set out the procedural violations and comitology issues. Each meeting added a new piece to the puzzle and allowed us to establish a close connection between CTRS and the Member States, the latter being the final decision-makers – whatever the Commission may think.

We seized every chance to make Orphacol a topic of discussion: more articles, more interviews. The Slovenian Perm Rep organised a training session on post-Lisbon secondary legislation, with its Permanent Representative present. This allowed Vicky Marissen and I to use the file as an illustration of wider comitology issues for 60 civil servants from various Perm Reps, under the watchful (and critical) eye of three participants from the Commission's Secretariat-General.

During these months, I personally grabbed every opportunity to speak about Orphacol or rather, to let Orphacol speak for itself: for example, at a public hearing on comitology organised by the European Economic and Social Committee (EESC); or during meetings in confidential circles where I was able to put questions to Catherine Day, the Commission Secretary-General, on the legality of re-submitting the same draft to a comitology committee.

A Manifesto for a Reform of EU Secondary Legislation, also important, was widely distributed. The visibility of the file was further reinforced by multiple contacts with the European Parliament: relevant MEPs and their assistants, as well as Parliament civil servants.

The end of 2012 was also devoted to raising awareness within higher ranks of the Commission, given that from the outset DG SANCO had refused to have contact with CTRS at any level. We identified potential interlocutors. Their common characteristic was that they all had access to the highest levels of the EU, where we expected them to communicate our double-barrelled message: Orphacol had been subjected to discriminatory treatment, and CTRS was determined to see the case through to the end (and win).

Of the five 'messengers' we identified, two pulled out, while the other three received a 4-page letter providing them with all the information to be transmitted to the highest levels of the EU. Was this information delivered? The question remains open, but the answer is probably 'no' **since the Orphacol file was surrounded by a cloud of unease: every observer who was even partly informed was already aware of the serious administrative flaws in the lower levels of DG SANCO. Nonetheless, every one of them (remember that this was on the eve of Commissioner Dalli's resignation) instinctively felt that certain**

upper parts of the EU iceberg were not unaware of the unfair treatment inflicted on CTRS.

Jean Quatremer's article in Libération: a real bombshell

The articles published on Orphacol were beginning to cause anxiety in high circles and the Commission felt the pressure mounting around the case. Jean Quatremer's article in Libération in January 2013 would prove to be a bombshell.

Jean Quatremer is an uncompromising journalist. If he finds an interesting topic, he does not hesitate to get involved. Orphacol immediately appealed to him as a citizen and as a journalist because it was an emblematic topic. Every article needs an 'angle' and it was rare to find a case like Orphacol that gave the reader such an insight into the decision-making labyrinth of the European Union.

Quatremer's strength lay in the fact that he had closely studied the file before meeting Antoine Ferry on 19 December 2012. Dr. Ferry, for his part, was completely transparent with Quatremer, giving answers to all of his questions. Even on the same day of that interview, Quatremer contacted DG SANCO and a few other civil servants. Their uneasy responses confirmed his suspicions. To maximise the effect, the article would be published a week after the New Year celebrations.

Spread out over two pages in Libération on 9 January 2013, the article's title was already enough to catch the attention: "The Orphan Disease, the Miracle Medicine and the Eurocrat". The sub-title was even more provocative: "The Commission is fighting doggedly against the marketing of a medicine that is the only known treatment for a life-threatening disease. Underneath the surface lurks an American lab controlled by the Seventh-day Adventist Church."

Throughout the article, Jean Quatremer summarised the case and set out all the issues. However, what really caused a fuss was that he revealed the name of the civil servant in charge of the file, who had incidentally just retired from her post (for unrelated reasons).

On the day of publication, trouble was brewing in the Commission press room where DG SANCO spokesperson Frédéric Vincent had to face a revolt. Badly prepared, he claimed that Orphacol was not the only treatment available and that there were other means of curing the illness. The result was a real journalistic scrum, with Jean Quatremer of Libération and Ophélie Spanneut of

Europolitics in the front row. We can be sure that Mr. Vincent did not get any compliments that day from his superiors!

Over the next few days, Jean Quatremer's article was re-published extensively in a wide range of daily European newspapers. Once again, the dimension of the Orphacol file had shifted: it was now a full-on battle, where only one side would win and the other would lose.

We know that the Commission was thinking about suing Jean Quatremer for defamation. In my view, he would not have been too angry about it. His file was so well-prepared and his article did not contain any factual errors. Therefore it would have been quite daring for the Commission to try to play with fire. The pressure on DG SANCO was starting to tell; in terms of tension, the tables were turning. That is the essence of lobbying!

April 2013: The public hearing at the Court in Luxembourg

After nearly forty years in European affairs, this was the first time I attended a public hearing at the EU Court of Justice. I presume it will not be the last, as the new system of secondary legislation has planted the seeds for increased litigation in Luxembourg. As I wrote in an 'Open Forum' in Europolitics in September 2012 on the issue of European governance: "When Europe gets caught in the mire, it is up to the Court of Justice to act".

On 12 April in Luxembourg, it was a full house. The Commission was represented by relatively junior civil servants – a sign that DG SANCO wanted to keep a low profile. This low profile was also reflected in the arguments of the lawyer representing the Commission. When cornered with complex questions, he found it difficult to respond credibly, even after long consultations of his badly organised papers. Poland, officially supporting the Commission, was not present at the hearing.

CTRS was represented by barrister Kelyn Bacon (of Brick Court Chambers) and by Bristows, with the 'back-office' team led by Marie Manley and her colleagues who anticipated the Court's questions, providing the necessary information when required. Around CTRS, four of the five countries accompanying the complainant had appointed their own lawyers and technical counsellors. Some of the associated countries, notably Austria, focused their arguments on the procedural issues, attempting to prove the decision's illegality due to the infringement of comitology procedures. Others, notably France, underlined that the Commission's decision refusing MA for Orphacol was based on

fundamental scientific, medical and regulatory errors. The rest based their arguments on both aspects of the action.

The three judges were very active during the hearing, addressing several questions to CTRS, the associated countries and the Commission. The very technical questions they asked illustrated their in-depth knowledge of the case (with which they were of course familiar from the first action); questions which required extremely precise answers. Surprisingly, the Court stuck to the substantive issues of the file and did not address the procedural aspect either directly or indirectly.

As an observer, what impressed me was that the 'pro-Orphacol camp' had managed its presentations and its responses very well, without any overlap between the five parties. There was an atmosphere of optimism following the hearing…

4 July 2013: The Court annuls the Commission decision refusing MA for Orphacol

The eve of the judgment and the morning of 4 July was a time of immense stress within the Orphacol camp. I personally was convinced of a positive outcome, but one never knows. Half an hour before the official publication of the judgment, we learned that the General Court had annulled the Commission Decision refusing market authorisation for Orphacol, thanks to Jean Quatremer's tweet: "Big blow for the Commission. The EU Court has annulled the refusal to authorise Orphacol." .

Specifically, the Court:

- ruled that CTRS had indeed demonstrated "Well-Established Medical Use" of cholic acid;
- ruled that CTRS had proved it was not able to provide full details on the efficiency and harmlessness of the medicine in normal conditions of use, due to "exceptional circumstances" provided under EU law;
- rejected the Commission's argument that the granting of MA for Orphacol would jeopardise the objectives of EU legislation on paediatric medication and the protection of innovation.

The Commission had clearly been dealt a knock-out blow, so much so that the Court found it unnecessary to examine the procedural issues. We will never know (or at least, not yet) whether or not the Commission acted illegally by putting forward a new draft decision following the two Member State rejections. Disappointing for the comitology purists, naturally, that the Court's ruling was limited to the technical arguments, but the fact that the Court did not address the procedural questions reduced the possibility of the Commission appealing the ruling.

There was great joy in my office too, despite our frustration that the General Court did not tackle the issue of whether or not the Commission's use of comitology procedures was legal. On 9 July, Jean Quatremer and I were Eddy Caekelberghs's guests for half an hour live on the RTBF programme Face à l'info. We had a lively, taboo-free discussion!

Would MA now be granted to Orphacol?

After the euphoria, a reality check. Of course the Court's annulment of the Commission Decision was an undeniable victory, but nothing was won yet. What needed to happen now was for the Commission to draft a proposal granting MA to Orphacol.

From 5 July, CTRS wrote to Commissioner Borg (Commissioner Dalli's successor) encouraging him to have a proposal drafted which was favourable to Orphacol, and to submit it for validation by the Member States via the written procedure.

The Commissioner responded positively. As promised, a text was drafted by his services and submitted to the Member States via a written procedure. Provided there was no opposition from Member States by 3 August, the proposal granting MA would definitely be adopted.

Everything seemed to be ok. Out of caution, CTRS continued to monitor the situation in case there were any unpleasant surprises. We awaited the final chapter with quiet confidence, but not necessarily with total calmness, given the obstacles that had stood in Orphacol's way and the distrust that had built up to this point.

The incredible final home stretch!

On 7 August, during my holidays, I received an email from Antoine Ferry entitled "Bad news". At the request of one Member State (which one, we did

not yet know), the Commission had decided to cancel the written procedure and instead hold a proper meeting of the Examination Committee at a date to be set. The news was bad for two reasons: MA would be delayed further and the uncertainty would persist. What seemed a fait accompli – MA for Orphacol – was no longer certain.

This development was followed a few days later by more bad news. Around mid-August 2013, we learned that Asklepion Pharmaceuticals, which had filed an application to obtain marketing authorisation for its own competing product at the European Medicines Agency, was on track to get a positive opinion quite soon. MA for Orphacol seemed to be slipping away; the American competitor was closing in.

The worst was yet to come

Our monitoring system, complemented by information provided by some very well-informed insiders, indicated to us that Orphacol's latest difficulties were not a coincidence.

What margins of manoeuvre did DG SANCO still have? We researched this on 16 and 17 August. Not without difficulty, we discovered two particularly worrying facts:

- First of all, we learned that Poland was the Member State that had requested the abandonment of the written procedure. Before, any change of procedure requested by a Member State had to be endorsed by the Commission, but this is no longer the case since the adoption of Regulation 182/2011 (the new comitology rules). It should be noted, however, that legal experts within the Commission stated the opposite when we asked them at the time. Yet again, we see the incredible complexity of the system.

- A detailed analysis of the post-Lisbon internal rules of procedure of comitology committees revealed that the Commission now has considerable scope for manoeuvre regarding quorum (evaluated on a case-by-case basis) and voting rules (the Commission can postpone a committee vote easily).

Around 20 August, CTRS learned that the Commission would submit its draft decision to the Standing Committee on 11 September 2013. In reality, CTRS found itself confronted with a potentially dramatic scenario: an unknown timeframe, the postponement of MA, an American competitor looming large and an Examination Committee where the rules on quorum and voting were flexible!

Once more, the media came to Orphacol's aid, this time via Europolitics which, right after the summer break, published a long article on 30 August 2013 entitled "Orphacol authorisation not a done deal". The article, written by Ophélie Spanneut, spelled out in great detail everything I have described above: the abandonment of the written procedure, the possible postponement of the vote and the American competitor.

Published in both English and French, we used the article to inform all the Brussels Perm Reps, as the information on the abandonment of the written procedure and the convening of the Examination Committee had been addressed by the Commission only to the national capitals. Many Perm Reps were not aware of the details of what was happening, many health attachés were still on holiday and as for the few national officials who were there, they thought the Orphacol case had already been resolved by the General Court in Luxembourg.

Asklepion Pharmaceuticals unexpectedly begins to lobby the national capitals and Permanent Representations

The situation now required a mobilisation of all our resources in order to contact, inform and persuade all twenty-eight Member State Permanent Representations.

Contact was mainly made via email and telephone, but we organised face-to-face meetings whenever possible (or necessary). I can never emphasise enough the importance of personal contacts and trust derived from mutual credibility. Throughout my career, I have seen not only how important luck is for a successful file, but also how much luck depends on daily hard work and perseverance.

Luck came in the shape of a meeting in a Perm Rep in the first week of September 2013 – a few days before the Examination Committee vote. Deep down, I did not feel this meeting was crucial, since the country in question had already made known its support for CTRS. However, we could not leave anything to chance; we had to mobilise again and again. I was greeted with the words: "I have just received a copy of a letter addressed by Asklepion Pharmaceuticals to my Minister. Were you aware?" I certainly was not! Who would have thought that after months of silence and days before the vote, Asklepion Pharmaceuticals would come charging back?

Asklepion Pharmaceuticals' letter was addressed in principle to all twenty-eight national health ministers, as well as to the Perm Reps in Brussels. It went back

over the issue of the previous relationship between the Cincinnati and Kremlin-Bicêtre hospitals and argued that Orphacol should be sent back to the EMA for a third analysis. Reading through it very rapidly in the official's office, the letter seemed surreal to me in every respect: its form, its content, its purpose and its list of recipients.

How were they informed? How did they proceed? Who was representing them? These questions remain open. With a little less vigilance and a little more complacency, there was every chance that CTRS could have seen its file delayed, even compromised for good. Personally, I never believed that the Commission would defy the General Court judgment; nor did I believe that both CTRS's and Asklepion Pharmaceuticals' applications would be submitted simultaneously to the Examination Committee. Nonetheless, the risk of the committee vote being postponed to a later date remained very real, so we were on our toes right up until the end.

The last week before the vote was especially active and curiously optimistic, as the positive signals began to arrive. We got news indicating that the Commission would hold a vote and that, apparently, any requests for information by certain countries regarding the General Court judgment would be addressed in a later meeting, once MA for Orphacol had been granted. The Perm Reps were beginning to talk to each other and we felt increasingly that a positive vote was expected. What is more, the very fact that the vote was taking place signified that MA would be granted, as this time the Commission was proposing a draft authorisation which the majority of Member States supported.

A remarkable finale: twenty-eight Member States unanimous in favour of Orphacol

On the afternoon of 11 September 2013, the SMS messages came in announcing victory. However, nobody could have predicted that it would be so glorious: twenty-eight Member States in favour. No votes against, no abstentions.

On 25 October 2013, the Official Journal of the European Union published a notification of the Commission Implementing Decision granting marketing authorisation for Orphacol. The file was officially closed.

So after 1,000 days of sweat, stress and struggle, the feeling of satisfaction is powerful. However, some questions remain – important questions!

- How could this have possibly happened? How is it that such a minor file (let us remember that only twenty-one patients are currently being treated with Orphacol) could generate such resistance from the Commission in the face of two negative Member State votes?
- How could the Commission put forward a first draft decision so poorly drawn up, technically speaking? How could the Commission submit a second draft decision while the first action was pending at the EU Courts?
- Why was CTRS made to endure the hostility of DG SANCO, and by extension the Commission, right up until the last moment?
- How and why did the hostility of DG SANCO, and by extension the Commission, extend from the very bottom levels of the Institution (Ms Brunko's Unit and her colleagues) right up to the top echelons where certain high-ranking officials and Commissioners clearly condoned the excesses of the case?
- How and why was Asklepion Pharmaceuticals able to obtain the support of DG SANCO and by extension the higher levels of the Commission? What reason(s) motivated the various players in the file to act against CTRS? Can we even imagine that the Seventh-day Adventist Church, Asklepion Pharmaceuticals' sole shareholder, itself played a role in the case?
- How and why did the civil servants involved in this file deliberately flout the codes of good conduct and administrative behaviour which they are bound to uphold by the Institution that employs them? Why did certain civil servants publicly make erroneous statements to MEPs? How and why was it that certain civil servants who acted in good faith and supported Orphacol seemed to be pushed aside?

In addition to these questions that require answers, there are other considerations regarding the EU decision-making process:

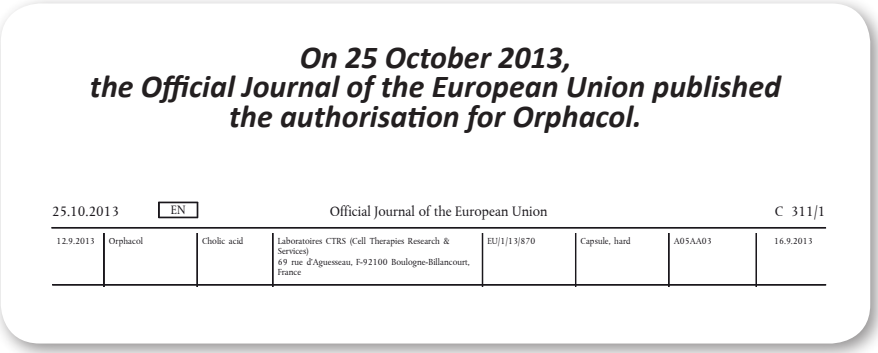
- First of all, the increased complexity of the new comitology system introduced by the Lisbon Treaty and the legal uncertainty it has generated. What is a delegated act? What is an implementing act? Can the Commission submit the same text several times? It is up to the Court of Justice to lay down the law, preferably as soon as possible.
- Orphacol has also demonstrated the extent to which secondary legislation is firmly in the hands of the EU bureaucracy. This is the case for delegated acts, which the Commission both proposes and adopts via opaque internal procedures. For implementing acts, the Commission has clearly shown it

knows how to erode the Member States' prerogatives in the comitology committees.

- Orphacol has brought to light the hidden power in Brussels, the huge importance of low-level civil servants and the lack of transparency that reigns at every level. The Lisbon Treaty has not increased democracy; rather, it has created complexity and opacity.
- Orphacol has also highlighted new lobbying techniques: more procedural and more legal than before. It confirms the importance of having the will to act. Lobbying is all about action. It underlines the major role of the media in putting pressure on the opponent, whether it is the national media or specialised European press.
- Finally, Orphacol reinforces the case for a compulsory lobby register in the EU – like in the United States – requiring certification of lobbyists and obligatory declarations of clients and contacts (applicable to the Institutions to), as well as civil and criminal penalties for violations.

What this 1,000-day battle shows, ultimately, is that David can defeat Goliath. That in itself is encouraging, and perhaps a source of inspiration for others!

On 25 October 2013, the Official Journal of the European Union published the authorisation for Orphacol.



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12.9.2013	Orphacol	Cholic acid	Laboratoires CTRS (Cell Therapies Research & Services) 69 rue d'Aguesseau, F-92100 Boulogne-Billancourt, France	EU/1/13/870	Capsule, hard	A05AA03	16.9.2013

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