SciencesPo
SCHOOL OF PUBLIC AFFAIRS

PUBLIC POLICY MASTER THESIS

MAY 2021

THE CONTRIBUTION OF COMPLIANCE LAW IN THE PREVENTION OF OPIOID CRISIS IN FRANCE

Théo Thouret

Master's Thesis supervised by **Marie-Anne Frison-Roche**, University Professor at Sciences Po Paris

Second member of the Jury: Maître **Arnaud de la Cotardière**, Partner at Linklaters

Master in Public Affairs – Public Administration

AKNOWLEDGMENTS

First, I would like to thank warmly Professor Marie-Anne Frison-Roche who supervised this master thesis and has showed available in every occasion to help me and advise me. She spent a lot of time to make sure that this master thesis would be a good quality work. Moreover, she has participated in my intellectual development by sharing her precious knowledge and opinions on the topic with me.

I also really want to thank Maître Arnaud de la Cotardière who accept to be the second member of the jury of this master thesis. I am sure that he will bring all his practical knowledge on the topic to permit a rich and qualitative discussion between the members of the jury and me and to bring a constructive criticism on my work.

I also would like to thank Sciences Po, particularly represented by Laura Atran-Fresco, Camille Damoiseau and Yann Algan, which give me the possibility to write this master thesis and to go in depth into this very interesting and crucial topic that is opioid problem in France and especially the Laboratory for Interdisciplinary Evaluation of Public Policies (LIEPP) which organized this possibility. Among LIEPP, I would like to particularly thanks Bruno Palier who spent time to provide me very precious methodological advices.

I would like to thank Sophie who accompanied me and supported me in this brief but intense intellectual adventure. Thanks to my mother, my father and my brother who got news of the advancement of this mas ter thesis. Finally, thanks to every people who, by their interest over this topic, pushed me to explain it and therefore help me to get a better understanding of the case (Caro, Bridget, Gauthier, Gabriel and all the others).

ABSTRACT

Although its opioids' consumption is much lower than in the United States, France faces a rising problem with opioids' use. Opioids are medical prescription painkillers derived from opium. Weak opioids (like Tramadol, Codeine or Morphine powder) are prescribed to ease serious pain and strong opioids (like Morphine, Oxycodone or Fentanyl) for very serious pain. Both, marketized since the end of 1990s, are much more powerful than traditional non-steroidal anti-inflammatory painkillers and present a higher risk of addiction and mortality if overused[1].

Despite of those risks, the opioids' consumption in France is dangerously increasing. Use of Tramadol, which is the most consumed opioid painkiller, increased by 68% between 2006 and 2017 and consumption of Oxycodone, very popular in the United-States, rose by 738% over the period even if its consumption remains quite low[2]. This increase is especially due to the rising use of opioids against non-cancer chronic pains and to its use as an antidepressant by an increasing number of patients although they were initially conceived to fight cancer and sharp pains[3]. This overuse of opioid medications is accompanied by a multiplication by 2,7 of the number of hospitalization due to overdoses between 2000 and 2017 and by a multiplication by 2,5 of the number of deaths between 2000 and 2015[4].

In 2017, weak opioids represented only 20% of painkillers' consumption in France and strong opioids only 2%[5]. However, health authorities have to react to avoid that this problem transforms into tragic crisis like in the United-States. This is why a comparison between the past situation in the United-States and the possible future solution in France is pertinent. The solution found in the United-States on the occasion of *Johnson and Johnson* trials was to hold liable drug manufacturers in Ex-post but also in Ex-ante for the misuse of the opioid drugs[6]. The judge, convinced of the existence of a "monumental goal"[7], aware of the weakness of the FDA[8] to face the problem and persuaded that drug manufacturers are the best positioned actor to solve the crisis, used Compliance Law[9] to internalize regulation into those firms, forcing drug manufacturers to find a way to guarantee the right use of opioids and holding them liable of any appearance or

1 Authier, N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

2 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé,* February 2019

3 Authier, N., "Antidouleurs opioïdes : vers une crise sanitaire en France ?", *The Conversation,* 13/09/2018

4 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé*, February 2019

5 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé,* February 2019

6 District Court of Cleveland County, State of Oklahoma (Judge Thad Balkman), August 26th of 2019, Mike Hunter (Attorney General of Oklahoma) versus Purdue Pharma (et al.), Teva Pharmaceutical (et al.), Johnson and Johnson (et al.), Allergan (et al.), Watson Laboratories (et al.), Case n°CJ-2017-816

7 This expression was used for the first time and theorized by Marie-Anne Frison-Roche in Frison-Roche M.A., « From Regulation Law to Compliance Law », 2017

8 Food and Drug Administration

9 A definition of Compliance Law could be found in Frison-Roche, M.-A., *Le Droit de la Compliance au-delà du Droit de la Régulation,* 2018

reappearance of a public disaster like this. The question is to know whether this solution is salient in France and if drug manufacturers are indeed the most pertinent actor to guarantee the right use of opioid drugs by patients.

In this master thesis, we will see that drug manufacturers' behavior does not seem to be the cause of the opioid problem in France because, contrary to the United-States, drug advertising to the health professionals and to the public is much more regulated and because drug manufacturers have a duty to warn health professional and patients. Moreover, it seems incredible to hold drug manufacturers liable in Ex-ante for the crisis because they do not seem so powerful to address the problem, especially because the situation depends on many other actors' behavior (physicians, pharmacists, regulator and user) that drug manufacturers cannot control. From this point, we will see that health professionals seem a much more crucial operator, more able to guarantee the right use of opioids. Compliance system in France should therefore lean on health professionals, implementing “monumental goals” decreed by ANSM[10] and supervised by professional orders.

KEY WORDS

Opioid Crisis, Compliance, Pharmaceutical Sector

10 Agence Nationale de Sécurité du Médicament et des Produits de Santé

TABLE OF CONTENTS

INTRODUCTION

Opioids are medical prescription drugs that are derived from opium and that are known very effective to ease and fight violent pains[11]. We can divide opioids into two different categories. Weak opioids, especially Tramadol, Codeine or Opium Powder, are often prescribed to ease intense pain while strong opioids, like Morphine, Oxycodone or Fentanyl are recommended to fight *very* violent pain. Both weak and strong opioids distinguish from other painkillers and especially from traditional non-steroidal anti-inflammatory painkillers, whose the two most famous molecules are Aspirin and Ibuprofen, by being much more powerful but also by presenting much higher risk of addiction and therefore of mortality if they are misused[12], even if weak opioids present less risks than strong ones because of their lower effect against pain.

Although opium has been used as painkiller for many decades before, its consumption has rose dramatically since the end of the 1990s in most occidental developed countries[13]. The country in which consumption reaches the highest level and knows the most important increase is without any doubt the United-States[14]. According to Angus Deaton, former Economics Nobel Prize, United-States consumed 80% of opioids in the world although its population only represents 5% of the world population[15]. However, Europe, even if its use of opioids is far from the one of the United-States, also sees its consumption increasing massively. More particularly, France is the fourth consumer of opioids painkillers in Europe behind Germany, Spain and United-Kingdom. Even if strong opioids are less used in France than in the United-Kingdom, in Germany, in Spain, in Denmark or in Sweden, France is the third country in Europe where weak opioids are the most consumed. Moreover, this consumption is drastically increasing in France since the beginning of the XXIst century. Consumption of Tramadol, the most used opioid painkiller in France, has increased by 68% between 2006 and 2017, for example. This rise is even more important for strong opioids whose the consumption increased by 150% between 2006 and 2015[16].

What is particularly important to understand here is that, even if this increase is partially due to an increasing of the number of people using opioids, the consumption rise is most often due to an increase of the use of opioid per patient. Indeed, since the end of the 1990s, opioids are more and more used to fight non-cancer chronic pain while they were initially conceived to fight sharp and cancer pain[17]. Moreover, an increasing number of

11 « Good Use of Pharmaceuticals: Medicines for Breakthrough Pain Due to Cancer », *Haute Autorité de Santé*, July 2014

12 Authier, N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

13 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé,* February 2019

14 Obradovic, I., " La crise des opioïdes aux Etats-Unis : d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

15 Deaton, A., *La Grande Évasion : Santé, richesse et origine des inégalités,* PUF, 2016

16 For state of the situation in France, see Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé*, February 2019

17 "Chronic Pain, in France. Recommendations of the National Academy of Medicine for Better Care of

patients distort the use of opioids to use them as antidepressant drugs and so to fight psychological pains more than physical pains[18]. These two kinds of patients therefore enter a frequent, regular and long run use of opioids. This increase of consumption per patient is especially problematic when we know that an overuse of opioids could lead to death or severe addiction, which is an issue in itself but which also may indirectly lead to death if this addiction has a tendency to push the patient to increase its use.

United-States is currently facing a true crisis due to the overuse of opioids. Since 1996, 300 000 Americans died because of opioid overdose, which is more than during the Viet Nam War, and this number is increasing years after years. Today, we estimate than 130 Americans dies per day because of opioids. Addiction is also more and more important, even with babies who are more and more to born with neonatal abstinence syndrome. Approximatively, a baby born already addict to opioids every 19 minutes in the United-States[19].

In France, the situation is much less dramatic because « only » 304 people died because of opioid overdose in 2018, which is far from the American statistics (156 times less)[20]. In this sense, France does not face a « crisis » but rather a « problem ». However, this number of deaths, by the way already alarming in itself, is increasing and nothing could guarantee that the "little" French problem could not turn into crisis like in the United States. Indeed, the number of deaths linked to opioids was multiplicated by almost 2,5 between 2000 and 2015 in France[21]. The American crisis has enabled us to detect the first symptoms of this tragedy and have given to us the opportunity to think, coldly, about how preventing that the problem becomes a crisis. Thinking coldly is always a better idea than thinking in the heat of the moment which very often offers exaggerated reactions. Obviously, opioid crisis, even if it should appear, could not turn into a systemic crisis because the deficiency of one actor cannot have an effect on all the other actors and put the entire system in peril but the multiplication of individual deficiencies could lead to a massive agglomerate effect that we should avoid. This is the reason why public powers, in France, should take advantage of this chance to think about the policies package that it could be salient to implement in order to prevent a public health crisis.

The first step before finding solutions is to understand well what is exactly the problem that we are currently facing. Here, it is really important to understand that the cause of the opioid problem in France is not the opioid drug in itself but its use. Indeed, it would be reasonable to think that the origin of the problem would be the marketization of a dangerous product (opioids) whose we know, or not by the way, that it was dangerous when it has been marketized and that this dangerous product would be dangerous whatever the way it would be used and even if its posology was respected. Thinking like that would immediately hold liable either the drug manufacturer who has created and marketized a dangerous product or the regulator which is the Autorité Nationale de Sécurité du Médicament et des Produits de Santé (ANSM) which was in charge of guaranteeing the security of medications and failed in appreciating the benefits/risks balance of the drug and labeled it unjustly by providing it a marketization authorization.

Patients", *National Academy of Medicine's Report*, 2018

18 Authier, N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

19 For a state of the situation in the United-States, see Obradovic, I., " La crise des opioïdes aux Etats-Unis : d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

20 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé,* February 2019

21 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé,* February 2019

This was the case during the Mediator affair when the Servier laboratories and the ANSM were jointly found liable by the Tribunal de Grande Instance de Nanterre on October 22nd of 2015 of leaving a "*defectueux*"[22] drug on the market whose « *ils ne pouvaient ignorer les risques*[23] »[24]. However, both in the United-States and in France, the origin of the problem does not come from the product in itself but from the way it is used by patients and health professionals. Indeed, opioids, in themselves, are necessary for ease and fight intense pain and the Haute Autorité de Santé (HAS) found that the medical service rendered by opioids is relevant for this purpose, especially after the failure of alternative treatments[25]. Moreover, the ANSM, by delivering a marketization authorization has judged satisfying the benefits/risks balance in the case of a regular use of the drug, that is to say if the drug is indeed used for what for why it was created : easing a patient without any contraindications' violent pain who respect the maximal dosage. This means that opioids are not dangerous in every case and that when they are used properly, they are not defective, and it is even very effective. In this perspective, if the problem does not come from a product's default, it comes from its use. As we have already mentioned, many patients and physicians misuse opioids. Either they use too much opioids or they use them for the wrong purpose, and this is the problem that we have to address. In other words, the question is not to know if the opioids painkillers should be removed from the market, and so we are not assessing here the ANSM's benefits/risks balance calculation, but rather how we should guaranteeing the right use of this kind of drugs. In this perspective, Nicolas Authier, psychiatrist and Professor specialized in addictology and pharmacology, said that the question is not to consume « *moins d'opioïdes mais de consommer mieux les opioïdes*[26] »[27].

Before continuing, it is probably important to give here some definitions and make some linguistic distinctions in order to avoid confusion in the following of this master thesis. All the definitions given in this paragraph are extract from the article R.5121-152 of the Code de la Santé Publique (CSP) and we will use them in the all this master thesis. First, we will understand « undesirable effect » as "*une réaction nocive et non voulue à un médicament*"[28]. The undesirable effect is known when the drug is marketized by all the stakeholders informed by the manufacturer and is globally accepted because of its lower significance in comparison with the benefit of the drug recognized by the ANSM who accept to label the product and then by the user who most often choose to use the medication despite of the undesirable effects, after having been informed of them, because he or she expects a benefit larger than the risks. Sometimes the undesirable effect is unknown by the patient who was not informed of it and discover it when he or she uses the drug. We talk about « unforeseen undesirable effect » which is « *un effet indésirable dont la nature, la sévérité ou l'évolution ne correspondent pas aux informations contenues dans le résumé des caractéristiques du produit* »[29]. A different notion is « misuse » which is an « *utilisation intentionnelle et inappropriée d'un médicament ou d'un produit, non conforme à l'autorisation de mise sur le marché ou à*

22 « Defective » (translation by the author).

23 « Whose they cannot ignore the risks » (translation by the author).

24 Tribunal de Grande Instance de Nanterre, 2nd Chamber, 22nd of October 2015, n°12/07723

25 « Good Use of Pharmaceuticals: Medicines for Breakthrough Pain Due to Cancer », Haute Autorité de Santé, July 2014

26 "Less opioids but to consume opioids better" (translation by the author).

27 Authier, N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

28 « A nocive or unwanted reaction to a medication » (translation by the author).

29 « Undesirable effect whose the nature, the gravity or the evolution do not correspond to the information given in the summary of product characteristics" (translation by the author).

l'enregistrement ainsi qu'aux recommandations de bonnes pratiques[30] ». « Abuse » is a category of « misuse » because it is « *un usage excessif intentionnel, persistant ou sporadique, de médicaments ou de produits mentionnés à l'article R. 5121-150, accompagné de réactions physiques ou psychologiques nocives*[31] » and « overdose » is another category of « misuse » and is an « *administration d'une quantité de médicament ou de produit, quantité par prise ou cumulée supérieure à la dose maximale recommandée par le résumé des caractéristiques du produit*[32] ». When a drug is misused, this means that the patient or the physician distorts the regular use of the medication voluntarily and choose to use it in a higher quantity or for another purpose than the recommended quantity or purpose.

Since we have said that the origin of the opioid problem was the use of the medicine, one question is immediately raised: what about the liability of the drug's user? After all, if the user got all the necessary information to make a free and informed choice and that he or she has decided to « intentionally » use the drug for another purpose than the recommended purpose or using it too much, it is complicated to say that he or she should not accept his or her fate. In the United-States, archetype of the liberal country, holding this kind of reasoning seems very coherent. Indeed, in United-States, but also globally in North America, Agency Theory is very strong, and people are considered as free and independent individuals able to gather and treat all the necessary information make free and rational decisions without any contingencies. The only condition for what individuals could not be able to make the right choice is if some information is hidden to them or not accessible. But, if all the necessary information is given, then individuals are supposed sufficiently mature to make the good choices[33]. In this perspective of perfect information, the freedom/liability couple is very strong. People are indeed free to adopt approximatively every behavior they want as long as they assume it afterwards. If you get damage from your choice, you cannot complain because you choose with full knowledge of the facts. You are liable because you have the faculties of being it.

However, in a more European context, such a speech is less acceptable. Indeed, the European culture is much more paternalistic than the American one and the user of a product is much more likely to be deresponsibilized. The reason why we have such a deresponsibilization is that information is never considered as perfect. Indeed, it is not sufficient that information is accessible in a European context. A free and rational choice needs that not only information is accessible but also that individuals is able to find it and treat it. Although in United-States, the tendency is to consider individuals as a priori endowed with reason, in Europe, we have built the "vice of consent theory"[34]. This means that under certain circumstances, individuals may not be able to consent freely and to choose what is the best for them. Sometimes, individuals do not have enough faculties to find all the necessary information either because they do not know where to find it or also because they do not know the existence of this information. Moreover, individuals could have not the sufficient abilities to treat the information even if it is given to them either because they do not have the sufficient knowledge on a topic that requires expertise (and

30 « Intentional and inappropriate use of a medicine concerning the authorized or prescribed dosage, the administration way, the information conformed to marketing authorization and the good practices recommendations" (translation by the author).

31 « Excessive and intentional, persistent or sporadic, use of a medicine which goes along with physical or psychological reactions" (translation by the author).

32 « Administration of a quantity of medicine, per dose or per day, which is superior to the maximal recommended dose in the summary of product characteristics" (translation by the author).

33 Thompson D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend? *Florida State University Law Review,* 1985, Article 6, Vol 13, Issue 1

34 Article 1109 of Code Civil

medicine is such a field) or because the circumstances deprive them of their faculties to make rational decision. The last point is very important when talking about painkillers. Indeed, it is reasonable to think that someone using opioids painkillers for the first time is suffering a lot and that this pain slants his or her faculties. Moreover, even someone who uses opioids painkillers for a long time as a narcotic is not able to consent freely because he or she is under the physical and psychological dependence of the substance. Pain and withdrawal feeling trouble the true benefits/risks balance by overestimating the benefits and underestimating the risks. Therefore, this two people are able to make choice that they can regret afterwards when the pain and withdrawal feeling will remove.

Being in an European context and considering that this solution is too much simple, we will rule out, in this master thesis, the possibility that the victim of opioid problem is a traditional « junky » that goes towards a substance that is known by everybody to be addictive and fatal. Indeed, as we have shown, most of opioid victims were not really aware of the risks of this kind of drugs, because all the information was not available or because they were not in capacity to analyze it. Moreover, opioid victims and traditional « junky » do not belong to the same sociological category. If we compare the sociology of the crack crisis in the 1980s-1990s and the sociology of the current opioid crisis, we can see a lot of differences according to Obradovic (2018)[35]. Indeed, the crack addicts was young, from urban and disadvantaged districts and most often from ethnic minorities. Opioid Crisis display a very different sociology. Victims of opioids are rural, middle-aged, from the working-middle class and white. It is not only a different sociology it is also a surprising sociology. Rural, middle-aged, white from the working-middle class is not supposed to fall into drug addiction. This is an additional reason to think that they fall into it involuntarily.

If user cannot be responsible of his or her own use, then who could be responsible of the guaranteeing of the right use of the drug? It is necessary to find the salient actor, the one who would be the more able to make sure that opioid pills are correctly used by patients who cannot, themselves, know fully what a right use is. On the occasion of the *Johnson and Johnson* trial in Oklahoma, American judge Thad Balkman found drug manufacturer liable of the tragic situation in the United-States and urge it to solve and prevent the crisis by using Compliance Law. Judge Balkman hold therefore, drug manufacturers liable of the right use of opioids[36]. We would not, in this master thesis, assess if this solution is pertinent for United-States, we will take it as an assumption. Rather, we will ask us if holding drug manufacturer liable of the right use of the drug is salient in France and if creating a Compliance system leaning on the drug manufacturer to prevent opioid crisis to come is a good idea.

In a first part, we will show that opioid problem rises a “monumental goal” to address for the Public Health Authorities in France and we will look at how it was address in the United-States. Then, in a second part, we will search who could be the crucial operator on who a Compliance system preventing opioid crisis to come could lean.

35 Obradovic, I., “ La crise des opioïdes aux Etats-Unis : d’un abus de prescriptions à une épidémie aiguë”, *Potomac Papers*, 2018, n°35, IFRI

36 District Court of Cleveland County, State of Oklahoma (Judge Thad Balkman), August 26th of 2019, Mike Hunter (Attorney General of Oklahoma) versus Purdue Pharma (et al.), Teva Pharmaceutical (et al.), Johnson and Johnson (et al.), Allergan (et al.), Watson Laboratories (et al.), Case n°CJ-2017-816

PART I: THE BIRTH OF A "MONUMENTAL GOAL" AND OF A WAY TO ACHIEVE IT

As we have said in the introduction, the aim of this master thesis is to find who is the crucial operator on who a Compliance system permitting to prevent opioid crisis in France, could lean. However, before starting this research, it is important to get the measure of the current opioid problem in France, to understand its extent and the risks to not addressing it quickly. Moreover, it is necessary to understand in what kind of doctrinal framework (Compliance Law), currently implementing in the United-States to solve the opioid crisis, we are placing our study. The aim of this first part is therefore to give some contextual and theoretical elements useful to our second part's demonstration.

CHAPTER I: THE CONTEXT – ADDRESSING THE OPIOID CRISIS

Since the very beginning of this master thesis, we said that France is facing an opioid problem and that it is very urgent to act to address it before it turns into a massive public health crisis. However, what is exactly the extent of the opioid problem faced by France and to what extent it sounds like an emergency to face it ? In this first chapter, we will try to endow the lector of this master thesis with some contextual and especially factual elements to appreciate the necessity to act. We will start by a state of play of the French situation before looking at the situation of the United States which is much more advanced in the process than us and which could enable us to see what the future situation in France could be if we do not act quickly and at the solution that was implemented to the American context.

I- THE EXTENT AND THE RISKS OF THE OPIOID PROBLEM IN FRANCE

As we said, France is facing a real problem with opioid medications that are more and more misused and overused by French people despite of the risks presented by a misuse and an overuse of this kind of very powerful and potentially really addictive drugs. Let's give some facts and figures to enable the lector to appreciate the extent and the risk of such a problem.

A- The Extent: The Consumption of Opioid Painkillers Increases in France

Before talking about the risks of an increase of opioid painkillers consumption, let's see to what extent this increase is important and alarming.

1- French People consume more and more opioids

Opioids are a category of painkillers, derived from opium, and conceived to ease and fight very violent pains like cancer or very sharp pain as intense and punctual back pain, for instance[37]. But opioids are also known to present, if they are misused or overused[38], a serious risk of addiction for their user and therefore a risk of mortality by overdose. There are two categories of opioids: weak opioids like Tramadol, Codeine or Opium Powder that are recommended to be prescribed against violent pain and strong opioids like Morphine, Oxycodone and Fentanyl which are recommended to be prescribed against *very* violent pain. The difference between weak and strong opioid is their level of powerfulness against pain but also of addiction and mortality risk. Strong opioids are much more powerful than weak opioids against pain but are also more likely to make their user dependent of its effect and to die because of overdose, because they are more concentrated. However, both weak and strong opioids are more powerful and more risky than other traditional painkillers and especially non-steroidal anti-inflammatory painkillers. Opioids, because of their origin from opium, are classified among narcotics used as medications by the article 5132-30 of CSP. This means that in addition to being only deliver to people having a prescription by a physician, opioids are subject to supplementary regulations. For

37 « Good Use of Pharmaceuticals: Medicines for Breakthrough Pain Due to Cancer », *Haute Autorité de Santé*, July 2014

38 Authier N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

example, weak opioids cannot be prescribed for more than one year and deliver for more than 28 days. Morphine and Oxycodone cannot be prescribed for more than 28 days and Fentanyl, which is one of the strongest opioid legally used as painkiller, must be deliver per intervals of 14 days (in the case of prolonged action medication) or 7 days (in the case of fast action medication)[39].

Opioids still represent a minority of the painkillers used in France. In 2017, only 22% of the painkillers consumed are opioids and the great majority of them are weak opioids (weak opioids represent 20% of the consumption of opioids and strong opioids only 2%). However, opioid consumption has risen massively since the end of the 1990s. If we look at, for example, the most consumed opioid painkiller in France, which is Tramadol, with 11,2 Daily-Defined Dose for 1000 inhabitants per day, its consumption increased by almost 68% between 2006 and 2017. Codeine, another weak opioid that was available over-the-counter until 2017 but which has become a prescription drug since, is 84% times more consumed in 2017 than in 2006. The rise is even more dramatic for strong opioids, even if the consumption of strong opioids is still much less important than the weak opioid usage. Overall, the consumption of strong opioids has increased by 150% over the period. But, the use of Fentanyl, the most powerful opioid authorized on the legal drug market, rose by 339% for transmucosal administration (and 78% for transdermal administration) and consumption of Oxycodone, which is very popular in the United-States and which is the molecule contained in the so controversial drug OxyContin, knew an even more impressive rise with a 738% increase over the period[40]. Those increases have led to the fact that, now, more and more people, in France, consume opioid painkillers. We have estimated that only in 2015, 9 966 944 people, in France, received a medical prescription containing opioid antalgics. This number represents 17,1% of the total French population[41].

2- Although it is also due to an increasing number of people using opioids, the increase in opioid consumption is most often due to a rise of quantities used per patients

It is important to understand that increase in opioid consumption is due to two phenomena. The first one is a broadening of the number of people using opioids. More and more people are using opioids[42]. Indeed, although opioids were only used, before the 1990s, to treat cancer pains or sharp and punctual pains, they start to be prescribed more and more to treat more benign pains since the end of the 1990s[43]. At the very end of 1990s and the very beginning of 2000s, many action plans to fight pain were launched in the developed countries[44]. The argument was that pain was undertreated and often minimized while it was a real and broad problem. Many people, and more than imagined, were suffering from different pains and they had a “right to not suffering”. Pain was

39 Article 5132-30 of CSP

40 For all statistics concerning opioids consumption in France, please see Monzon, E., “Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques”, *Report of Agence Nationale de Sécurité du Médicament et des Produits de Sant,* February 2019

41 Barreau M, Chenaf C, Kabore J.L, Bertin C, Delorme J, Riquelme-Arbre M, Eschalier A, Ardid D, Delage N, Authier N, Pharmacoépidémiologie de l’usage des antalgiques opioïdes en France, Trends in opioid analgesic use, *Lettre du pharmacologue*, 2017, Vol. 31

42 Barreau M, Chenaf C, Kabore J.L, Bertin C, Delorme J, Riquelme-Arbre M, Eschalier A, Ardid D, Delage N, Authier N, Pharmacoépidémiologie de l’usage des antalgiques opioïdes en France, Trends in opioid analgesic use, *Lettre du pharmacologue*, 2017, Vol. 31

43 Thurel C, « « Du mauvais usage » des opioïdes forts dans le traitement des douleurs chroniques bénignes (non cancéreuses) », *Douleurs*, 2007, Vol 8, n°2, pp.101-107

44 A French example of Pain Management Action Plan is the Pain Management Plan implemented between 1998 and 2000 by the French Ministry of Health

considered as very subjective and the idea that the patient was the only person who can legitimate know what is good for him or her, born[45]. Therefore, the prescription of painkillers but also of opioids became more flexible and opioids start to be prescribed for less intense pains. In 10 years, prescriptions of opioids for non-cancer pains increased by 88%[46].

But, the increase in opioids consumption is also due to an increase of the quantity of opioid used per patient. More people are using opioids but, most often, those who are using opioids, use them in a higher quantity. Here, we talk about those who increase the number of doses per day or those who increase the quantity of drug per dose but not only. We are also talking about patients, who are more and more, who start using opioids on a regular, frequent and long run basis. Some patients do it following a physician's prescription who recommend them to do it. It is the case of patients using opioids to treat non cancer chronic pain. As we said, opioids were created to ease cancer pain, or eventually very intense but exceptional and temporary pains. Indeed, because of the addictive potential of opioids, they were not conceived to be used in the long run[47]. However, since the end of the 1990s, many physicians start to prescribe opioids to fight non cancer chronic pains like chronic lumbagos, osteoarthritis pains, or neuropathic pains. In 2017, weak opioids are prescribed to chronic pain in 13,4% of the cases while strong opioids are prescribed to treat chronic pain in 42,9% of the cases and those figures are increasing[48]. This new use of opioids painkillers could be explained by two reasons. First, many physicians inspired from the recommendations of the diverse pain management action plans which took place at the end of the 1990s and whose we talked just before. Every pain deserves a remedy, especially those who are persistent. But Nicolas Authier detects another potential reason. According to him, the lack of alternatives between very soft painkillers (like Ibuprofen, Paracetamol or Aspirin) and hard painkillers representing by opioids is one of the causes of massive prescription of opioids for non-cancer chronic pains. Indeed, most often, soft painkillers are powerless face to chronic pain and the only medication stronger is opioid. You do not have intermediary painkillers which could perfectly fit to chronic pain which is itself between benign pain (treated by soft painkillers) and very violent pain (treated by opioids)[49].

But there is a second type of patients using opioids painkillers on a regular, frequent and long-run basis. However, contrary to the precedent group of patients, who misuse opioids but misuse them following a physician's medical recommendation or prescription, this group of patients misuse opioids and medical recommendations. We are here talking about patients using opioids as antidepressant or anxiolytic substance. Opioids have indeed a sedative and relaxing effect because of their origin from opium and some patients, who most often have discovered opioids as painkillers, continue to use them but only because of their psychological benefits. Nicolas Authier has met some patients who told him that opioids "*les aidaient à dormir, à être moins anxieux et à être de meilleur*

45 Lohman, D, « S'il vous plait ne nous laissez pas souffrir… L'accès au traitement de la douleur est un droit humain », *Human Right Watch Report,* 2009

46 Chenaf et al., "Prescription des antalgiques opioïdes en France entre 2004 et 2017 : évolution et impact en termes de morbi-mortalité *», European Journal of Pain*, 2018, Vol 23, Issue 1

47 « Good Use of Pharmaceuticals: Medicines for Breakthrough Pain Due to Cancer », *Haute Autorité de Santé*, July 2014

48 Chenaf C, Kabore J.L, Delorme J, Pereira B, Mulliez A, Zenut M, Delage N, Ardid D, Eschalier A, Authier N, Prescription opioid analgesic use in France: Trends and impact on morbidity–mortality, *European Journal of Pain,* 2018

49 Authier N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

humeur[50]"[51]. We can almost talk about psychological depends to opioid here and we may expect that these patients misusing opioids for their antidepressant effects will continue to use them on a regular and long run basis with the risk to falling into addiction if they are not already (psychologically) addict.

A final reason could be used to explain the intensification of opioids consumption. This argument is more structural. In 2009, the ANSM and the European Medicines Agency (EMA) decided to definitively withdraw Dextropropoxyphene from the French and European drug market. This molecule, especially contained in Di-Antalvic drug and consumed by approximatively 15% of the French population, representing 95% of the European total consumption for this drug, is a weak opioid and was removed from the market exactly because of its risk of overdose[52]. However, some physicians replaced Dextropropoxyphene by other opioids like Tramadol, Codeine or Opium Powder that are known to be more powerful[53]. Here, we join the precedent argument that we wrote in this master thesis saying that a lack of alternatives pushes physicians to prescribe more opioids or stronger opioids.

B- The Risks: The Misuse of Opioid Painkillers May Lead to Dependence and Death by Overdose

Now, let's see what the risks and the potential and effective consequences of a such increase of opioid painkillers consumption are.

1- Opioid painkillers present a serious risk of addiction if they are misused by patients

As we have said, total consumption of opioid painkillers is increasing in France since the end of the 1990s and this increase is mostly due to a new use of this kind of drugs, much more on a long run basis than before. If this factual information is so alarming for health authorities, it is because opioid painkillers, if they are overused, either because patients increase their number of doses per day or because they start to consume opioid painkillers on the long run, present a serious risk of dependence. Nicolas Authier, which is specialized in addictology, distinguish two kind of addiction. The first one is a physical addiction, which is, according to him, the first step of the dependence. At this stage, patients' organisms have been used to opioids and patients needs more opioids to feel the effect of them on pain which is decreasing as the total consumption is increasing. At this stage, patients mostly increase their consumption in order to fight a persistent pain that the traditional dose of opioids cannot ease anymore because of the habituation of the body to the opioid substance. However, according to Nicolas Authier, this first stage often leads to another, from which it is much more difficult to extract. This second stage is psychological addiction. At this step, patients start to use opioids for themselves. Patients do not suffer anymore in reality but are persuaded that they will suffer if they do not use opioid painkillers. They start building their life around opioids consumption. It is also at this stage that patients start using opioids for their psychological effect (antidepressant, anxiolytic and relaxing effects)[54].

50 "Help them to sleep, help them to be less anxious or to have a better mood" (translation by the author).

51 Authier N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

52 « Press Release European Medicines Agency Recommends Withdrawal of Dextropropoxyphene-containing Medicines", *EMEA*, 25 of June 2009

53 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé*, February 2019

54 Authier N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération*, 23/02/2019

What is alarming is that both physical and psychological dependence are increasing in France since the start of the 2000s. Indeed, the number of cases of misuse reported to the addiction monitoring network doubled between 2006 and 2015[55]. A priori, opioids do not present risks of physical and psychological addiction if they are used in compliance with the recommendations formulated and for the purpose for what they were created. However, as we already saw before, both patients and health professional more and more misuse opioids painkillers. Health professionals overprescribes opioids painkillers and patients often misused them, either because they are not informed of the danger of misusing or because the pain or the addiction push them to infringe their physician or pharmacist's recommendations. This misuse of opioids painkillers by patients was particularly visible for Codeine when it was still possible to buy it over the counter. Before 2017, self-medication with Codeine and use of Codeine without health professional advice was possible. In 2016, a study has shown that 13,3% of patients who self-medicated with Codeine were overusing it[56]. Here, we can easily consider that this overuse of Codeine was mostly due to a lack of information about appropriate use, either because patients did not get the advice of a health professional or because they did not ask for it. The same year, we found that Tramadol, most used opioid in France, was overused in 49% of the cases[57]. If overuse leads to addiction and that a such amount of patients is overusing it, this could mean that a pretty large number of people, in France, are actually addict to opioids. Moreover, another indicator to approach the extent of addiction in France is to consider the extent of doctor shopping. Doctor shopping is the behavior adopted by addict people who visit different doctors either because a first one did not accept to prescribe opioid painkillers to him or her or because he or she wants more opioids. This method exploits the failure of physician's coordination and the power of freedom of prescription to get a higher and not legal quantity of opioids. It is clear that people behaving like that are addict and a higher rate of doctor shopping let foresee a higher rate of addiction among the population. French Social Security has estimated the doctor shopping indicator at 4% for Morphine, 1,7% for Oxycodone and 1,5 for Fentanyl in 2013. Social Security judge that those number start to be worrying when they are greater than 1%[58]. It is therefore quite clear that we have a rising problem of addiction due to opioid painkillers in France.

2- Opioids painkillers may lead to death if they are overused by patients

Addiction is a serious problem in itself for the victim and for the society because of its physical effects, its desocialization effects and of its risks to increase illegal or criminal behavior. But it is also a key issue in the sense that addiction lead the consumer to increase its dosage, because he or she does not feel anymore the effect of the drug because of the habituation of his or her organism, and therefore make risk of overdose more and more possible. Opioid overdose most often manifest by a respiratory arrest that could go until the death of the victim. If we look at the number of hospitalizations for 1 million inhabitants due to the consumption of a prescribed opioid, we will see that this number passed from 15 to 40 between 2000 and 2017, which means a multiplication by 2,7 since the start of the XXth century. Among the 2762 cases of intoxication due to opioids

55 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé*, February 2019

56 Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé*, February 2019

57 Roussin, Doazan d'Ouince, Géniaux, Halberer, « Evaluation of Abuse and Dependence in Addiction Monitoring Systems: Tramadol as an Example", *Thérapie*, 2015, 70(2), pp.213-221

58 Ponté, Lepelley, Boucherie, Mallaret, Lapeyre-Mestre, Pradel, Micallef, « Doctor Shopping of Opioid Analgesic Relative to Benzodiazepines: A Pharmacoepidemiologic Study Among 11,7 million Inhabitants in the French Countries", *Drug and Alcohol Dependence,* 2018, 187, pp. 88-94

notified to the Pharmacovigilance National Bank, 49% were due to weak opioids, 47% to strong opioids and 4% to an association of weak and strong opioids. However, the evolution shows that the notification rate for strong opioids increased more drastically than for weak opioids. The notification rate increased by 139% for Tramadol, by 757% for Opium Powder and by 1229% for oxycodone. The share of overdoses caused by opioids among the total number of overdoses also increased over the period. The Pharmacovigilance National Bank has estimated that this share passed from 40/10 000 to 87/10 000 between 2005 and 2016. Even if opioids still represent a weak part of overdoses, they have nevertheless increased by 117%, either a multiplication by 2,2, which means that this substance could have a higher, and perhaps a major place in the drug habits in the future[59].

Even if overdoses do not always lead to death of the victim, the number of people who died because of an overdose of opioid painkillers is increasing. The number of deaths caused by opioids in France was multiplicated by 3, passing from 1,3 for 1 million inhabitants to 3,2 for 1 million inhabitants between 2000 and 2015. We have estimated that 406 people died because of opioids in 2006, knowing that Tramadol killed 37 people, Morphine 22 people, Codeine 16 and Oxycodone 8. This number is really impressive. In order to compare, opioids kill each year 10 times more people than flu. In 2016, over 100 deaths due to medications, 14 were caused by opioids and this share is increasing[60].

II- THE AMERICAN SOLUTION: A COMPLIANCE SYSTEM LEANING ON THE DRUG MANUFACTURER

To address a domestic problem, it may be interesting to look at abroad if there is or there was a similar problem to inspire from the solution found an implemented. United-States is currently facing a very serious crisis due to the overconsumption of opioids. In this section, we will study the solution found by Americans to solve and prevent this crisis.

A- The American Context: Not a Problem but a Crisis

Before looking at the solution found by Americans to solve and prevent opioid crisis, let's just look at the extent of the crisis in the United-States and the context in which a such decision was made.

1- United-States are touched by a similar serious problem with prescription opioids even if opioids are much more lethal in the United-States than in France for the moment

As we have said, United-States is currently facing a massive and very serious opioid crisis among its population since the end of 1990s. Although more drugs are available over-the-counter in the United-States than in France, opioids are nevertheless still a prescription drug in the United-States. Opioids are used to treat chronic and more benign pain since the mid-1990s, where *Purdue Pharmaceuticals,* a drug manufacturer specialized in pain management, created a new drug "OxyContin", containing Oxycodone, which were presented as much less addictive than other opioids because of its action during 12 hours

59 For all statistics about overdoses due to opioids in France, please see Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé*, February 2019

60 For all statistics about deaths due to opioids in France, please see Monzon, E., "Etat des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of Agence Nationale de Sécurité du Médicament et des Produits de Santé*, February 2019

permitting to limit the number of doses per day[61]. *Purdue Pharmaceuticals* insisted on the problem of undertreatment of pain which was a massive problem in the United-States at the time, according to them, and recommend their drug, without any risk, still according to them, for the treatment of all kind of pain and not only cancer pain[62]. Purdue Pharmaceuticals obtained a marketization authorization from Food and Drug Administration (FDA) in 1995[63] and started a large promotion campaign towards health professionals but also patients, quickly followed by other drug manufacturers[64].

Very rapidly and gradually, prescription and therefore consumption of opioids, accompanied by misused practices by patients and health professionals, increased sharply in the United-States. Today, 2 million Americans consume opioid painkillers, either 1% of the total population, and 12% of this 2 million actually misuse those painkillers. In these conditions, addiction rose importantly. This phenomenon is especially visible by the number of babies affected by neonatal withdrawal syndrome[65] who are 27 000 per year. This means that one baby born addict to opioids each 19 minute in the United-States. 7 babies over 1000 are affected since 2013. But, the number of deaths by overdose due to opioid painkillers have also increased importantly since the end of the 1990s. The number of deaths because of opioids overdose has been multiplicated by 5 between 1999 and 2018. Since the start of the XXIst century, 300 000 Americans died because of prescribed opioids, either 130 Americans per day, according to the Center for Disease Control and Prevention (CDCP) affiliated to the FDA. In order to be able to compare, the total number of deaths *per year* because of opioids overpasses the total number of American victims during the Viet Nam War. We estimate that opioids are currently liable for 1,5% of the total number of deaths in the United-States each year. Moreover, opioids are responsible of the first diminution of life expectancy since centuries in the United States[66].

2- The United-States is knowing a substitution effect towards more powerful and illegal substance that France does not know yet and that make the crisis entering into a new dimension

This explosion of mortality is partially due to the direct effects of opioids but also partially due to its indirect effects. Indeed, many Americans start to become addict with prescription opioid painkillers and then, because they cannot get prescription drugs anymore or because they want a substance with a greater effect, turn towards more powerful and illegal substances. The first illegal narcotic targeted is heroin. Its consumption increased massively since 2010 in the United-States due to the entering into the illegal heroin market of a new kind of consumer, the former prescription opioid painkillers' users. This increasing consumption has of course tragic effects because the number of babies born already addict to heroin has been multiplicated by 10 since 2000 and because mortality due to heroin has been multiplicated by 4 in 5 years between 2010 and 2015. But, since

61 Hale M.E., Fleischmann R., Salzman R., et al., « Efficacy and Safety of Controlled Release Versus Immediate Released Oxycodone: Randomized, Double-Blind Evaluation in Chronic Back Pain", *Clin J. Pain*, 1999, 15, pp.179-183

62 Van Zee, "The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy", *American Journal of Public Health*, 2009, Vol 99, No. 2

63 Kolodny, Courtwright, Hwang et al., "The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction", *Annual Review of Public Health,* 2015

64 Van Zee, "The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy", *American Journal of Public Health,* 2009, Vol 99, No. 2

65 Being affected by Neonatal Withdrawal Syndrome is the fact to born immediately addict to a substance because the mother of the baby consumed it during pregnancy

66 For all statistics regarding opioid crisis in the United-States, please look at Obradovic, I., "La crise des opioïdes aux États-Unis: d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

2013, the consumption of new substances, still more powerful, has increased among opioid addicts: the one of synthesis opioids. Among those synthesis opioids we can cite Carfentanil, for instance which is 1000 times much more concentrated than Fentanyl, which is the most powerful legal opioid and which is itself 100 times more powerful than Morphine. The consumption of synthesis opioids increased by 73% between 2014 and 2015 and by 103% between 2015 and 2016 according to the Center of Disease Control. This new kind of consumption reveal very lethal. Indeed, in three years, between 2013 and 2016, the number of deaths due to synthesis opioids was multiplicated by 6. We counted 3 100 deaths in 2013 and 19 413 deaths in 2016, either 3 deaths for 100 000 inhabitants in 2016. In France, we have not really seen yet this substitution effect with other more powerful and illegal substance[67].

As we have seen, opioid crisis in the United-States is without any common measure with the problem faced by France. Indeed, opioids kill, in the United-States, 156 times more than in France while the American total population is only 5 times greater than the French total population. Some people could say here that as the American and the French problems are at a different scale, the two situations are not comparable and that so it is unreasonable to ask us if the American solution could be exportable to France. This argument could be indeed justified if the French situation was at the end of its evolution. However, as we saw in the precedent section, the French problem is rising. French consumption of opioids does not stop to increase and the number of deaths because of opioids in France is more and more important years after years. These dynamics show that the French problem has not reached its summit and that the statistics are converging towards those of the United-States. Then, it is quite reasonable to think that United-States are just at a most advanced level in the crisis than France but that France will probably join one day United-States. In this perspective, United-States is just the "trailer" of what could be the future situation in France if no policy inflexion is made and France represents just a step by where United-States passed in the past. Opioid crisis is a track in what France and United-States are not at the same check-point but are both walking in the same direction. Finally, United-States and France are not different point in space but different point in time, in our case. If we consider things like that, it is reasonable to look at the solution implemented by the United-States even if the extent of the crisis is for the moment not the same because the problem faced by the United-States would be the problem faced by France one day.

B- The Johnson and Johnson Case: Holding Liable in Ex-Post and Ex-Ante the Drug Manufacturer

Face to the inaction of policy makers, the first protagonist who makes a decision concerning opioid crisis in the United States is the judge. For the last years, many attorneys general from different American States[68], at many victims' request, have decided to sue opioid manufacturers[69] for their liability in the current opioid crisis that the country faces. Among them, State of Oklahoma decided to sue *Johnson & Johnson* group.

1- Parties' arguments

67 For all statistics regarding substitution effects towards heroin or synthesis opioids, please look at Obradovic, I., "La crise des opioïdes aux États-Unis: d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

68 Among the Attorneys General suing Pharmaceuticals groups for liability in the opioids crisis, we can cite those of Oklahoma, Ohio or New York, for instances.

69 Among the Pharmaceutical groups that are sued, we can quote *Purdue Pharmaceuticals*, *Johnson & Johnson* or *Teva Pharmaceuticals*, for instances.

Brad Beckworth who is the lead attorney for the State of Oklahoma said: "We have shown that *Johnson & Johnson* was at the root cause of this opioid crisis". The plaintiff's argument was that opioid manufacturers, during their promotional campaign, diffuse a false and misleading information towards health professionals and patients leading to minimize the current risks of the opioid painkillers marketized. Johnson & Johnson were accused to hide information about the risks, to minimize the risks, or to overpromote the benefits of the drug in order to make them wrongly and artificially much more important than the risks. As Abbe R. Gluck who is professor of Health Policy and Law at Yale Law School said, "the critical finding is that *Johnson and Johnson* engaged in false, deceptive and misleading marketing". The attorney general took advantage of the dramatic extent of the crisis and emphasize the profits made by manufacturers thanks to opioid painkillers since the marketization of these drugs for non-cancer chronic pain. Brad Beckworth has explained that "[*Johnson & Johnson*] made billions of dollars from it over a 20-year period".

The defense of *Johnson & Johnson* rests on diverse arguments. We can distinguish three of them. First, *Johnson & Johnson*, even if it often recognizes the fact that United-States is facing a serious crisis due to opioids, refuses to assume the entire consequences of the opioid crisis saying that they play a minimal role in it. They explain that they are not the only manufacturer to produce opioids and that, at least, the liability is to divide between each opioid seller, including illegal and legal drug traffickers, and that affiliates, which also act independently have to carry alone their own part of liability. For example, *Johnson & Johnson* underlines the fact that its medicines "have accounted for less than one percent of total opioid prescriptions in Oklahoma as well as in the United-States"[70]. Second, they emphasize the fact that the opioid painkillers they marketized have played a major role in pain management for many and most patients, as foreseen by the manufacturer when it has created the painkiller. Johnson and Johnson argue that it is important to not disregard the "unique role its medicines play in the lives of people who need them"[71]. Finally, they remind the fact that they never broke Law and that they always act in compliance with the federal rules produced by Parliament and FDA. They insist on the fact that FDA approved and labeled their products and that either it is a token of quality and safety, either it is to the FDA to assume the liability of the crisis to have authorized or to have not removed from the market a drug that was dangerous. In any case, according to them, drug manufacturers could be considered as liable if their action was approved a priori by a Federal Authority. *Johnson & Johnson* support that the "State's claims violate fundamental principles of due process by seeking to hold a company liable for conduct permitted under Federal Law and regulations" [72]. Moreover, *Johnson & Johnson* precise that they have always made available any necessary information concerning risks of the drug to health professionals as Law requires it[73].

2- Verdict: holding Johnson & Johnson liable in Ex Post and in Ex Ante

The final verdict was given on August 26th of 2019, by Judge Thad Balkman from the

70 Exhibit 99.1 "Johnson & Johnson To Appeal Flawed Opioid Judgement in Oklahoma", New Brunswick, NJ, August 26, 2019

71 Exhibit 99.1 "Johnson & Johnson To Appeal Flawed Opioid Judgement in Oklahoma", New Brunswick, NJ, August 26, 2019

72 Exhibit 99.1 "Johnson & Johnson To Appeal Flawed Opioid Judgement in Oklahoma", New Brunswick, NJ, August 26, 2019

73 Here, it is particularly important to know that, in the United-States, drug manufacturers have a duty to warn health professional but not directly patients. We are talking about « learned intermediary doctrine » which was consecrated by case law.

District Court of Cleveland County, in the State of Oklahoma[74]. What is important to understand here is that judge Balkman's decision is in two parts. First, judge Balkman holds liable defendants in Ex Post for the opioid crisis currently occurring in the State of Oklahoma. Judge Balkman, leaning on Supreme Court precedent[75], extends the extent of public Nuisance Law "beyond the regulation of real property" to include *Johnson & Johnson*'s behavior into it. At the origin, public Nuisance Law is enforceable in the case where an action cause damage to property rights of a victim. Following this definition, public Nuisance Law is not enforceable to *Johnson & Johnson* because the firm's behavior did not exactly harm property right of the opioid victim. However, judge Balkman reminds that, according to Law, a nuisance "consists in unlawfully doing an act, or omitting to perform a duty, which act or omission annoys, injures or endangers the comfort, repose, health or safety of others; or, in any way renders other persons insecure in life, or in use of property"[76] and that in precedent public Nuisance Law has been enforced "with no claims of damages to property rights"[77]. In this perspective, then, public Nuisance Law is enforceable to *Johnson & Johnson*'s behavior. Admittedly, public Nuisance Law enforcement requires the use of public property. But, judge Balkman shows that *Johnson & Johnson* used Oklahoma infrastructure to create the nuisance. Then, it is just necessary now to show that *Johnson & Johnson* indeed "unlawfully did an act or omitted to perform a duty" to enforce public Nuisance Law to them. Here, Judge Balkman "conclude that Defendants engaged in false and misleading marketing of both their drugs and opioids generally, and the Law makes clear that such conduct is more than enough to serve as the act or omission necessary to establish the first element of Oklahoma's public Nuisance Law" and therefore "find that defendants actions annoyed, injured or endangered the comfort, repose, health or safety of Oklahomans". Judge Balkman holds liable *Johnson & Johnson* here for the misuse of the drugs by Oklahomans and sentences them to fix the damages caused. Here, we are in front of an Ex Post sanction. This means that the judge punishes the defendants for a past action that already caused a damage.

Although this Ex Post sanction sounded as a first ever in the case law, the second part of the verdict is still more interesting. Indeed, more than holding *Johnson & Johnson* liable in Ex Post of the opioid crisis and sentencing them to repair the damages already caused by their action, judge Thad Balkman also holds *Johnson & Johnson* liable in Ex Ante by forcing them to prevent any future and potential occurrence of this kind of crisis. At the end of his verdict, judge Balkman said that "commissioner White testified that, in her opinion, the State's Abatement Plan will abate the nuisance, save countless lives of Oklahomans in the future, save countless people from becoming addicted to opioids in the future, and eliminate the negative impact the nuisance has had on the State of Oklahoma". Here, judge Balkman forget what happened in the past to focus on the future situation. The fact is now to avoid new damages and prevent the crisis in Ex Ante. In this statement, he also sets an objective which is "saving countless lives of Oklahomans and saving people from becoming addicted to opioids in the future". After saying that, he recognizes that "Oklahomans' lives can be saved if the State obtains the resources needed "to use evidence-based programs to abate this crisis"". By saying that, judge Balkman express the fact that the entities that are normally supposed to address the problem, Health Authorities and more broadly the Politics, is unable to address it, here principally because of a lack of financial resources. But he finds that the defendant seems to be able to bring what is missing because he finishes his verdict by sentencing *Johnson & Johnson* to pay

74 District Court of Cleveland County, State of Oklahoma (Judge Thad Balkman), August 26th of 2019, Mike Hunter (Attorney General of Oklahoma) versus Purdue Pharma (et al.), Teva Pharmaceutical (et al.), Johnson and Johnson (et al.), Allergan (et al.), Watson Laboratories (et al.), Case n°CJ-2017-816

75 Ellis v. Ellison, 1921 OK 279, §3, 200 P. at 161

76 50 O.S. 1981 §1

77 Reaves v Territory, 1903 OK 92, 74 P. 951

$572,102,028 each year for at least 20 years and all the unforeseen costs that could occur in the future. Therefore, *Johnson & Johnson* is sentenced to pay for a damage that has not occurred yet, and which will perhaps not be occurred at all, and whose they are, obviously, not the cause because this damage does not occur yet. The fact here is that *Johnson & Johnson* are not convicted to pay to repair a damage but to prevent it to occur and that they are not targeted by the judge because they are the cause or the potential future cause of a damage but because they are able to address the problem. What is enforced here by judge Balkman (enforcing an actor to pursue a goal, that is not necessarily the goal that it will naturally pursue, set by politics but that politics cannot reach, because this actor seems the best positioned to do it) is named Compliance Law.

CHAPTER II: THE THEORETICAL FRAMEWORK – COMPLIANCE LAW

In the precedent chapter, we have explained the context in which our study is embedded. Opioid consumption and misuse are dangerously rising in France and are accompanied by more and more addiction cases and deaths by overdoses. Because United States and France are just two different time point in the evolution of opioid crisis, it is reasonable to compare the American and the French situations, first to measure the danger of what could come in the future and second to analyze the solution found by Americans to address their problem. As we have shown, a great part of the solution found by judge Thad Balkman during the *Johnson & Johnson* trial leaned on Compliance Law. But before seeing if Compliance Law would be salient in our French problem, it seems reasonable to endow the lector, which is perhaps not particularly comfortable with this recent and revolutionary branch of Law, with some theoretical elements permitting to understand what Compliance Law is exactly.

I- COMPLIANCE LAW: THE INTERNALIZATION OF "MONUMENTAL GOALS" IN "CRUCIAL OPERATORS" WHICH ARE MORE ABLE THAN REGULATORS TO REACH THEM

Compliance Law was theorized by doctrine very recently. Actually, Compliance Law is itself just starting to emerge at the time where this master thesis is written. Compliance Law emerges empirically through case law, guidelines from administrative authorities or legislative texts. At the beginning, Compliance Law was not a theorized and structured normative corpus but rather an aggregate of practices which just had in common the fact to propose a similar and new way of regulation placing the firm, and not on the public authorities anymore, at the heart of the system. Since 2016 and the Marie-Anne Frison-Roche's article "Compliance Law"[78], doctrine try to name, define and structure these new practices to build a coherent and structured new branch of Law.

A- The Apparition of a Monumental Goal

Compliance Law starts with the rise of a monumental goal. We can define "monumental goal" as an ambitious and principle-based objective.

1- Monumental goals, because they are complicated, urgent and sometimes global are ambitious objectives

"Monumental goals" are most often pretty ambitious and it is the reason why they are called "monumental". Some examples of "monumental goals" could be "protecting the environment from global warning", "fighting against corruption in the world" or "preventing terrorist attacks". In these cases, the objectives are ambitious because they consist in addressing complicated, urgent and, sometimes, international problems or crisis.

First, "monumental goals" are, most of the time, complicated. Here, it is not important to

78 Frison-Roche, M.A., *Compliance Law,* 2016

confuse a "complicated problem" and a "complex problem". "Complicated problems" are technical problems. To solve them, we need a high quantity of technical knowledge and experience and sometimes a lot of work by people having this high quantity of technical knowledge and experience. However, this kind of problems, if the right people are working on it, is solvable because, as a mathematical problem, it has a solution, even if it is not known by us a priori. "Complicated problems" have one solution that it is just necessary to find. It is a matter of transpiration. "Complex problems", however, are problems due to the coexistence of contradictory but legitimate positions on a topic. To solve them, we need to balance those contradictory opinions or to decide between one of them. Here, the solving is not a question of engineers but a question of politics because only politics is legitimate to make a decision on a "complex issue". "Complex issues" do not have only one right solution but most of the time many. It is then necessary to choose the one which is the least worst solution (which hurt the less) or the best solution (which conciliate the most). But, in every case, solving a "complex problem" needs to use opinions and it is the reason why "complex issues" are the field of politics. Here, it is not a matter of transpiration but a matter of inspiration. "Monumental goals" are complicated problems that results from the decomplexification of a complex problem. Let's take an example here. Financial crisis is a complex problem. Indeed, some economists would say that they are due to the internal process of our capitalist economies, that they are attesting of the normal working of the system and that they are the normal and best way of regulating the market[79]. Others will say that financial crisis are catastrophic for economic activities and that they are detrimental for working people who can lost their jobs, their house and end up in misery with a huge debt to reimburse and that in this perspective, it is essential to avoid crisis[80]. We are face to two contradictory but legitimate point of view on the same question and therefore in front of a "complex problem". By building Banking Union in 2014[81], politics chose in favor of the second opinion and decided that crisis must be avoid. This "complex problem" was solved and does not exist anymore. However, this problem was replaced by a complicated one because, even if we are persuaded that there is a way to avoid crisis, no one knows how indeed avoid the crisis. It is now the time for experts to relay politics to find the solution to this "complicated problem". In this case, the monumental goal "avoiding financial crisis" is a complicated problem that results from the decomplexification of a complex problem.

The global aspect of some problems[82] makes it even more difficult to solve because as we do not have "global State", their solving leans on international cooperation of actors from different States whom the objectives are different or contradictory and not benefiting from common space of communication, coordination and collaboration or from a powerful institution of control entitled to distribute sanctions in case of defective behavior from an actor.

Finally, "monumental goals" are urgent problems. Because they are global and complicated they, most of the time, remained unsolved. However, this absence of solution present risks of very detrimental consequences in a more or less close future. Global warming is for example unsolved and the fact that we did not find yet a solution to global warming is dangerous and worrying when we know that global warming could lead to the flood of many littoral regions, to dryness in countries where the water is already scare and to the death of biodiversity. The conjunction of danger and the fact that this problem is still unsolved is emergency.

79 Minsky H., *Stabilizing an Unstable Economy*, Yale University Press, 1986
80 Galbraith J.K., *The Great Crash, 1929*, Pelican, 1961
81 Article 114 and article 127, paragraph 6 of the Treaty on the Functioning of the European Union
82 Frison-Roche M.A., « From Regulation Law to Compliance Law », 2017

2- "Monumental goals" are principle-based objectives

One of the specificities of the "monumental goals", except that they are ambitious, is that they are principle-based. This means two things: "monumental goals" are necessarily set by politics and "monumental goals" are voluntarily conceived as general and vague.

As we have said just before, "monumental goals" are the result of the decomplexification of a complex problem. As a complex problem may only be solved by politics, this means that "monumental goals" are necessarily set by politics. But, politics is not an engineer. Politics does not give instructions about a way to achieve something. Politics just states what is the general willingness of the sovereign population that it represents[83]. And, politics states this general willingness thanks to a principle[84]. What it is particularly important to understand here, it is that "monumental goals" are not a policy or a measure taken in order to address a problem. A "monumental goal" is simply the expression, by a legitimate and powerful institution, of a willingness. Most of the time, we are used to see politics accompanied its general statements by concrete measures and tools to implement it. It is its executive aspects. However, executing is not the first essence of the politics. The first essence of the politics is to decide what is the general opinion of the population and to express it. Politics' mission is to search what it wants and to tell it. Here, we are touching the fact that "monumental goals" are most often ethical principles[85]. When the politics states that it does not want corruption anymore, it is not because corruption is detrimental for the economy but just because it is considered as morally bad and unfair. "Monumental goals" are a matter of values and life's principles. It is also the reason because politics never justify them, besides the fact that it is the politics and that politics never has to justify. Once the general willingness is told, it becomes an assumption that must give the actions of the different actors and it is not a topic to debate anymore. The agents must take it as it is, without questioning it and do what they have to do to achieve the goal or to not impede its realization, according to the role they have. Working to achieve it is the role of the crucial operator as we will see just after while not impeding is the duty of anyone else. But the mission of the politics stops when it has stated the general willingness, especially under Compliance Law[86].

One of the other characteristics of the principle-based "monumental goal" is that it voluntary remains vague and general. It is general because, as we said, it is said by politics and that the mission of politics is to create general principles and not instructions notebooks. But the fact that "monumental goals" remains vague permits to those who are able to pursue it and who have the knowledge to know how to pursue it to express their talent. We will see just after the role of the crucial operator who is entitled – and sometimes enforced – to work in order to achieve the "monumental goal". Crucial operator, especially because of the generalness of the "monumental goal" and of its imprecision concerning its implementation, is free to choose the most appropriate way to achieve it[87]. Politics wins because it finds a solution to its unsolved problem and the crucial operator sees its compliance constraint soften by the freedom it has to realize the politics' goal.

B- The Inability of the Regulator to Reach the "Monumental Goal"

83 Rousseau, J.-J, *Du Contrat social*, Flammarion, 2011 (original edition: 1762)
84 Frison-Roche M.A., « From Regulation Law to Compliance Law », 2017
85 Frison-Roche M.A., « From Regulation Law to Compliance Law », 2017
86 Frison-Roche M.A., « From Regulation Law to Compliance Law », 2017
87 Frison-Roche M.A., « From Regulation Law to Compliance Law », 2017

As we said in the precedent section, Compliance Law starts with the statement by politics of a "monumental goal". The question is now to know who will be in charge of realizing the goal set by politics. In this perspective, it could seem obvious to entitle an independent and administrative authority to achieve the "monumental goal" or to reinforce the mission of the existing regulator if there is already a regulatory authority in the sector. Here, we will be in the frame of Regulation Law, which was now pretty well admitted by doctrine since the founding Marie-Anne Frison-Roche's works in 2001[88]. Regulation is a balance, by a regulator, between competition principles and other principles different from or anti competition in a sector. "Monumental goal" could be one of these other principles and its balancing with competition may be entrusted to the regulator. However, regulators are sometimes too weak to be entitled with such a mission. When we are facing a complicated, global and especially, urgent "monumental goal", the crucial point is to be efficient and effective. But, is the regulator the most effective actor to achieve the goal? Sometimes, regulators could suffer from asymmetry of information in comparison with operators which make them unable or less able to pursue the aim set[89]. Indeed, in some cases, some operators, that we will name later "crucial operators" because they effectively are on the ground and implicated in the activity of the sector, are more able than the regulator to pursue the goal.

1- The regulator can lack of professional expertise

First, by their practice or because of their expertise, operators can have an empirical or theoretical knowledge than the regulator does not have, about what is the best way to achieve the goal. Regulator is an external authority that is too far from the ground and that could be out of the realities of the way things happen in the sector. Moreover, regulators sometimes do not have the necessary expertise or technical background to understand what the operators do or to know what the operators should do. In this perspective, regulators could do more harm than good. This detrimental lack of information for the regulator, is particularly visible in sector where the operators are professionals like health, for instance[90]. Physicians are considered as the best positioned, especially because of its knowledge, to know what to do in a situation concerning healthcare. The regulator, who is not a doctor, is unable to tell the physician how he or she should or must act.

2- The regulator may be unable to collect necessary information

Secondly, because they act in the sector, operators can have information that is necessary to the realization of the goal or being in capacity to collect it, contrary to the regulator. Let's take an example, here. Fighting against corruption – which is a monumental goal – requires to prove that an important amount of money is circulating between one person who has a power of decision-making and another who has interest that a certain decision, that the first person is entitled to make, was made. Regulator cannot see this circulation which is private and that would obviously be hidden to it. However, the two protagonists cannot hide this to the bank who can see that money is circulating between these two accounts or that an amount is withdraw from one account while the same amount is paid into the other account. Here, operator have information that the regulator cannot have. Even if it does not have information, the operator sometimes can manage to have it while regulator cannot. For example, the bank could force every person who wants to make a transfer to declare it to the bank for a priori checking[91].

88 Frison-Roche, M.A., « Le Droit de la Régulation », 2001
89 Frison-Roche, M.A., « From Regulation Law to Compliance Law », 2017
90 Greener, I., *Public Management*, Hound mills: Palgrave Macmillan, 2013
91 Frison-Roche, M.A., « From Regulation Law to Compliance Law », 2017

3- The regulator does not have a direct contact with some actors

Finally, operators can have the opportunity, on the occasion of their activity to act in a sense that will make the realization of the goal progress. This opportunity appears, most of the time, when the achievement of the "monumental goal" requires that another actor – than the firm and the regulator - change his or her behavior. However, the regulator does not have a direct contact with this actor to incentivize or force him or her to change this behavior while the firm has one. Let's take an example. The fight against global warming requires that energy consumers decrease their consumption of energy. In this case, regulator cannot really force the consumer to decrease its consumption nor incentivize him or her to dot it. However, energy distributors, because they have a direct contact with the consumer and because they can use the service they offer as a compensation to the change of behavior by the consumer, are in a better position than the regulator to incentivize the consumer to act for global warming. It is the reason why France has implemented in 2005 the *Certificats d'économie d'energie* (Energy Saving Certificate Program)[92] that the energy distributors are forced by the Ministry to obtain from consumers. Because of their local implementation and of their economic power, firms can obtain some change in consumer's behavior that the regulator cannot get.

4- The regulator is limited by national borders

As we have said just before, some "monumental goals" are global. However, realizing a global "monumental goal" requires that the entities which works for that would be global too. Fighting against pollution must be done at the world scale because pollution does not know any human borders and circulates across countries. If one State (A) makes strong ecological policies but that its neighbor (B) does not do it, the problem would be not solved because pollution from country B would go to country A and because seeing this situation, country A would be tempted to give up its strong ecological policies seeing that, anyway, pollution would be present in country A[93]. The only way to avoid this free-rider problem is to have a global regulator. But regulator is linked to the State which is itself limited by its national borders. On the contrary, some firms are multinational and not limited by national borders. They act in every or at least many countries and could be more able, as they are global, to pursue the global "monumental goal".

Therefore, as traditional regulator cannot act effectively, politics needs another actor, best positioned to realize the "monumental goal". This powerful and able actor will be named "crucial operator".

C- The Existence of a "Crucial Operator"

As we have said, Compliance Law takes on its full meaning when Politics, through its regulator, is not able to address a problem or to reach the "monumental goal" that it is expecting. Face to this Public failure, while traditional policy making would try to reinforce public power, sometimes failing, Compliance Law accepts the fact that the Politics is too weak and will never be strong enough to reach the goal. Instead, Compliance Law prefers looking around to see if there is another actor that would be more powerful or better positioned than Politics to reach the goal. And, if this kind of actor would exist, Compliance

92 Article 14 to 17 of Law n°2005-781 of 13th of July 2005 de programme fixant les orientations de la politique énergétique

93 Olson, M., *The Logic of Collective Action: Public Goods and the Theory of Groups*, Cambridge, MA: Harvard University Press, 1965

Law calls it "crucial operator" and legally enforce it to pursue the "monumental goal" that the Politics cannot pursue itself.

1- It is the ability which distinguish the "crucial operator" from the others

In the case we precedingly saw, judge Balkman considers that *Johnson & Johnson*, and more broadly the drug manufacturers that they represent, are the appropriate actor to prevent a new opioid crisis and that they are in the best position, among all the other actors implicated, to make sure, with the most efficiency, that such a crisis does not occur anymore. In compliance Law, we talk about "crucial operator" to name this "best-positioned actor"[94]. Considering drug manufacturer as a "crucial operator", it is considering that drug manufacturer is able, by constraining its own behavior or by constraining the behavior of others, to get the expected results. It is judging drug manufacturers powerful enough to reasonable expect that they can do something.

What is particularly important here is that, comparing to the traditional Tort Law, it is not the fact to be generator of a damage that hold you liable to repair it, it is the fact to be able to prevent a risk that hold you liable to avoid it[95]. Therefore, the couple fault/damage is replaced by the couple capacity/risk. Tort Law is enforceable when we are in presence of a fault and of a damage[96] while Compliance Law is enforceable when we have a risk and an actor able to prevent it[97]. This way of thinking is very revolutionary because what we said before means that it is possible to punish someone or to force him or her to do something even if he or she is not the cause of the damage created or that will be created. Compliance Law distinguish causation of a damage from liability. Whilst under traditional Tort Law you may be liable only if you caused a damage and being a cause of a damage hold you immediately liable of it, under Compliance Law, you can be liable without being the cause of a damage and being a cause of a damage without being liable because you are not powerful enough to make a difference. This great difference between Tort Law and Compliance Law is due to the fact that Tort Law exclusively uses Ex Post liability when Compliance Law uses quasi-exclusively Ex Ante liability[98]. When what is important is past for Tort Law, what's matter is future for Compliance.

Moreover, crucial operator is not chosen because the "monumental goal" is close to the one it already pursues. "Monumental goal" is not necessarily complementary or in concordance with the goal of the "crucial operator". Sometimes, "monumental goals" are radically different from the initial essence of the "crucial operator" and sometimes, "monumental goals" are even contradictory to the goal that the "crucial operator" is already pursuing. It is the reason why Compliance Law could have a constraint aspect.

2- The "crucial operator's" work is characterized by a large freedom but also by a huge liability

Moreover, most often, when the judge sentences a "crucial operator" to Compliance, he or she never indicates to the "crucial operator" what is the path to take in order to achieve the objective assigned. The reason why, the judge does not do that is that, most often, nor him nor anybody else has even a blurred idea of what could be the path to take. This means that being a "crucial operator", it is not only being considered as able to walk

94 Frison-Roche, M. -A., "Proposition pour une notion : l'opérateur crucial", *Recueil Dalloz*, 2006, n°27

95 Frison-Roche M.A, « Du Droit de la Régulation au Droit de la Compliance », 2017

96 Cabrillac, R., *Droit des obligations*, Dalloz, Third Edition, 2018

97 Frison-Roche M.A, « Du Droit de la Régulation au Droit de la Compliance », 2017

98 Frison-Roche, M. -A., « Le couple Ex ante - Ex Post, justificatif d'un droit spécifique et propre de la régulation », 2006

towards the destination, it is also and especially being considered as able to find the best and fastest path to reach the destination. The judge therefore let the "crucial operator" free to choose the path that seems to it the most effective to get the goal fast[99]. So, the only thing that the judge set here, it is a "monumental goal" to achieve and a system of sanctions to incentivize the "crucial operator" to indeed do its best to reach the target[100].

The most effective way to make sure that the "crucial operator" will work hard towards the goal is to tell it that we already hold it liable in the eventuality of any occurrence of a problem. Compliance Law works like that because Ex Ante liability sounds like a strong incentive but also to make control much easier. Indeed, supervisor most often suffers from asymmetry of information and especially moral hazard[101]. In comparison to the "crucial operator" who is considered competent and powerful to find a way to reach the goal and indeed reach the goal, supervisor is not considered as having this knowledge because if it has it, there will be no need to implement a Compliance system, regulator would implement some appropriate measures itself. In this perspective, supervisor cannot judge of the means used by the crucial operator because it does not have any idea of what the salient tools to used are. The only thing that supervisor can do is so judging the results of the "crucial operator"[102]. It can do that because the supervisor knows what the goal is. The aim in our case is "not having any crisis anymore". In the *Johnson & Johnson* case, judging the results is pretty simple: if there is no crisis, the drug manufacturer is considered as successful in its work to prevent a crisis; if there is a crisis, drug manufacturer failed in his duty to prevent and is therefore hold liable. Even a child or a machine could do that. Compliance therefore leans on a strong freedom/liability couple. The "crucial operator" has a full freedom to choose the way to reach the goal but assume a strong liability if it fails.

Of course, obligation of results could be particularly cruel. First, we hold liable someone who is not necessarily the cause of the damage and who is sometimes called, because of his or her ability, to repare a problem caused by other ones, and moreover, we would punish him or her if he or she fails to achieve the goal imposed? It seems all the more unfair that the supervisor and the regulator, most of the time and because of the asymetry of information whose they are suffering, do not know if their goal is indeed achievable by the "crucial operator". It is the reason why regulator and supervisor often satisfied themselves to impose an obligation of means to the "crucial operator" instead of an obligation of results, which seems less credible, realistic and fair than obligation of mean. It is then asked to the "crucial operator" to do its best to achieve the goal and it would therefore be punished only if the "crucial operator" cannot prove that it did everything it could to reach the goal and that the realization of the goal is conditionned to elements independent to its willingness. Obligation of means is delicate to make effective for public authorities which are not aware of the real efforts made by the "crucial operators" and which cannot measure what are the reasonable effort that could be expected from the "crucial operators", once again because of asymetry of information, and obligations of means seems less incentivizing for the crucial operators but it seems definitively fairer, that is still precious in a "rule of Law".

In a way, Compliance Law is therefore internalizing Regulation Law into "crucial

99 Borga, N., Marin, J.-C., Roda, J.-C. (dir.), *Compliance : l'entreprise, le régulateur et le juge,* Dalloz, 2018

100 Frison-Roche, M-A, « Compliance et Incitations : un couple à propulser » in Faculté de droit de l'Université Toulouse-Capitole et Journal of Regulation & Compliance, *Les incitations, outils de la Compliance,* 12/12/2019

101 Ross, S., and Mitnick, B., "Origin of the Theory of Agency", University of Pittsburgh, 2006

102 Frison-Roche, M.-A. (dir.), *Régulation, Supervision, Compliance,* Dalloz, 2017

operator"[103]. The crucial operator becomes a second-level regulator because it is now in charge of the achievement of the "monumental goal" instead of the regulator judged less able to do it and a new operator is created to monitor the "crucial operator" and make sure that the "monumental goal" is achieve or, at least, pursued: the supervisor.

II- WHY DOES COMPLIANCE LAW SEEMS INTERESTING IN OUR FRENCH OPIOID PROBLEM?

Now that we have seen what Compliance Law is, let's see if this branch of Law could sound interesting for us in our French opioid problem. Compliance Law is interesting if two conditions that we have presented just before are fulfilled: the rise of a "monumental goal" and the inability of the current regulator to achieve it. In this section, we will show that opioid problem has created a "monumental goal" that the current regulator is unable to pursue. It is after having showed this that we will be enabled to search who would be the "crucial operator" able to realize the objective set, in the next part of this master thesis.

A- The French Opioid Problem Rises a "Monumental Goal": The Right Use of Medicines

Opioid problem in France has risen a "monumental goal" which is the right use of medicines. Making sure that drugs are correctly used is not a new ambition. Indeed, many drugs present risks if they are misused even those which are not classified as narcotics because of undesirable effects. However, opioid problem has risen the right use of medications as a "monumental goal" because misusing opioids seems much more dangerous, for the patient but also for society when we see the number of deaths caused and that are likely to come in a close future.

1- Guaranteeing the right use of medicines is not a new ambition

Drug history is driven by the idea that drugs are ambivalent. Obviously, drugs are considered as a life-saving remedy that permits to cure ill and injured people, but medications inspire defiance from citizens suspecting dangerous effects of it. Indeed, drugs miracle hangs by a thread. Everything is a matter of use. The patient needs to use it sufficiently to enable the drug to have an effect on his or her organism to cure him or her but not too much because an overuse could lead to, sometimes serious, detrimental effects. If the patient uses the drug correctly, it will be cured and if he or she misuses it, he or she risks experimenting serious problems, including death. An extreme and the other.

Indeed, the border between drugs and poisons is very thin. Bertrand Lebeau Leibovici explains that history of drugs and history of narcotics are closely imbricated because many molecules that are considered as illicit narcotic now were legal drugs in the past and that a lot of molecules that serves today as medications were previously considered as dangerous and illegal narcotics. According to this physician, expert in addictology, the words "drugs" and "narcotics" are conventions and that every drug could be considered as narcotic and every narcotic could be considered as drug because both fulfill the same function, enabling people to feel better, and that their qualification is just a matter of convention and of what a society is morally ready to accept and what it is ethically not ready to tolerate[104].

103 Frison-Roche M.A, « Du Droit de la Régulation au Droit de la Compliance », 2017
104 Bertrand Lebeau Leibovici, « Drogues : sortir de la prohibition ? », in *Chimères*, 2010, n°74, pp. 113-121

Public authorities have therefore the choice between authorizing medications in order to cure people but with the risk that some patients abuse and forbid medications in order to prevent every kind of abuse but taking the risk that people who really need to be cured could not access a way to recover. Public authorities balanced these two options by taking a decision caught in the middle: medications would be authorized but they will be delivered only after the control and the authorization of a labeled physician. Indeed, "*le pharmacien ne peut délivrer un médicament ou produit autre que celui qui a été prescrit [par une personne habilitée]*[105]"[106]. Controlling use via an expert intermediary is therefore the solution found to solve this dilemma. Drugs are safe and effective only if these medications are rightly used, knowing that this right use itself does not permit much gap from the norm. The difference between drugs and poison is very thin: the poison is the misused drug and the drug is the appropriately used poison.

2- Opioid problem has risen right use of medicine at the rank of "monumental goal"

Therefore, the idea that drug could be dangerous and that their safety and efficiency is conditioned to a right use that is very precise and that which hangs by a thread, is not new. Guaranteeing the right use of medicine is a goal for many decades. However, is it a "*monumental* goal"? The opinion of this master thesis is that opioid problem has transformed the right use of drugs from a goal to a "monumental goal".

First, the massive number of people dying because of opioid overdoses or who risk to be touched by addiction or death by overdose in the future is massive as we saw in the precedent chapter of this master thesis[107]. These statistics has made the right use of medications more and more crucial. Indeed, the right use of opioid is the key issue of the opioid problem in France. If health professionals and patients respect the recommendations and use opioids seriously and correctly, there is no risk that opioids cause addiction and death by overdose: opioid problem would be not a problem anymore. However, if health professionals and patients transgress recommendations and start to misuse opioid painkillers, then there is a high probability that opioids create an addiction and cause a death by overdose. In this second case, it is highly probable that current opioid problem turns towards a future opioid crisis. It is therefore essential to guarantee a right use of opioid painkillers by health professionals and patients in order to prevent an opioid crisis in France like in the United States[108]. Because guaranteeing right use of opioids is the crucial condition to avoid a health tragedy and because the tragedy risked in case of non-fulfillment of this condition is massive in number of victims, we can therefore consider "the right use of opioid painkillers" as a "monumental goal" which must be reached as a priority by the different actors playing a role in the conception, the manufacturing, the sell, the prescription, the delivery and the consumption of opioid painkillers.

According to Compliance Law, if right use of opioids becomes a "monumental goal", then everything that is possible and necessary should be done to reach the goal. We are here in a teleological conception of Law where the end justifies the means and the legitimacy of the means used depends on the end and only on the end. If the mean is necessary to the end, then it is legitimate to use it and it must be used, regardless of other considerations.

105 "The pharmacist cannot deliver a medicine or a product which was not prescribed [by an entitled person]" (translation by the author).

106 Article L.5125-23 of the CSP

107 Monzon, E., "États des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Report of ANSM,* February 2019

108 Authier, N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération,* 23/02/2019

On the contrary, the mean is judged useless and is abandoned. The only criterium of evaluation of a mean is effectivity, efficient and usefulness. This conception is very different from traditional Law for which the end does not matter and for which the most important is procedures[109]. However, for the moment, right use of opioid painkillers does not seem to be indeed sufficiently respected[110]. On the contrary, the driving concept of patient-health professionals relationship is rather the respect of the patient's right to not suffer enacted since the end of the 1990s[111] and the freedom of choice for the patient considered as sufficiently enlightened on the medicine knowledge and on its own feeling to choose the best treatment for him or her[112]. The proof of this non respect of right use of opioid painkillers is the current opioid problem faced by French health authorities that we presented previously and which is manifestly due to a disregard towards recommendations of safe use of opioids. Making right use of opioids "monumental goal" and adopting a more teleological vision of Law have the aim to make right use of opioids *effective*.

B- The French Opioid Problem Puts ANSM in Front of Its Powerlessness

At this stage, we have identified a "monumental goal" which is "guaranteeing the right use of opioid painkillers". The first step to know if Compliance Law is interesting in our case is accomplished. Now, it remains to assess the ability of the regulator. French administrative authority in charge of medicines is the ANSM. At the European level, the European Medications Agency (EMA) fulfills the same missions than ANSM does in France. Here, we will remain focus on the French case but everything that we will be able to say on ANSM is true for EMA and we will consider this two institutions substitutable. Each time ANSM would be evoked in this master thesis, let's considering that there are these two regulators that are mentionned together and that it is drug regulator (both at the national and European level) which is concerned. What is particularly important to understand here is that ANSM is not only in charge of the right use of drugs but also in charge of the entire regulation of French pharmaceutical sector. Even if the right use of medicines is part of its mandate[113], ANSM is especially interesting by safety of the drug in itself by evaluating the security and the efficiency of the drugs[114]. The aim of ANSM is indeed to make sure that products offered to patients are safe, especially by delivering marketization

109 Frison-Roche M.A., « Dessiner les cercles du Droit de la Compliance » in *Études en l'honneur de Philippe Neau-Leduc. Le juriste dans la cité*, coll. « Les mélanges », LGDJ-Lextenso, 2018, pp. 483-496

110 Muszczak, A., « Enquête sur les pratiques de prescription d'opiacés des médecins généralistes,dans le traitement des douleurs chroniques non cancéreuses: à propos d'une étude de faisabilité dans le Grand-Est. » *Sciences pharmaceutiques*, 2015

111 Lohman, D., « S'il vous plait ne nous laissez pas souffrir… L'accès au traitement de la douleur est un droit humain », *Human Right Watch Report*, 2009

112 Thompson, D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend?, *Florida State University Law Review*, Article 6, Vol 13, Issue 1, 1985

113 Article L.5311-1 of CSP: "L'agence participe à l'application des lois et règlements et prend, dans les cas prévus par des dispositions particulières, des décisions relatives à l'évaluation, aux essais, à la fabrication, à la préparation, à l'importation, à l'exportation, à la distribution en gros, au courtage, au conditionnement, à la conservation, à l'exploitation, à la mise sur le marché, à la publicité, à la mise en service ou à l'utilisation des produits à finalité sanitaire destinés à l'homme » *(translation by the author : « the ANSM participate to the application of law and, in the cases foreseen by special dispositions, make decisions concerning the evaluation, trials, manufacturing, preparation, exportation, distribution, brokerage, packaging, conservation, exploitation, marketing, advertising, delivery and use of drug used by humans")*.

114 Article L.5311-1 of CSP: "L'agence procède à l'évaluation des bénéfices et des risques liés à l'utilisation des produits à finalité sanitaire destinés à l'homme" *(translation by the author: "the agency evaluates benefits and risks linked to the use of health product")*.

authorizations[115] and by realizing pharmacovigilance studies and reports[116]. In this task, the privileged ANSM's interlocutor is drug manufacturer. Indeed, ANSM, not assessing the use but the safety of the drug in every circumstances, has more interest to focus on the conception and production part of the drug circuit and less on the prescription, delivery and using part because if drugs are make safe upstream, then they will be necessarily safe downstream. Here, we can see that ANSM is not really the regulator of the good use of opioids, for the moment. However, as they are no other institutions in charge of guaranteeing the right use, may ANSM be charged of this new and essential mission?

1- ANSM lacks of expert knowledge to regulate the right use of opioid drugs

Making ANSM competent to ensure the right use of the medication would say that health professionals and patients should become the new privileged interlocutor of the agency. However, this change includes a major problem that is the asymmetry of information between the two parts of the relationship[117]. As we said just before, to be able to regulate a sector and to implement a "monumental goal" in it, a regulator should detain the same amount of information on the way to act in the sector than the operator. However, in our case, the ANSM does not have the professional knowledge of the physicians or of the pharmacists. Professional knowledge in this sector is not available to everybody just by wanting it. Medicine needs a high degree of expertise that could be obtained after many years of education and training and sometimes with many years of experience in the field. In this perspective, regulator, which is not physician cannot say to the health professional how he or she should or must behave. Moreover, even if the regulator would have the necessary and sufficient knowledge, it cannot see each patient to ensure that each of them indeed needs an opioid painkiller. It cannot feel what the patients feel, neither. Regulator does not have sufficient legitimacy because it does not know and cannot know what the best decision to make is. The only way to make regulator legitimate is that health professionals regulate other health professionals[118]. In other words, health professionals should regulate themselves. Here, we say that regulator is *caught* by operators. But, the pertinence of a regulator is its independence and autonomy from the field. A regulator is most often implemented in a sector in order to regulate it externally, politically and neutrally. If a sector is autoregulated, you cannot guarantee this external, neutral and political control over the sector and you cannot avoid that operators abuse of their power of autoregulation[119]. Here, we join the decision between efficiency and control. Either, you have a control but no full efficiency, or you have full efficiency but no control. Compliance seems therefore useful to solve this dilemma by internalizing regulation into expert operators (for efficiency) while supervising them (for control)[120].

2- To regulate the opioid consumption, ANSM would need some information that it does not have

115 Article L.5121-5 of CSP: « toute spécialité pharmaceutique ou tout médicament fabriqué industriellement […] doit obtenir, avant mise sur le marché ou distribution gratuite, une autorisation de mise sur le marché délivrée par l'ANSM […]" *(translation by the author: "every pharmaceutical specialty or every drug manufactured industrially [...] must have, before marketization or free distribution, a marketization authorization delivered by ANSM […]".)*

116 Article L.5311-1 of CSP: "l'ANSM guarantit la mise en place d'un système de vigilance" *(translation by the author: "[the ANSM] ensures the implementation of vigilance system").*

117 Greener, I., *Public Management*, Hound mills: Palgrave Macmillan, 2013

118 Greener, I., *Public Management*, Hound mills: Palgrave Macmillan, 2013

119 Stigler, G., « The Theory of Economic Regulation", Bell Journal of Economics and Management Science, 1971, Vol 2, Spring, pp.3-21

120 Frison-Roche, M.-A. (dir.), *Régulation, Supervision, Compliance,* Dalloz, 2017

Opioid problem may come from two behaviors from two different actors. First, opioid problem could be due to a misuse of opioid painkillers by the patient who does not follow the recommendations formulated by its physician[121] or who manage to get opioids via different physicians (we have called this later behavior "doctor shopping" in the first chapter of this master thesis)[122]. Second, opioid problem could be due to a wrong exercise of medicine by physicians who prescribe much more opioids that they should, either because they are not aware of the real danger of overconsumed opioid painkillers[123], or because they behave as true dealers, taking advantage of their right and freedom of prescription to prescribe opioid painkillers against money[124]. In facts, these two different behaviors (those of physician and those of patient) are imbricated. Indeed, some patients abuse of opioids because their physicians did not warn them sufficiently because they, themselves, did not have conscience of the potential danger of their prescribing or prescribed to much opioids, involuntarily, creating an addiction, that lead to an abuse of opioid painkillers. Moreover, we can understand very easily how doctor shopping and exercise of medicine as a business could be linked, addicted patients and unscrupulous doctors being accomplice of each other in a vast traffic of opioids.

Addressing these two problems requires, for the ANSM, to have access to two different information: patient's consumption statistics and physician's prescribing statistics. Indeed, if the ANSM does not know which patients are abusing and which doctors are prescribing wrongly, then how can the ANSM address the problem? Sanctioning a physician or prevent them to prescribe too much or taking care of patients who present symptoms of addiction or risks of abuse is possible only if the entity in charge of regulate can gather and collect all the information about consumption and prescribing. However, ANSM does not have this information which is hidden to it. As doctors have a freedom of prescription[125] and a duty to professional secret[126], they do not have to transfer the information about their prescription to the regulator. In the same way, pharmacists do not have to indicate to the regulator who has bought opioid drugs in their store. Here, the regulator suffers from asymetry of information because it does not have some crucial information, which is hidden to it for legal but also for technical reason, but that other actors detain or can easily gather. Compliance could be a way to force these actors to share this information with Public Authorities.

3- ANSM does not have a direct contact with patients

As we said, ANSM's favorite interlocutor for the moment is the drug manufacturer in order to make sure that drugs marketized are safe and effective. We can, obviously, imagine that ANSM also talks to health professionals. However, it is difficult to expect from ANSM

121 Monzon, E., "Etats des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Rapport de l'ANSM*, Février 2019

122 Ponté, Lepelley, Boucherie, Mallaret, Lapeyre-Mestre, Pradel, Micallef, « Doctor Shopping of Opioid Analgesic Relative to Benzodiazepines: A Pharmacoepidemiologic Study Among 11,7 million Inhabitants in the French Countries", *Drug and Alcohol Dependence,* 2018,187, pp. 88-94

123 Monzon, E., "Etats des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Rapport de l'ANSM*, Février 2019

124 Obradovic, I., " La crise des opioïdes aux Etats-Unis : d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

125 Article R.4127-8 of PHC: « Dans les limites fixées par la loi, le médecin est libre de ses prescriptions qui seront celles qu'il estime les plus appropriées en la circonstance » *(translation by the author : « in the limits set by law and considering of the science data, the physician is free of its prescriptions which will be those he or she estimates the most appropriated under the circumstances").*

126 Article R.4127-4 of PHC: "Le secret professionnel institué dans l'intérêt des patients s'impose à tout médecin dans les conditions établies par la loi" *(translation by the author: "each physician must respect the professional secret, implemented in the interest of the patients, under the conditions set by law")*.

that it should be in contact with patients. Regulation is possible when you are in a close sector with few, or at least, determined, operators. But every citizen is likely to be a patient and ANSM cannot expect something from them. ANSM can inform the patient, launching sensibilization campaign[127] but all this measures only can influence patients, persuade them or incentivize them but in any cases these measures can force them, directly or mechanically, to act in the desired way. But constraint is necessary to prevent opioid crisis. Indeed, influencing patients does not and cannot work for the simple reason that patients who overuse opioids are suffering or addict and that their consumption is irrational. Of course, they are aware of the danger of over consuming opioids for the great majority, but they are caught either in a process of violent pain or in a process of addiction that is stronger than their sense of rationality and that push them to act differently from what they seem fair and reasonable. The regulation of consumption should be direct or mechanical. We will call direct regulation the fact to simply and arbitrarily forbid the use of opioid to an agent. On the contrary, we will call mechanical regulation the fact to create some measure in order to make sure that patients cannot behave differently than correctly. But ANSM cannot neither regulate directly nor mechanically because either it does not have the sufficient information for that (see just above) or because they are not present on the ground to study each patient's case, because every case is different and should not be treat in the same way.

127 Monzon, E., "Etats des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Rapport de l'ANSM*, Février 2019

PART II: IN SEARCH OF A "CRUCIAL OPERATOR"

In the first part of this master thesis, we have shown that France is facing a rising problem with opioid consumption that presents serious risks of addiction and of deaths by overdoses. We have seen that facing a similar but deeper problem, United-States have chosen the way of Compliance Law to address their crisis. Since this point, our question is to know if the application of Compliance Law is possible in our French opioid case. After having presented theoretically Compliance Law, we have shown that our opioid case fulfills the two conditions permitting to assume that Compliance Law is applicable. Indeed, opioid problem has creating a "monumental goal" which is guaranteeing the right use of opioid painkillers, and the current regulator, ANSM, especially because of asymmetry of information problem, is unable to pursue it. Now that we have shown that Compliance Law sounds interesting for our case, the remaining question is: on which actor, a Compliance system should lean in France? In other words, who is the "crucial operator" which will internalize regulation and overcome the deficiencies of ANSM? As we start to see in the precedent part, Americans have judged drug manufacturer liable in Ex Ante for preventing opioid crisis. Let's see if such an idea seems the most appropriate in France.

CHAPTER I: THE INCREDIBILITY OF HOLDING DRUG MANUFACTURERS LIABLE IN EX-ANTE IN FRANCE

In this chapter, we will assess the pertinence of considering the drug manufacturer as "crucial operator" in our French opioid crisis. We will see if, as in the United-States, something more could be expected from drug manufacturers to prevent an opioid crisis. We will see that drug manufacturers, in France, already have a lot of duties that they do not have in the United-States – and this is the reason why, United-States choose to place them as a central piece of Compliance system – and that it is unreasonable to expect more from them.

I- CONTRARY TO THE UNITED-STATES, DRUG MANUFACTURERS, IN FRANCE, ALREADY HAVE A LOT OF ESSENTIAL DUTIES CONCERNING CIRCULATION OF INFORMATION ABOUT THEIR DRUGS

The *Johnson & Johnson* trial has created a lot of duties for the drug manufacturers, especially because they did not have many constraints before. In France, the situation is different. Indeed, as Nicolas Authier says: "*le système de régulation des médicaments nous protège plus qu'aux Etats-Unis: en France, la publicité médicale est interdite et la manière dont les laboratoires communiquent avec les médecins est contrôlée*[128]"[129].

A- Drug Manufacturers Have a Duty to Warn Patient and Health Professional About the Risks of Their Products in France and Not Only Health Professional Like in the United States

In the United States, drug manufacturer's duty to warn is limited and it is a reason why it is credible to expect more from them to prevent an opioid crisis. However, drug manufacturers, in France, already have a lot of essential duties in making information circulate between the different actors who will use it (health professionals and patients). In this perspective, the question about the reasonability to expect more from the laboratory is asked.

1- In the United-States, drug manufacturers do not have a duty to warn patients

In the United-States, drug manufacturers are not legally expected to warn patients about the risks and the way to consume the prescription drug they sell. Concerning over-the-counter drugs, drug manufacturers are required to inform patients of the right use of the drug because no intermediary is expected to play a role between the patient and the drug manufacturer. Indeed, the advice of a pharmacist is not required before buying an over-the-counter drug and a direct contact between drug manufacturer and patients is created. As someone must inform the patients and as the drug manufacturer is the only actor to be able to do so, it is then the drug manufacturer which is in charge of warning patient for

128 « The drug regulation system protects us more than in the United-States: in France, drug advertising is forbidden and the way drug manufacturers communicate with physicians is controlled" (translation by the author).

129 Authier, N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?", *Libération*, 23 of February 2019

over-the-counter drugs[130].

However, concerning prescription drugs, another actor appears – the physician – and he or she becomes an intermediary between the drug manufacturer and the patient. The question is then: who is in charge of warning patient between drug manufacturer and physician? In 1974, during the *Reyes v Wyeth Laboratories* affair, the judge has decided that "as a medical expert, the prescribing physician can take into account the propensities of the drug as well as the susceptibilities of his patient. He is the task of weighing the benefits of any medication against its potential dangers […] Pharmaceutical companies then, who must warn ultimate purchasers of dangers interests in patent drug sold over the counter, in selling prescription drugs are required to warn only the prescribing physician, who acts as "learned intermediary" between the manufacturer and consumer"[131]. Here, the judge creates what the doctrine will theorized as "the learned intermediary doctrine"[132]. The fact is that physicians are judged more able than the drug manufacturer to warn the patient because they have a direct contact with them which will facilitate the transmission of information and because they are the best positioned to adapt their advices to each patient's specific cases. Moreover, it is judged that drug manufacturer's warning could be contradicted by physicians and that, as drug manufacturers are not able to control the actions of physicians, it seems better to give the duty to warn the patient directly and exclusively to the doctor, who becomes the learned intermediary responsible of the warning of patients.

Therefore, especially during the *Dunkin v Syntex Laboratories* trial, the judge expressed clearly that it is physicians and not drug manufacturers who are liable to warn patients by saying that "the duty to warn the patient, if one exists, lies with the physician and not with the drug manufacturer"[133]. Many other decisions went in this direction too[134]. The judge has also had the opportunity to reinforce the absence of duty to warn for the drug manufacturer by saying, during the *Buckner v Allergan Pharmaceutical* affair, that "since physicians do have an absolute duty to inform patients of all possible side effects in every instance, failure to do so in a particular instance should not give rise to a duty in the manufacturer"[135]. So even if the physician does not warn the patient and that the drug manufacturer has known this failure, drug manufacturer remains not constraint to warn the patient. Therefore, drug manufacturer does not have any duty to warn patients of the risks and the way to use prescription drugs in the United-States[136] except for seven prescription drugs that are list in the paragraph 21 of the Code of Federal Regulations[137].

However, even if the duty to warn patients lies on the shoulders of health professionals and in any case on the shoulders of drug manufacturer, drug manufacturers still have the

130 Thompson, D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend?, Florida State University Law Review, 1985, Article 6, Vol 13, Issue 1

131 Reyes v Wyeth Laboratories, 498 F. 2nd 1264, 1276 (5th Cir. 1974)

132 Thompson, D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend?, Florida State University Law Review, 1985, Article 6, Vol 13, Issue 1

133 Dunkin v Syntex Laboratories Inc. 443 F. Supp. 121, 123 (CWD. Tenn. 1977)

134 Koury v Follo, 158 SE 2nd 548 (NC 1968), Sharpe v Pugh, 155 SE 2nd 108 (NC 1967)

135 Buckner v Allergan Pharmaceutical Inc, Florida 5th District Court of Appeal, 498 F 2nd 1264, 1276 (5th Cir), 419 US 1096 (1974)

136 Stone v Smith, Kline and French Laboratories, 447 So 2nd 1301 (Ala 1984), Singleton v Airco Inc, 314 SE 2nd 680 (Ga Ct App 1984), Kinney v Hutchinson, 449 So 2nd 696 (La Ct App 1984), Serna v Roche Laboratories, 684 P 2nd 1187 (NM Ct App 1984), Ross v Jacob, 684 P 2nd 1211 (Okla Ct App 1984)

137 Isopreterend inhalation drugs (§201.305), oral contraceptive (§310.501(a)), oral postcoital contraceptive (§310.501(b)), medroxyprogesterone acetate injectable contraceptive (§310.501(a)), intrauterine devices (§310.502), estrogenic drugs (§310.515), progestational drugs (§310.516)

duty to warn health professionals in order to enable them to reverberate this information to patients. This was assumed in the *Schenebeck v Sterling Drug'*s affair, for instance, when the judge remind that drug manufacturers have a duty to warn health professionals[138]. Even if drug manufacturers are not liable of the last step of the circulation of the information, it is clear that they initially detain the information and that they are the unique actor to detain it and that it is their duty to make it public and to make it available to the "learned intermediaries" who will be enable to understand it and to popularize it to non-learned patients". The drug manufacturer gives the appropriate information to the learned intermediaries who diffuse it afterwards.

This system is characteristic of United-States' cultural conception of Law. Indeed, in the United-States, duty is considered as a necessary evil which should be reduced to minimum. The existence of a duty is necessary for efficiency but multiplying the number of actors who must fulfill this duty is ineffective and considered as a hindrance to individual freedom. Therefore, the number of people forced should be reduced at the minimum permitting to guarantee an effective functioning of the system. Duty to warn could be given to physician *and* drug manufacturer but it is not vital. Indeed, if you give it only to the physician and that physician fulfill it indeed – and Americans believe in this because they trust the actor – then it is unnecessary and – if we consider constraint as an evil – detrimental to give it also to the manufacturer. European would think differently, with less trust, preferring multiplying number of actors forced because two people constraint are more valuable than one only and because constraint is not seen as a hindrance to individual freedom but as a favor done to the community.

However, this absence of duty to warn patients by manufacturers is probably one of the causes of opioid crisis in the United-States. Currently, drug manufacturers can do more than they are actually forced to do to prevent an opioid crisis – for instance, warning patients directly and jointly with health professionals – and it is the reason why they will be found liable in Ex Ante by judge Balkman.

2- In France, drug manufacturer already plays an important role in the circulation of information about drugs towards health professionals and patients

Contrary to the United-States, drug manufacturers in France already have a lot of duties regarding the circulation of information about their drugs.

a- Like in the United-States, drug manufacturers, in France, are forced to warn health professionals

The first interlocutor of drug manufacturer should be health professionals that drug manufacturer must inform about the potential dangers and risks of the drug and about the appropriate use of them.

First of all it is important to say that drug manufacturer must compulsorily make available for each health professional who is supposed to prescribe or deliver its product, a summary of product characteristics, according to the *Arrêté* of 6 of May 2008 taken in application of article R.5121-21 of CSP. This decree precises that the summary of product characteristics must include contraindications, warning and special precautions, drug interactions, undesirable effects, information concerning overdose (symptoms, emergency behavior, antidote…). The summary of product characteristics is the equivalent of medication label for patients and permits to doctors to be aware of the risks of each drug

138 Schenebeck v Sterling Drug Inc, 423 F 2nd 919 (8th Cir 1970)

and of the way it is supposed to be used to be effective and safe.

Face to this legal obligation to warn health professionals, drug manufacturers have also adopted, in 2019, a *Charte d'information promotionnelle* (CIP)[139]. This charter was signed between the drug manufacturer's trade-union (LEEM) and the Centre Economique des Produits de Santé (CEPS) which is a public institution. The legal value of this charter is not very high but it shows the intention of the drug manufacturers, through their trade-union, to participate to the reinforcement of drug promotional information quality in order to guaranteeing a good use of drugs by health professionals. Indeed, the CIP lists the good practices that pharmaceutical sales representatives should adopt when promoting drugs to health professionals. First, pharmaceutical firms engaged in guaranteeing competent pharmaceutical sales representatives. Indeed, the CIP says that "*l'entreprise dispense systématiquement une formation nécessaire à l'actualisation de ses connaissances réglementaires et scientifiques*"[140]. Pharmaceutical sales representatives should have the scientific but also legal knowledge appropriated to their function and the firm engages to train them if they do not have the competences required. By the way, the firms engaged to control this knowledge. Indeed, "*l'entreprise met en oeuvre une évaluation annuelle permettant d'attester que le salarié dispose des connaissances*"[141] according to the charter. In their work near to the physicians, representatives should clearly inform about the risks of the drug promoted. "*Est, en outre, obligatoirement remis aux professionnels de santé, tout document jugé nécessaire par l'ANSM*"[142]. In general, "*l'information favorise la qualité du traitement médical dans le soucis d'éviter le mésusage du médicament*"[143]. This means "*informer sur les posologies, les contre-indications, les effets undésirables, la durée du traitement*"[144] and ensuring that "*les informations concernant l'usage du médicament et notamment les effets indésirables, les précautions d'emploi et les contre-indications sont mentionnées clairement*"[145]. Moreover, representatives are supposed to "*présente et propose de remettre l'ensemble des documents de minimisation des risques prévus par les plans de gestion des risques ou les plans de minimisation des risques*"[146]. But, according to the charter, sales representative's mission does not stop with diffusing top-down information from drug manufacturer to health professionals. Indeed, sales representatives are also expected to get back bottom-up information from health professionals' experiences with the drug to transmit their feed backs to their firms. The charter says: "*ces personnes reportent à l'entreprise toutes les informations relatives à l'utilisation des médicaments dont elles assurent la publicité, en particulier, en ce qui concerne les effets indésirables et les utilisations hors AMM qui sont portées à leur connaissance*"[147] to enables their firms to "*se donner les moyens de mesurer ses actions*

139 Charte de l'information promotionnelle (2019), signed between Les Entreprises du Médicament (LEEM) and Le Centre Economique des Produits de Santé (CEPS).

140 "The firm systematically trains to actualize scientific and legal knowledge" (translation by the author).

141 "The firm implements an annual evaluation to attest that the employee gets the right knowledge" (translation by the author).

142 "All document judged necessary by ANSM, or other institution, must be given to health professionals" (translation by the author).

143 "The information given must favor the quality of the medical treatment in order to avoid misuse of the drug" (translation by the author).

144 "Inform(ing) about posology, contraindications, undesirable effects, length of the treatment" (translation by the author).

145 "Information concerning drug use and especially undesirable effects, use precautions and contraindications are clearly mentioned" (translation by the author).

146 "Presents and propose to give all the documents about minimization of risks foreseen by the risk management plans or risk minimization plans" (translation by the author).

147 "Those people report to the firm all the information concerning the use of the drug that they promote, especially concerning undesirable effects and off-label uses that they know" (translation by the author).

contribuant au bon usage, à la détection des prescriptions non conformes à celui-ci et sur les mesures visant à les corriger[148]"[149]. So, sales representatives should play the role of intermediaries between drug manufacturers and health professionals by diffusing information from manufacturers but by collecting feed-backs and experiences from health professionals. They are not only commercial representatives, they also are a messenger, the support of the dialogue between manufacturers and practionners. In this perspective, they are a key actor of the circulation of information in terms of medications. It is perhaps this crucial intermediary position which push the charter to consider sales representatives as the best positionned actor to relay some information to the doctors. The charter indeed says that "*conformément à la législation en vigueur notamment les articles L.162-17-4-1 du Code de la Sécurité Sociale), si des prescriptions non conformes à l'AMM sont constatées, l'autorité administrative peut demander à l'entreprise concernée de communiquer auprès des professionnels de santé pour rappeler le cadre de prescriptions défini par l'AMM et le cas échéant pour diffuser des messages correctifs qu'elles jugent utiles. Ces actions d'information spécifiques mises en oeuvre par l'entreprise ou le groupe d'entreprises en direction des prescripteurs peuvent être dévolues aux personnes exerçant une activité d'information par démarchage ou prospection. Le CEPS peut en demander la communication*"[150]. In the same way, the charter explains that "*lorsque l'entreprise constate des prescriptions non conformes au bon usage d'une spécialité, elle peut demander aux personnes exerçant une activité d'information par démarchage ou par prospection visant à la promotion de relayer aurpès des professionnels de santé les mesures d'information appropriées et en informe sans délais l'ANSM*"[151]. The attentive lector did not miss it: this kind of system is Compliance. Indeed, drug manufacturers are in charge of monitoring the use of their drug and to find a solution if it is not the case to remedy to this problem because they are better positionned than regulation agencies to collect information about the use of the medications and to warn practionners because they have sales representatives who are on the ground, who speech to the doctors, who see their practices and who know what is the information to give to them to help them to improve their use and who have the opportunity to give it.

Beyond information given through the summary of product characteristics and through sales representatives, drug manufacturers have the obligation to implement a pharmacovigilance system over their products even after their approval and marketization. Indeed, article R.5121-162 of the CSP forces the drug manufacturers to *"mettre en œuvre un système de pharmacovigilance pour s'acquitter des obligations qui lui incombent en matière de pharmacovigilance, et notamment pour procéder au recueil et à l'évaluation scientifique de toutes les informations relatives aux effets indésirables dans un but de prévention et de réduction des risques »*[152]. According to the article R.5121-164 of the

148 "Find a way to measure its actions contributing to good use, to the detection of non-compliant to good use prescribing and to measure its actions to correct them" (translation by the author).

149 Article L.5121-14-3 of CSP

150 "In compliance with current Law (especially article L.162-17-4-1 of *Code de la Sécurité Sociale*), if non-compliant to marketing authorization prescribing are observed, administrative authority may demand to the concerned firm to communicate to health professionals to remind prescribing legal framework defined by marketing authorization and, if it is necessary, to diffuse corrective messages which are judged useful. Those information actions may be implemented by the firm or the firm group for the attention of prescribers may be delegated to people in charge of door-to-door sales or prospection. The *CEPS* may ask for the communication of this information." (translation by the author).

151 "When the firm observe prescribing which are not compliant with the good use of a medicine, it may ask to the people in charge of door-to-door sales or prospection to relay to health professionals appropriate information and must inform the ANSM immediately" (translation by the author).

152 « Implement a pharmacovigilance system which collect and evaluate the undesirable effects with the double aim of prevention and reduction of risks" (translation by the author).

CSP, each drug manufacturer should have a person (either a physician, a pharmacist or someone justifying a competence in pharmacovigilance) who will organize post-approval risk studying and who will inform health professionals as well as ANSM about risks discovered. Moreover, each drug manufacturer is required to give frequent and regular reports to ANSM concerning permanent evaluation of risks according to a European directive of 2010 and must actualize its marketization authorization to the ANSM each time state of knowledge about risks and efficiency changes. Here, Law forces drug manufacturers to establish a risk mapping and to implement a risk management system. CSP defines risk management system as "*un ensemble d'activités de pharmacovigilance dont l'objectif est d'identifier et de décrire les risques liés à un médicament ou un ensemble de mesures dont le but est de prévenir ou de minimiser ces risques, y compris l'évaluation de l'efficacité de ces mesures. Cet ensemble de mesures et d'activités est proportionnés aux risques avérés, au potentielrisques du médicament et à la nécessité de disposer d'une information à propos de la sécurité après AMM*"[153].

What is important to understand here is that obligations of drug manufacturers are here much more important than traditional duties expected from classic firms. Indeed, we can expect that a firm is liable for its product until it is marketized and that the only thing that we can expect from it is that the product sold is without any risks when it is marketized. But it seems difficult to hold it liable for a risk that was impossible to detect at the moment of the marketization and that appears much later, especially if the drug has been approved by an administrative authority like ANSM. However, for drugs, manufacturers are expected to ensure that their product is safe at any time after marketization and at each time a patient would consume it. Following a drug to evaluate it frequently and regularly to ensure that it is still safe seems normal but what it is less common is to charge the manufacturer to do it. We can indeed expect that this is the role of the regulator to evaluate the risks post-approval and that the only responsibility of the manufacturer would be Ex Post if a risk is detected with a fault. However, because it has certainly more abilities to do it, it is drug manufacturer which is responsible for that in Ex Ante. Here, we are already in a Compliance system where regulation of drugs is internalized in firms which must do their best to prevent a risk and which could be hold liable if any problem would occur. Let's note here that drug manufacturer must evaluate each drug, give the information about these evaluations and find a way to reduce the risks found. It is a huge task, contradictory to what is supposed to be a manufacturer, for a firm which is just supposed creating a drug to, besides, find the risks, even those which appear after the marketization and which were unforeseen at the moment of the marketization, make them public and find a solution to fight them or to prevent them.

b- But, in France, drug manufacturers are also expected to warn directly the patient

More than warning ANSM and health professionals, drug manufacturers are also expected, in France, to warn directly the patient, contrary to the United-States. The expected way of communication between a drug manufacturer and a patient is usage instructions contained in each drug box sold. The article R.5121-148 of the CSP says that "*la présence d'une notice est obligatoire*"[154]. Article R.5121-149 of CSP completes this precedent obligation by saying that "*la notice comprend les instructions nécessaires pour*

153 "A group of pharmacovigilance activities whose the aim is to identify and describe risks linked to a drug or a group of measures whose the aim is to prevent or minimize those risks, including efficiency evaluation of those measures. This group of measures and activities is proportionate to the known risks, to the potential risks of the drug and to the necessity to have information about security after marketization authorization" (translation by the author).

154 "The presence of usage instructions is compulsory" (translation by the author).

un bon usage (posologie, mode et voies d'administration, fréquence, durée, conduite à tenir en cas de surdosage, conduite à tenir en cas de sous dosage, la mention si nécessaire d'un risque de syndrome de sevrage, la recommendations de consulter un médecin ou un pharmacien)"[155]. The existence of this medication label and its compulsoriness have their origin in the fact that CSP specify that a marketization authorization could include the duty to "*mettre en oeuvre des mesures garantissant l'utilisation sûre du médicament*"[156] or "*tout autre condition ou restriction destinée à garantir une utilisation sûre et efficace du médicament*"[157]. This obligation to warn patient by a medication label could be accompanied by the obligation for the drug manufacturer to give a "*une mise en garde spéciale, si elle s'impose pour ce médicament*"[158] according to the article R.5121-138 of CSP.

If the drug manufacturer does not provide sufficient and necessary information over its product, its liability could be engaged by the user of the product under the legal regime of Product Liability defined by Directive of 25th of July 1985 transposed in French Law in the articles from 1386-1 to 1386-18 of *Code Civil* and in the Law n°98-389 of 19 of May 1998. Under product liability the drug manufacturer's liability could be engaged if the product sold is defective. For this, the victim must prove that the product is defective and that this default caused a damage to him (default, damage and causality link between default and damage)[159]. Article 1386-4 of *Code Civil* declares that "*un produit est défectueux lorsqu'il n'offre pas la sécurité à laquelle on peut légitimement s'attendre*"[160]. A product could be considered as defective either because its conception contained a default but also because sufficient warnings concerning dangerousness or necessary using instructions were not provided to the consumer. This idea of defectiveness because of insufficient information was confirmed by case law. The *Cour de Cassation* said in 2009 that "un produit sans les informations suffisantes à propos de sa dangerosité est défectueux même s'il n'a pas de défaut intrinsèque[161]"[162], knowing that informing only health professional is not sufficient and that the manufacturer must also warn the patient to see its liability saved, according to the same court[163]. Concerning causality link between default and damage, the *Cour de Cassation* explained in 2008 that it is not necessary anymore to prove a certain causality link provided that there are "*présomptions graves, précises et concordantes*"[164] like temporal proximity between use of the drug and damage, number of victim, non existence of family precedents or good health condition of the victim before the use of the drug, aware that it is really difficult to prove a legal causality when scientific causality is uncertain or when scientific causality proof is not available to everybody's knowledge[165].

---

155 "The usage instructions must include necessary instructions for a proper use (posology, administration way, frequency, duration, appropriate behavior in case of overdose, the mentioning of a risk of withdrawal syndrome if necessary, the recommendation to ask information to a physician or a pharmacist before using)" (translation by the author).

156 "Implement measures to guarantee the safe using of the medication" (translation by the author).

157 "All other condition or restriction to guarantee safe and effective using of the medication" (translation by the author).

158 "Special warning if it is necessary for this drug" (translation by the author).

159 Article 1386-9 of *Code Civil*

160 "A product is defective if it does not provide the security legitimately required" (translation by the author).

161 "A product without sufficient information about its dangerousness is defective even if it does not have intrinsic default" (translation by the author).

162 Cass. 1ere Civ., 9 of July 2009, n°08-11073

163 Cass. 1ere Civ., 22 of November 2007, n°06-14174

164 "Serious, precise and consistent presumptions" (translation by the author).

165 Cass. 1ere Civ., 22 of May 2008, n°05-20317, n°06-10967, n°06-14952, n°06-18848 and n°05-10593

Therefore, drug manufacturer is liable in France for the warning of health professionals but also of patients and could be charged if it did not do it. If course, some exceptions exist and drug manufacturer's liability could be reduced or cancelled in certain cases. The first exoneration may be caused by a fault of the victim. Indeed, article 1386-13 of CC exposes that "*la responsabilité du producteur peut être réduite ou supprimée compte-tenu de toute les circonstances lorsque le dommage est causé conjointement par un défaut du produit et par la faute de la victime*"[166]. However, "*la responsabilité du producteur envers la victime n'est pas réduite par le fait d'un tiers ayant concourru à la réalisation du dommage*"[167] according to article 1386-14 of *Code Civil*. This means that drug manufacturer is not responsible if the user commit a fault but is still responsible if a physician or a pharmacist commit a fault during the process of prescribing. Moreover, and it is very interesting in our opioid case, "*le producteur peut être responsable du défaut alors même que le produit a été fabriqué dans le respect des règles de l'art ou de normes existantes ou qu'il a fait l'objet d'une autorisation administrative*"[168] according to article 1386-10 of *Code Civil*. This means that the fact to be labeled by an administrative authority does not exonerate the drug manufacturer from liability on its product and this means that if an existent but not seen default is discovered after the marketization authorization, it is not the fault of the regulator who did not found the default or who labeled a product wrongly but the fault of the drug manufacturer. In general, article 1386-11 of *Code Civil* lists the circumstances under which drug manufacturer's liability could be reduced or cancelled. According to this article, "*le producteur est responsable de plein droit à moins qu'il ne prouve: 1) qu'il n'ait pas mis le produit en circulation, 2) que, compte tenu des circonstances, il y a lieu d'estimer que le défaut ayant causé le dommage n'existait pas au moment où le produit a été mis en circulation par lui ou que le défaut est né postérieurement, 3) que le produit n'a pas été destiné à la vente ou à toute forme de distribution, 4) que l'état des connaissances scientifiques ou techniques au moment où il a mis le produit en circulation n'a pas permis de déceler l'existence du défaut, 5) ou que le défaut est dû à la conformité du produit avec des règles impératives d'ordre législatif ou réglementaire. Le producteur de la partie composante n'est pas non plus responsable s'il établit que le défaut est imputable à la conception du produit dans lequel cette partie a été incorporée ou aux instructions données par le producteur de ce produit*"[169]. The point that we will develop a little bit more here is the point n°4. This point means that drug manufacturer could be found liable only for default that were foreseeable at the time of marketization of the product. If nothing in the state of knowledge at the time of marketization could lead to think that there was a default, then it is unreasonable to hold drug manufacturer guilty of having marketed the product anyway because it could not know that a problem was existing. This point is the most used by attorneys to defend drug

166 "The manufacturer's liability could be reduced or cancelled, taking into account every circumstance, when the damage is due, jointly, by a product's default and by the victim's fault" (translation by the author).

167 "The manufacturer's liability towards victim is not reduced by the fact that a third party participated to the realization of the damage" (translation by the author).

168 "The manufacturer could be liable even if the product was manufactured in accordance with the standard practice or with the existent rules or if it was administratively authorized" (translation by the author).

169 "The manufacturer is liable except if he or she proves that: 1) he or she does not marketize the product, 2) taking into account of the circumstances, it is reasonable to consider that the default did not exist when the product was marketed by him or her, 3) the product was not supposed to be sold or distributed, 4) the state of scientific and technic knowledge at the moment of marketization did not permit to detect the existence of a default [development risk], 5) the default is due to the compliance of the product to legislative or regulatory rule. A component's manufacturer is not liable if he or she proves that the default is due to the global conception of the product or to the injunctions of the product manufacturer" (translation by the author).

manufacturers and the fact to know whether a company was supposed to know that something constituted a default or a danger is very often debated in trials. This point n°4 is a strong weapon in the hands of drug manufacturers to escape from liability because of the largeness of the interpretation permitted by it regarding what is supposed to be known. Moreover, this point n°4 may permit to the firm to claim that what is assessed by point n°4 is whether there is something in the state of knowledge of the time which permits to know that the firm was supposed to know the potential danger or defectiveness of its product and not whether the firm is able act on this state of knowledge. Indeed, it is sufficient to the drug manufacturer to prove that knowledge was missing to escape from liability without having to prove that this knowledge could not be found by the firm in question with a little bit more effort and precautions from it. The ability of the firm to fill the failure of the current state of knowledge is not assessed, only the stock of knowledge is considering. Nevertheless, courts try to be exigent with drug manufacturers by considering a upgraded version of state of knowledge. For instance, the *Cour d'Appel de Toulouse* in 2000 has explained that the evaluation of knowledge "*doit être faite de façon purement objective sans tenir compte des qualités et aptitudes du producteur*"[170] and that "*l'état des connaissances scientifiques et techniques est celui au niveau mondial le plus avancé au moment où le produit a été mis en circulation*[171]"[172].

B- Drug Advertising is Much More Regulated in France than in the United-States

As we have seen, drug manufacturers are only expected to warn health professionals in the United-States and that this represents a problem. Moreover, warning is not very effective if the drug manufacturer simultaneously engages in promotional information that could "nullify" the warnings provided in the same time. But, in the United-States we are unfortunately in this case with an evidence of overpromotion of opioids towards doctors but even more towards potential patients. In this perspective, expecting more from drug manufacturers – and especially that they stop their overpromotion – makes sense. However, in France, where drug advertising is already much more regulated than in the United-States, the room for manoeuvre is much more narrow.

1- In the United-States, drug manufacturer takes advantage of a huge freedom in its drug promotion activity

The Food, Drug and Cosmetic Act (FDCA), adopted in 1938 and which still is the reference text in terms of medications regulation, entitles the FDA to regulates advertising over prescription drugs in order to guarantee that promotion is "truthful, balanced and accurately communicated". However, the text does not distinguish non controlled drugs and controlled drugs concerning promotion. This means that a potentially dangerous drug, which presents many risks, like opioids painkillers, is regulated by the same rules regarding advertising than common and without any foreseable risks. Moreover, this text remains largely unapplicated. Indeed, the FDCA plans that every promotional material for prescription drug must be approved by FDA. However, many promotional materials are not examinated or too quickely examinated by FDA. The reason of this unapplication of FDCA is the limited staff of FDA. For instance, in 2002, only 39 people were in charge of reviewing approxiamtively 34 000 pieces of promotion materials[173]. Face to this limited and

170 "Should be done objectively without taking into account of the qualities and abilities of the manufacturer" (translation by the author).

171 "The state of scientific and technic knowledge is the most advanced at the world level at the time when the product is marketed" (translation by the author).

172 CA, Toulouse, 22 of February 2000, n°1999/01293

173 Van Zee, "The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy", American Journal of Public Health, 2009, Vol 99, No. 2

almost unapplicated text, it is reasonable to say that promotion is almost unregulated and free in the United-States in terms of prescription drugs.

It is just necessary to have a look at the promotion of opioid painkillers to illustrate this statement. Here, we will especially focus on the way Purdue Pharma had promoted OxyContin, the most popular opioid painkiller in the United-States, since 1996. According to the statistics collecting by Purdue Pharma, the sales of OxyContin passed from $48 million in 1996 to approximaively $1.1 billion in 2000[174]. But, according to the Medical Letter on Drugs and Therapeutics concluded in 2001, this increase is not due to the merit of the drug in itself which does not offer additional benefits than another opioid painkillers, contrary to what was claimed by Purdue Pharma and its scientists at the start of the marketization[175]. Rather, this massive increase of sales is due to an aggressive promotion campaign lead by Purdue Pharma[176]. For the unique year 2001, for instance, the firm spent over $200 million to promote its drug[177]. This huge promotion campaign took the form of conferences when scientists paid by Purdue Pharma presented and promoted OxyContin to physicians. Between 1996 and 2001, Purdue Pharma has organized more than 40 of this kind of conferences in various states of the country[178]. Approximatively 5000 health professionals attended thoses conferences[179]. The strategy implemented by Purdue Pharma consisted in profiling prescribers[180] to detect those who, because of the sociology of their patients or because of their prescription habits, were more likely to be seduced by OxyContin[181]. But, Purdue Pharma also hired many sales representatives to visit doctors and promote OxyContin. Between 1996 and 2000, the number of sales representatives in Purdue Pharma passed from 318 to 671 while the number of physicians targeted passed from 33400 to 94000 physicians[182]. Those sales representatives were incentivized by large bonuses. In 2001, the average annual bonus of a sale representative was $71500 and Purdue Pharma paid, the same year almost $40 million of incentives towards sales representatives[183]. Those sales representatives distributed to health professionals many goodies[184] and almost 34000 coupons which were a free limited in time prescription for a 7 to 30 days supply[185]. Many of Purdue Pharma promotion material was not reviewed by FDA. For instance, in 1998, Purdue Pharma diffused 15 000 copies of a promotional video without submitting it a priori to FDA. In 2002, FDA studied the video and found that the risks of OxyContin were minimized in this video and that the so called benefits of the drugs were overestimated. Moreover, Purdue Pharma engaged in a huge campaign of promotion towards potential patients and public by putting the issue of pain

174 ‘‘OxyContin Marketing Plan, 2002.’’ Purdue Pharma, Stamford, CN, 2002

175 Porter J. and Jick H., « Addiction rare in patients treated with narcotics », N Engl J Med, 1980, 302:123

176 ‘‘OxyContin Marketing Plan, 1996-2001.’’ Purdue Pharma, Stamford, CN

177 ‘‘OxyContin: balancing risks and benefits,’’ in Hearing of the Committee on Health, Education, Labor, and Pensions, United States Senate, February 12, 2002, p 87 (testimony of Paul Goldenheim, Purdue Pharma).

178 Florida, Arizona, and California

179 Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem. Washington, DC: General Accounting Office; December 2003. Publication GAO-04-110

180 Stolberg SG, Gerth J. High-tech stealth being used to sway doctor prescriptions

181 Van Zee, “The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy”, American Journal of Public Health, 2009, Vol 99, No. 2

182 Van Zee, “The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy”, American Journal of Public Health, 2009, Vol 99, No. 2

183 Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem. Washington, DC: General Accounting Office; December 2003. Publication GAO-04-110

184 Van Zee, “The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy”, American Journal of Public Health, 2009, Vol 99, No. 2

185 Van Zee, “The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy”, American Journal of Public Health, 2009, Vol 99, No. 2

management on the political agenda, by telling to the people that they have a right to not suffer and that they should ask for OxyContin to their physician to ease their pain.

Throug this example of very large and aggressive promotion campaign, we can estimate the idea that warnings and promotion go together. A drug manufacturer can put all the effort wanted in warnings health professionals and even patients, if this same drug manufacturer eganged in the same time a similar or larger effort in promoting the same drug, the benefits in terms of prevention gained through warnings will be "nullified" by this promotion. This argument was taken by Californian District Court of Appeal in 1964 during the *Love v. Wolf* affair. In this affair, the judge decided that "even where an adequate warning is originally given by manufacturer, this warning may nonetheless be nullified by subsequent advertising and promotional activities which downplay the risks of the drug or which encourage its application to ailments for which the drug is ill suited". Indeed, "though *Parke-Davis* adequately warned of the drug's risks in its medical advertisements, it engaged in a number of activities which considerably diminished the perceived dangers of the drug". Finally, "the court concluded that *Parke-Davis*' overpromotion may well have induced the doctor to disregard the warnings previously given"[186].

Here, we can see that drug manufacturers are not very constrainted in United-States concerning promotion and advertising of their drugs. Once again, they can do more than they currently do to prevent an opioid crisis, starting by stopping their over and sometimes false and misleading promotion towards health professionals and patients and guaranteeing a realistic promotion that warn and inform correctly the patient and health professionals concerning the right use of opioid painkillers. In this perspective, building a Compliance system leaning on drug manufacturer in the United-States seems credible and pertinent. However, situation is, once again, very different in France where promotion and advertising of prescription drugs like opioid painkillers is already very regulated. In this case, the question of the interest and of the salience to hold liable in Ex Ante the drug manufacturer is asked.

2- In France, promotion and advertising of prescription drugs are already much more regulated than in the United-States

Contrary to the United-States, France already regulates prescription drugs advertising and promotion. First, the CSP offers a very precise definition of what is advertising in its article L. 5122-1. According to this article, advertising is "*toute forme d'information y compris le démarchage, de prospection ou d'incitation, qui vise à promouvoir la prescription, la délivrance, la vente ou la consommation de ces médicaments à l'exception de l'information dispensée, dans le cadre de leurs fonctions, par les pharmaciens gérant une pharmacie à usage intérieur*"[187]. This definition is rather complete because it include either the diffusion of information from the drug manufacturer to health professionals or patients or the use of incentives by drug manufacturer. Moreover, the article concerns every types of information whether it is target to the physicians, the pharmacists or the patient. Advertising to the public is allowed only for over-the-counter drugs who fulfill two conditions: being non-reimbursable by social security system and not being subject to an interdiction of advertising by ANSM[188], who can forbid the use of advertising for certain kind of drugs, even if they are over the counter and non-reimbursable by social security

186 Love v Wolf 38 Cal Rptr. 183 (Cal Dist. Ct App 1964)

187 "Every form of information, including door-to-door sales, prospecting or incentive, in order to promote the prescribing, the delivery, the sell or the consumption of a drug, excluding information given by the pharmacist holding a indoor usage pharmacy, within the scope of his or her functions" (translation by the author).

188 Article L.5122-6 of CSP

system. Advertising to the public is totally prohibited for prescription drugs. It is therefore impossible to promote opioid painkillers to the public in France, contrary to the United-States.

Advertising to the health professionals, who are considered as more enlightened than public on medical questions and as more able to balance the words of drug manufacturers is, however, allowed for prescription drugs under certain circumstances. First, advertising for prescription drug is only allowed towards the physicians who are entitled to prescribe the drug[189]. If the prescriber is not entitled to prescribe the drug, advertising him or her is the same than advertising someone from the public. Moreover, the information given to the health professional must be adapted to him or her[190].

Since 2012, right to advertise prescription drugs to health professionals is conditionned to the obtention of an advertsing visa delivered by ANSM[191]. Contrary to the United-States, no advertising is tolerated as long as ANSM has not examinated every promotion material and given its agreement. A priori agreement is necessary to diffuse any advertisement. Among all the things that ANSM examines before the diffusion of promotional materials to health professionals, there is the exactness of the information given to health professionals. Indeed, every information given to health professionals by drug manufacturer must be exact[192]. But, drug manufacturers does not have only to diffuse information exactly, they also have to give all the information concerning their product when they advertise it, even the information which does not represent a selling argument and even some information that could discourage to buy the drug. For instance, drug manufacturers must compulsorily precise the warnings, undesirable effects and posology[193]. Here, we can appreciate the fact that pharmaceutical sector is a regulated sector. Indeed, in a non-regulated sector, therefore under Competition Law, advertising is free and it would be non conceivable to ask to a firm to give compromising information to its potential buyer at the occasion of advertising. Giving some compromising information has the same effect that telling to the potential buyer to not buy the product. However, under Regulation Law, which is the balancing between Competition principle and other principle, it would be conceivable to ask to the firm to give compromising information at the same time than promoting its product if this compromising information could permit to achieve another objective considered like as important as the Competition principle. We have here a promotion that is allowed to achieve the Competition principle and compromising information that is required to be given at the same time to achieve the other principles that are here right use of the medications or public health, for instances.

Finally, advantages and incentives to the prescribers are forbidden and free-samples could be given to the health professional by the drug manufacturer only if it is the health professional who ask for it[194]. This means that the drug manufacturer could not persuade prescribers by offering them free trials to test the drug. Free sample distribution to patients is of course prohibited[195].

As we can see, drug advertising is already regulated in France. In the United-States, promotion is almost free so, it seems interesting to expect more from drug manufacturers to provide a fair information. But, in France, drug manufacturers seems to do already their

189 Article R.5122-10 of CSP
190 Article R.5122-8 of CSP
191 Article L.5122-9 of CSP
192 Article R.5122-9 of CSP
193 Article R.5122-8 of CSP
194 Article L.5122-10 of CSP
195 Article L.5122-10 of CSP

best in terms of circulation of quality and necessary information.

II- CURRENT DUTIES OF THE DRUG MANUFACTURER SEEMS SUFFICIENT, ESPECIALLY REGARDING WHAT IS CREDIBLE TO EXPECT FROM IT

As we saw in the precent section, drug manufacturers already have a lot of obligations. But are these obligations sufficient? In other words, can we expect more from the drug manufacturer than what it is already expected from it?

A- Current Duties Imposed to Drug Manufacturers Seem Sufficient

Drug manufacturers play a major role in making information circulate about their drug between the different actors who will use it (physicians, pharmacists, patients...). These current obligations seems essential in order to prevent the occurrence of an opioid crisis like in the United-States. It is the reason why it is crucial that these duties would be maintained.

1- Current duties imposed to drug manufacturers concern circulation of information that are essential in order to prevent an opioid crisis

As we saw in the precedent section, what is especially and almost exclusively expected from drug manufacturers is that they deliver all the necessary information over the product that they marketized and that will very probably be used by health professionals and patients. Indeed, the major part of the ANSM's mission, except guaranteeing that the drugs are safe and effective, is 1) to ensure that the drug manufacturer correctly warn the patients and the health professionals about the risks and contraindications of their drug and about the way to use it rightly in order to being able to take advantage of the benefits of the drug and in order to avoid risks and undesirable effects, and 2) to make sure that drug manufacturers do not push patients or health professionals to use or overuse the medication they sale by overpromoting it. Thereofre, the contribution of drug manufacturers in guaranteeing a right use of medications and particularly a correct use of opioid painkillers is to be found in their obligation to make available all necessary information about drugs, their benefits, the risks they present whatever happens, the risks they presents if they are over or misused and therefore the correct way to use them.

Circulation of information seems essential to prevent opioid crisis in France. Indeed, most of the reports from different public institutions and from different specialists comittees establish circulation of information as a priority and as a condition *sine qua non* to prevent opioid crisis. For example, the ANSM's report proposes, among other measures, to "*renforcer la formation des professionnels de santé sur la prescription et la délivrance des antalgiques opioïdes*"[196], to "*améliorer la diffusion de l'information auprès des professionnels de santé*"[197] and to "*améliorer la diffusion de l'information auprès du grand public*[198]"[199]. If we look at the Health ministry's roadbook for prevention and action against opioid overdoses, the recommendations are pretty similar. The report proposes to "*informer et sensibiliser les professionnels de santé sur le bon usage des thérapeutiques*

196 "Reinforce health professionals' training in prescription and delivering of opioid painkillers" (translation by the author).

197 "Improve the diffusion of information towards health professionals" (translation by the author).

198 "Improve the diffusion of information towards public" (translation by the author).

199 Monzon, E., "Etats des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Rapport de l'ANSM*, Février 2019

opioïdes"[200] and to "*développer des outils d'information et de formation sur les surdoses d'opioïdes et la naloxone en s'appuyant notamment sur le savoir expérimental des usagers*[201]"[202]. Once again, the circulation of information is part of the recommendations to prevent opioid crisis.

Circulation of information is of course necessary. Opioid crisis is due to an overuse or to a misuse of opioid painkillers. We can suppose that the great majority of victims did not abuse or misuse opioid painkillers voluntarily[203]. It is reasonable to assume that opioid victims became victims because they did not know that their behavior was likely to lead to addiction or overdose. Opioid victims are not aware of the risks of misusing or overusing opioids and probably they are also not aware of what is overusing or misusing opioid painkillers. In other words, opioid users did not get the information about the right use of opioid medications. The fact is probably the same for health professionals, physicians and pharmacists who were not aware of the risks or of the way to use correctly opioid painkillers.

2- Drug manufacturers can play a great role in making this information circulate and it is therefore reasonable to expect that they play this role

As we saw, information must circulate and being available to patients and health professionals. The actor who is the better positioned to inform patients and health professionals, especially because it detains this information and because it has the ability to give it to them, it is the drug manufacturer. Indeed, drug manufacturer has created the drug. If one actor would know the most the product, its qualities and its drawbacks, it is, without any doubt the drug manufacturer which spent many years researching the best treatment, developing it and testing it. Moreover, the drug manufacturer conceived a medication to a specific end and it knows, better than anyone else, what is this end. Then, drug manufacturer detain the necessary information. Besides, drug manufacturer also have the opportunity to diffuse this information.

First, drug manufacturers have a very extensive and developed network of sales representatives. These sales representatives are very often in contact with health professionals, especially in order to promote the drugs marketized by the drug manufacturer. Drug manufacturers can demand to their sales representatives to take advantage of the opportunity of their appointments with physicians and pharmacists to inform them about the risks, the contraindications and the posology of their products. Once again, ANSM cannot really do this job, especially because it does not have a real and physical contact with practionners where it could have the occasion to talk to them about risks and good use. The only thing that ANSM can do is to establish recommendations and communications but it cannot ensure that every doctor will have access to it and pay attention to this recommendations and communications. And, in fact, most often, they do not pay attention to the recommendations, because they do not know that they exist and therefore they do not apply them[204]. ANSM could organize big

200 "Inform and sensibilize health professionals about the right use of opioid therapeutic" (translation by the author).

201 "Develop information and training tools about opioid overdoses and naloxone basing especially on the user's experimental knowledge" (translation by the author).

202 Feuille de route 2019-2022 du ministère des solidarités et de la santé : prévenir et agir face aux surdoses d'opioïdes

203 Here, we exclude people who want to kill themselves and junkies that represents only a minority of opioid overdoses victims as we have proved it in the introduction of this master thesis

204 Muszczak, A., « Enquête sur les pratiques de prescription d'opiacés des médecins généralistes,dans le traitement des douleurs chroniques non cancéreuses: à propos d'une étude de faisabilité dans le Grand-

conferences, of course, but this would represent an organizational, material and human cost that would be considerable, especially when it is so easy to take advantage of the already constituted and, ready to be used, network of sales representatives created by drug manufacturers. Drug manufacturers are the best positionned to inform health professionals, then they are asked to do it.

Second, drug manufacturers are equally able to inform patients. By including usage instructions in any box of drug sold, it is sure that every patients who would consume it, will have access to the necessary information. ANSM is, once again, unable to inform patients as well as the drug manufacturer. Indeed, the regulator is unable to target who are the people who use or would potentially use opioid painkillers to inform them. A warning from the ANSM targeted to the right individuals has very few probabilities to be a success, especially because people do not know really who is ANSM, but a warning address to every individual is almost sure to be a failure. Most of people will not have access to it and those who will hear the message from ANSM will probably not paying attention to it, being sure that they are not concerned, even if they are or will be, in fact, concerned in the present or in a close future. Even if they pay attention to it, the probability that they have forgot the information when they will need it is very high. It is therefore much more easy and probably much more effective to relie on drug manufacturer for this task of informing patients. Drug manufacturer has the possibility to target the people concerned by the warnings because only them are buying their drug.

It is therefore absolutely credible and even essential to expect from the manufacturer that it makes available all the information necessary to keep safe while using the medication. Because it is necessary and because drug manufacturer is able to do it and even the most able to do that. This statement is confirmed by the case law. Indeed, in 1968, the *Conseil d'Etat* has expressed that the drug manufacturer "*ne peut pas, pour soutenir que la responsabilité de l'Etat serait engagée à leur égard, se prévaloir utilement des fautes lourdes que l'Etat aurait commises en accordant sans contrôle et en ne retirant pas assez tôt le visa du ministre à la specialité en question et en n'assurant pas la surveillance de la fabrication*[205]"[206]. By saying that drug manufacturers remain liable for their product even after the label of public authorities, the judge shows that drug manufacturers are much more powerful than the regulator in the task of making information circulating. First, the judge recognizes the fact that ANSM could make a mistake in delivering a label without being liable of this mistake. These absence of liability shows the fact that ANSM is not totally enlightened to always make the right decisions. Moreover, with this decision, the judge recognizes the powerfulness of the drug manufacturer by holding it liable. If the drug manufacturer is liable is because, contrary to the public authorities, it is able to avoid problems. This decision of the *Conseil d'Etat* by saying who is liable, is saying, in the same time, who is powerful because liability and powerfulness always go hand in hand.

B- Is It Possible to Expect More from Drug Manufacturers? It Seems that Drug Manufacturers is not a So Crucial Operator and that the Situation Also Depends on Other Actors' Behavior that Drug Manufacturers Cannot Control

In the precendent section, we have seen that it was reasonable, as it is done currently, to

Est. » Sciences pharmaceutiques, 2015

205 "Cannot, to maintain that the liability of the State is compromised, usefully claim the very serious misconduct that the State would commit according without any control and not removing enough early the ministerial visa to the medicine or not carrying out the monitoring of the manufacturing" (translation by the author).

206 CE Ass, 28th of June 1968, Société des établissements Février-Decoisy-Chamion et Société d'assurances mutuelles de la Seine et de la Seine-et-Oise, n°67677-67678

force drug manufacturers to inform health professionals and patients. But, is it possible to expect more from them? Can we, as in the United-States, holding drug manufacturers liable in Ex Ante for each case of addiction or death due to a misuse of the opioid painkillers which will probably occur in the future. Holding drug manufacturers liable in Ex Ante suppose that drug manufacturers are able to avoid every misuse of opioid painkillers themselves or able to control or force those who are able to avoid every case of misuse. In this section, we will see that it is not the case in France.

1- Misuse of opioid painkillers depends on user's behavior that drug manufacturer cannot control

Drug manufacturers can make available to the patients all the information that is necessary to make right decision in its consumer practice, if the patients decide to not taking the information that is offered to him or her or to voluntarily ignore it, what can drug manufacturer do? Misuse is always possible because it is not only a matter of making information available, it is also a matter of willingness to intercepting this information and being voluntary to respect it. Drug manufacturer cannot force user to behave correctly. It could inform him or her of the risks, doing its best to discourage him or her to disregard the instructions but it cannot force him or her to effectively conform to the recommendations. If the user wants to misuse the drug, he or she will do it and drug manufacturer cannot prevent him or her to do it.

The Agency theory saying that user, if they have enough information, are sufficiently enlightened to make a free and rational choice and will necessarily make the choice they consider the best for them. Another person that them is not legitimate, according to the Agency theory, to say to the individual what is good for him or her because anybody else than the individual is better positionned to know what is good for him or her. Each individual is different and knows what is good for him or her. This Free choice theory is especially developed in the United-States and was particularly significant in the Donald E. Thompson's works who has imported this Agency theory in the Health field[207]. The Agency theory has two consequences in pharmaceutical sector: first, drug manufacturers can only deliver all the necessary information to the individual – and they have to do it – and, second, drug manufacturers are illegitimate to judge the individual on his or her behavior and to prevent him or her to do something because each individual should be free and is rational enough to make the right decisions, the right decisions being what are the most appropriate for them. Therefore, drug manufacturers are philosophically illegitimate to do something more than informing patients concerning garanteeing the right use of medication, according to Agency theory. They have to inform but they philosophically cannot do more.

But, if drug manufacturers are philosophically restricted, they also are technically constraint. Ensureing effectively that patients use correctly opioid painkillers would mean being able to monitor every consumer of opioid medications. However, drug manufacturers cannot follow every patients and control that they do not abuse of their traitments. First, because Law does not entitle them to do that and because it is not very desirable to transfer such a big power of controlling people and people's health to a private drug manufacturer while only State is entitle to force people to do something[208] and while even the State cannot gather information about citizens' health state. Second, because, even if they had such a legal power, drug manufacturers could not have the

207 Thompson, D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend?, Florida State University Law Review, 1985, Article 6, Vol 13, Issue 1

208 Weber, M., Le savant et le politique, La Découverte/poche, 2003 (original edition: 1919)

technical ability to follow every patient. Drug manufacturer is not at home, behind every patient to advise him or her or to prevent him or her to take more pills than what is recommended. By the way, the drug manufacturer does not have any contact with the patients to interact directly with him or her and not only by the intermediary of a written instruction paper. Actually, drug manufacturer does not even know the name of the patients consuming their drugs. But, we know that direct contact is much more effective than written instructions paper to conquer people and especially patient's obedience.

2- Misuse of opioid painkillers depends on health professionals' behavior that drug manufacturers cannot control

Opioid problem partially depends on patients' behavior. But, it also greatly depends on health professionals behavior. Physicians and pharmacists are intermediairies between drug manufacturers and patients. As specialist with full of knowledge about medicine and drugs, they are supposed to advice and follow patients in their traitment. More than this, health professionals are assumed to substitute to the patients in his or her medical choices face to the drug manufacturers as the patients is considered as not sufficiently enlightened to make these choices. They are also expected to substitute to the drug manufacturer face to the patients as the drug manufacturer cannot be physicially face to each patient to give advice to the patient. In other words, drug manufacturer relies on the health professionals for the right prescription and delivery of the medications and patients trust physicians and pharmacists in their prescriptions and delivering. Therefore, the opioid consumption in France depends on the health professionals' behavior. If physicians and phamracists prescribe and deliver opioid painkillers correctly, there will not be a massive opioid crisis in France. But, if they prescribe and deliver wrongly opioid painkillers, it is possible that a massive problem would occur because it is reasonable to think that patients will follow in priority the advice of the health professional with who they are in direct contact, in interaction and that they often personnally know rather than those of the drug manufacturer much less personified.

In the option when drug manufacturer's message and health professional's message are in contradition, drug manufacturer may only suffer from the situation and can make any effort that it wants, the crisis will occur, independantly of their will. Indeed, drug manufacturers cannot control each practionner to monitor if they are behaving the right way. As for patients, they do not have technical ability to do that. But they also do not have right to do that. The *Code de déontologie des médecins*, taken up by the article R.4127-8 of CSP, precises that "*Dans les limites fixées par la loi et compte tenu des données acquises de la science, le médecin est libre de ses prescriptions qui seront celles qu'il estime les plus appropriées en la circonstance*[209]". This means that physicians benefit from freedom of prescription and that no one could force them or even monitor them in their prescription activity. If prescribers are totally free of prescribing what they want without any limits, then if they decide to do it effectively with opioid painkillers and to prescribe it massively, drug manufacturers could not do anything to prevent it.

Whether it is for patients than for health professionals, drug manufacturers seems unable to monitor or force them to behave the right way. In this perspective, it seems not reasonable to hold them liable in Ex Ante for any appearance of opioid crisis. First, because such a measure would be ineffective. Indeed, the situation does not only depends on the motivation of drug manufacturers and you can promise any sanction than

209 "In the limits of law and considering the current science state of knowledge, the physician is free of prescribing. Those prescribing will be in concordance with what he or she judges appropriate under the circumstances" (translation by the author).

you want, as the situation depends from other actors than drug manufacturer cannot monitor and force, you will punish the drug manufacturer but without improving the situation at all. Second, these measure will be not fair because you will responsabilize someone without giving it back the means to achieve the goals set. Liability and ability could not be separable.

CHAPTER II: A MUCH MORE « CRUCIAL OPERATOR » – THE HEALTH PROFESSIONAL

In the precedent chapter, we have seen that drug manufacturer does not seem to be the « crucial operator » on which it seems pertinent to relie. Even if drug manufacturer is able to make information circulate about the right use of drugs between the different actors and that it is essential that drug manufacturers continue in this direction, we have seen that the situation also and most often depends on other actors – patients and health professionals – that drug manufacturers cannot legally, philosophically and technically monitor and force. As drug manufacturers appear not powerful, they does not answer anymore to the definition of «crucial operator» that we have given in the precedent part of this master thesis. Face to the rising opioid problem, we cannot stand without actor on which building a Compliance system. We will therefore continue to inspect the others actors of the sector to find our « crucial operator ». Especially in this section, we will be interest in studying the possibility that health professionals – physicians and pharmacists – are crucial operators. We will see that they represent a much more interesting actor than drug manufacturer to build a Compliance system that will be actual and effective.

I- PHYSICIANS AND PHARMACISTS' BEHAVIOR MAY HAVE A REAL IMPACT ON THE OPIOID PROBLEM

As we have shown, the health professionals' behavior plays a crucial role in the right use of opioid painkillers. As we can assume that patients will trust and follow the recommendations of health professionals, if physicians and pharmacists respectively prescribe and deliver carelessly or massively opioid medications, the direction followed by the French opioid problem will not be the same at all. In the same way, if health professionals advise their patients in conformity with recommendations and follow their treatment to prevent as soon as possible a potential abuse, or if they not, the result will not be the same.

A- Health professionals can act in rationalizing their prescriptions and deliverings

Opioid painkillers are prescription drugs. This means that physicians can control their consumption. If opioid painkillers prescription was perfect, no opioid problem would occur. However, we are actually facing a serious problem. This means that physicians' prescription are not enough careful.

1- General practionners are the physicians initiating the more opioid prescription

Amandine Muszczak studied in 2015 the general doctors' practices to see if they were in compliance with recommendations formulated by health authorities concerning the prescription of opioid painkillers[210]. She asks directly the general practionners. Amandine Muszczak launched her study in the *Grand-Est* and not in the whole country. The question that we first should ask is: is this spatial sample representative? Sociology of patients in

210 Muszczak, A., « Enquête sur les pratiques de prescription d'opiacés des médecins généralistes,dans le traitement des douleurs chroniques non cancéreuses: à propos d'une étude de faisabilité dans le Grand-Est. » *Sciences pharmaceutiques*, 2015

the Grand-Est is very different from sociology of patients in the rest of France. However, the sociology of the *Grand-Est*[211] is very similar to the sociology of opioid abusers[212]. Indeed, the Grand-Est is a former industrial region, with a high representation of white defavorized working-class far from big cities. The *Grand-Est* is probably the region of France where there are the most people likely to crashing into opioid addiction, just looking at the sociological characteristics. So, even if the *Grand-Est* is not representative of the whole France, it is a good laboratory of study, especially because we meet the same population than in very touched by opioid crisis regions of United-States.

Amandine Muszczak's results are alarming. Indeed, according to her, physicians are not enough careful in their prescription of opioid painkillers. Before presenting more in details her results, it is first important to remind the place of general practionners in the prescription of opioids. According to the ANSM report already quote in this master thesis[213], opioid treatment is initiated by a liberal general practionners in 59,1% of the cases for weak opioids and in 62,9% of the cases for strong opioids. In order to be able to compare, hospital physicians represent respectively 20,1% of weak opioids prescriptions and 21% of strong opioids prescribing. Comparing to specialists, general doctors prescribe much more opioids. They represents 86,3% of the weak opioid prescribing and 88,7% of the strong opioids prescribing, which is much more than dentists, for instance, who represents 2,8% of the weak opioid prescribing and 0,3% of the strong opioids prescribing. There are two ways of interpreting the fact that general practionners generally prescribe more opioids than specialists. First, it is possible to say that the fact that general practionners prescribe more opioids is normal because they represent the first step in the healthcare pathway ant that they therefore see more patients than specialists do. But, it is also possible that this more important quantity of prescriptions by general practioners in comparison to specialists is characteristic of general practionners who would be more likely to prescribe opioid painkillers all other things being equals. Indeed, it is probable that general practionners prescribe more opioids per patients than the specialists. In any case, whether the general practionners prescribe more opioids per patients or not, the fact that the majority of opioid treatments are initiated by them is important to us in our willingness to detect a « crucial operator » able to prevent an opioid crisis in France. Indeed, it seems that quantity of opioids circulating in France depends on the general practionners' behavior and so, it also seems that the regulation of this quantity should pass by general practionners.

2- General practionners do not always follow the recommendations from health authorities concerning the prescription of opioid painkillers

Unfortunately, according to the results found by Amandine Muszczak in 2015, it seems that general practionners, far from limiting the quantity of opioids in circulation, tends to prescribe much more opioid painkillers than necessary. Amandine Muszczak starts showing that general practionners do not respect health authorities' recommendations concerning non-cancer chronic pain. While general practionners should always evaluate pain intensity of their patients, 9% of them never do it before prescribing a treatment. They are also very few to ask for the advice of a pain specialist (only 6%). Even if it is true to say that some regions present a lack of such specialists, this statistics seems to low to

211 Montlibert, C., « Chômage et licenciements. La crise de la Lorraine sidérurgique : Longwy, 1978-1980. » In: *Annales. Économies, Sociétés, Civilisations*. 39e année, N. 5, 1984. pp. 1044-1068

212 Obradovic, I., " La crise des opioïdes aux Etats-Unis: d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

213 Monzon, E., "Etats des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Rapport de l'ANSM*, Février 2019

assume that general practionners respect the recommendations concerning the request to a pain specialist in any case of doubt. The most worrying figures come when Amandine Muszczak asks the general practionners if they evaluate the risk of addiction to opioids into their patients before prescribing them such a radical and potentially dangerous treatment. Indeed, even if 48% - which is not already very high – physicians evaluate the risk only during the treatment, they are only 15% to evaluate it just before the treatment and 9% to evaluate it before and during the treatment. Overall, only 4% of general practionners interviewed evaluate the risk of addiction of their patients before, during and after their treatment and 24% of physicians never evaluate the risk of addiction of their patients. This last figure is particularly worrying. Amandine Muszczak also found that 53% of general doctors evaluate the risk of addiction at each appointment with the same patient and that 37% evaluate it when the patient is asking for an increase of posology. If we gather this two behavior, only 10% of general physicians evaluate the risk at each appointment with the same patient and in any case of patient asking for an increase of posology. 59% of general physicians reconsider systematically their prescribing of opioid painkillers in case of risky medical history, 35% do it sometimes and 4% only for third level opioids (which are the strongest ones). After having asked doctors about their behavior face to non-cancer chronic pain, she also asks to the same doctors what is their behavior concerning opioid prescribing. Once again, she concludes that general practionners, in general, do not respect health authorities' recommendations. First, for non-cancer chronic pain, 85% of general practionners prescribe frequently Tramadol, 74% prescribe frequently codeine, 89% prescribe morphine (74% sometimes and 15% frequently), 70% prescribe oxycodone (57% sometimes and 13% frequently) and 74% prescribe fentanyl patches (59% sometimes and 15% frequently) although it is not recommended for naive from opioids patients. These figures seems very important face to the recommendations. Indeed, strong and very strong opioids are not recommended to treat headache, for instance, but they are still prescribe by, respectively, 68 and 82% of physicians. Moreover, second example: 67% of physicians prescribe benzodiazepines in association with opioids even if it is not recommended.

Despite all these statistics, Amandine Muszczak points the fact that physicians are rather comfortable with opioids prescribing. Indeed, according to her results, 68% of physicians are comfortable with it and only 2% are not comfortable at all. This is understandable because physicians are normally informed about risks of opioids and about the way they have to use them. They have indeed followed some academic teaching where they learn enough about drugs to have a good knowledge in this field. Moreover, even if the drug is perfectly new, general practionners are informed by drug manufacturers about the risks and the posology of this drug. For instance, general doctors have access to the summary of product characteristics that the drug manufacturers must send to them. As drug manufacturers must give a neutral and exact information, it is reasonable to think that general practionners are correctly informed about opioid painkillers posology and risks. Therefore, general practionners know what is the right behavior to adopt concerning opioids and if they do not adopt this correct behavior, it is maybe because they do not want it. Here we have found in the doctor the crucial agent that we were looking for. Doctors are « crucial operators » because the success or the failure of the right use of opioids system depends on them. Clearly, the Muszczak's work shows that general physicians do not do enough to prevent opioid and that they can clearly do, easily, more than they do. It is perhaps reasonable here to expect more from them, so.

B- Health professionals can act in informing and following patients

In the precedent section, we have seen that health professionals could be helpful in the prevention of opioid crisis in France by mastering their prescriptions (if they are

physicians) or delivering (if they are pharmacists). However, they could also be helpful by increasing and improving the information they give to patients and by following them during the entire treatment.

1- Health professionals are the best positionned to make sure that every patient gets the necessary information concerning the use of opioid painkillers

As we have already said before, health professional is this «learned intermediary»[214] between the far drug manufacturer and the naive patient. As they are in direct contact with the patient and as they can know their medical identity (because they are in direct contact but also because they follow the same patients for many years), they also are in capacity to adapt the treatment to the individuality of each patient or to agence the treatment case by case according to the singularities of the patient they face[215].

Besides, health professionas have the sufficient knowledge and enough trust capital from patients, as they are professionals, to play this role of relaying information from the drug manufacturer to the patient and to advice patients[216]. Patients cannot always understand instructions from drug manufacturers. In this case, health professionals should popularize the cold words of drug manufacturer and explain them to the patient in order to the patient could understand them correctly. The health professional is here the best positionned actor because he or she is the unique or the closer enlightened actor the patient has access to.

Moreover, the patient does not always have the reflex to check the medical instructions from the drug manufacturer before using the drug[217] (because he or she is suffering, because he or she does not know that such instructions are contained in the box, because he or she does not have the motivation to read all the instructions while the probability that this is useful is low, because he or she is persuaded that he or she already know what is written or because he or she judges not necessary to know this information either because he or she does not care about it or because he or she minimizes the probability to indeed be in the situation mentionned in the medical instructions). In this perspective, health professional should anticipate that the patient will not read the instructions and summarize them to him or her in order to be sure that the patient get the necessary information before using the drug. If the patient also read the information after that the health professional has summarized it, it is not time wasted because, face to the potential danger of misused opioid painkillers it is better informing twice than once.

To sum up, the health professional should be available to every patient if necessary to give him or her information about use of opioid painkillers. And, even if the patient does not ask for information, because it is not often the case, the health professional should ensure that the patient gets the information before using the drug by providing him or her anyway, even if it is the second time that the patient gets this information.

214 Thompson, D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend?, *Florida State University Law Review*, 1985, Article 6, Vol 13, Issue 1

215 This argument was essential in Reyes v. Wyeth Lab., 498 F.2d 1264, 1276 (5th Cir. 1974), for instance.

216 This argument was essential in Roien v. Burroughs Wellcome Co., 856 S.W.2d 607, 609 (Tex. App.-Waco 1993, writ denied).

217 Mahut, S., « Comment les patients utilisent-ils la notice des médicaments ? Enquête qualitative compréhensive réalisée auprès des patients des Yvelines et du Val d'Oise », Thèse pour le diplôme d'Etat de docteur en médecine, soutenue en 2016, à l'université de Versailles Saint-Quentin en Yvelines ; Muller C., Chantrel F., Bazin-Kara D, Ott J., Krummel T., Imhoff O., Richter S., Hannedouche T., Dimitriov Y., « Influence de la lecture des notices des médicaments sur l'adhésion thérapeutique », *Néphrologie & Thérapeutique*, Volume 11, Issue 5, September 2015, Page 401

However, Amandine Muszczak found that physicians give not enough information to patients concerning opioid painkillers. 11% of general practionners do not inform their patients about foreseen undesirable effects of this kind of medication, 28% do not inform them about the risk of tolerance, 35% tell about efficiency, 54% of physicians do not talk about benefit/risk balance and 54% also do not warn about risk of dependance. All of this information are yet expected from general practionners by health authorities[218]. Therefore, making information about use of drug circulating easily may be the second thing that we can expect from health professionals after having expected from them to rationalize their prescriptions and delivering.

2- Health professionals are the best positionned to follow the patient during his or her treatment and make sure that no abuse is committed

Ensuring that patients gets the necessary and sufficient information to use correctly the drug is not sufficient to avoid opioid crisis in France. Indeed, even if they have the information, patients could choose consciously or not, to disregard it and to abuse anyway of opioid medications. However, health professionals could prevent that patients misuse opioid painkillers. More than this, health professional is the only actor who can do that and therefore whose it is reasonable to expect it. But, how physicians and pharmacists could indeed prevent that patients do not overuse opioid pills? Actually, the ability of health professionals depends if they are physicians or if they are pharmacists.

A physician cannot really avoid the abuse. Obviously, he or she can stop to prescribe opioid pills to a patients who abuse of it or who present risk to become very soon addict to opioid medications. But, except this power – which is already very important – the physician cannot really force the patient to act correctly, especially in our times when consent and freedom of a patient considered as always more and more enlightened about health questions[219]. However, the physician can yet try to dissuade patients to adopt a behavior that could make them srink into addiction. The physician can use its knowledge, of medicine in general but also of the patient, to detect the risk of addiction. Then, the physician can use the trust that the patients have in regards to them to advice them and dissuade them to continue their behavior when a risk of sinking into addiction is detected.

To do that physicians need to follow the patient during its treatment[220]. We have said that this seems difficult for the drug manufacturer who is far from the patient. But, the physician, who have the same knowledge in medicine than the drug manufacturer, is also closer to the patient to be technically able to follow him or her during his or her treatment. The physician has a limited number of patients, and even fewer patients how are using opioids, and can reasonably pretend to follow them seriously during their treatment, also because their patients are geographically close to them. The only thing that is necessary is that physicians could legally follow the patient. For the moment, they cannot force the patient to be accountable of their use of the drug and cannot really monitor the patient during the treatment phase. The reason is that such a following could be considered as an

218 Muszczak, A., « Enquête sur les pratiques de prescription d'opiacés des médecins généralistes,dans le traitement des douleurs chroniques non cancéreuses: à propos d'une étude de faisabilité dans le Grand-Est. » *Sciences pharmaceutiques*, 2015

219 Thompson, D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend?, *Florida State University Law Review*, 1985, Article 6, Vol 13, Issue 1

220 This is for example recommended by OFMA in Bonnet, N., « Médicaments antalgiques opïodes : ce qu'il faut savoir ce qu'il faut faire », *RESPADD and OFMA*, 2018 and by ANSM in Monzon, E., "Etats des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Rapport de l'ANSM*, Février 2019

illegitimate ingerence into the private life of the patient. But, face to the « monumental goal » that we present, what is the most important?

If the physician's control is not enough to be sure that patient use correctly opioid painkillers as physicians can just monitor and not enforce patients, the action of pharmacist could be, here more decisive. Indeed, pharmacists are in charge of delivering opioid pills and they have the legal monopole of this delivering. This means that if they do not deliver a pill, an abuse from the patient is technically impossible. Indeed, if the patient has no pill or only the pill that he or she is supposed to consume to ease and only ease his or her pain, he or she cannot overuse of it. It is therefore pertinent, if our aim is to prevent and avoid opioid overuse, to create or agence a system such as abuse is impossible. This means that this system should be build such as the patient does not have more pills than necessary and than recommended in order to no sinking into addiction[221]. The concretization of this require coordination between pharmacists and between pharmacists and physicians.

In the following section, we will present some recommendations and propositions to create such a Compliance system. This system presents some constraints that we will study and discuss in the following section, too, after having proposing and presenting in details our potential solution.

II- THE NECESSITY TO CREATE A COMPLIANCE SYSTEM TO MAKE EFFECTIVE THE CURRENT HEALTH PROFESSIONALS' OBLIGATIONS

In the precedent section, we saw that it is reasonable to expect more from health professionals in the regulation of opioid medications. First, because they can do more than they do and second because their action could be decisive. If physicians and pharmacists are indeed « crucial operator », we should create a Compliance system such as they will be forced to help in the prevention of opioid crisis.

A- Health professionals already have some duties on which a Compliance system could rely

Studying current duties before regarding what we can impose to health professionals is important first to be aware of the existing regulations framework but also to create continuity. Indeed, former obligations could legitimate new ones and new ones could be created in the wake of former ones. Like that, we can creating a credible and coherent legal framework that does not bring about a revolution everything that already exist.

1- Physicians already have obligations on which a Compliance system could lean

It seems clear that the profession of physician is not a profession like others and that it is probably more than a job occupied to make money. Health is a high proccupation and, in this perspective, it is too precious to let physician free from specific duties in addition to its private and economic rights. In other words, health sector is one of this sector considered as too essential to be let to the regulation of traditional Competition Law like other sectors less essential[222]. Medicine is considered as a first necessity service that anybody should

221 We especially refer here to fractional drug delivery which is already compulsory for very strong opioids especially Fentanyl

222 This idea that some sector should be excluded from market and competition rules was theorized by Roth, A. E., The theory of stable allocations and the practice of market design, 2012 and at the basis of Regulation Law developed by Marie-Anne Frison-Roche in Le Droit de la Régulation, 2001, Dalloz, n°7

access easily and almost freely, whatever its resources. It is the reason why article R.4127-19 of CSP says that « l*a médecine ne doit pas être pratiquée comme un commerce*[223] *»*. It is clear that physician should be able to live correctly from their activity and that, therefore, they need to make a minimum of money. But, it is also clear that the research of profit and the selection by exclusion by price is excluded in a soo important sector than health. Then, it is clear that health sector is a specific sector and that physicians should have specific duties.

Among the duties that physicians have and that are particularly interesting for us in our opioid problem prevention, there is an obligation to restrict its prescriptions. Of course, the article R.4127-70 of CSP precises that the physician « *ne doit pas, sauf circonstances exceptionnelles, entreprendre ou poursuivre des soins, ni formuler des prescriptions dans des domaines qui dépassent ses connaissances, son expérience et les moyens dont il dispose*[224] » but regulations go beyond with the article R.4127-8 of CSP, by saying that « *il doit, sans négliger son devoir d'assistance morale, limiter ses prescriptions et ses actes à ce qui est nécessaire à la qualité, à la sécurité et à l'efficacité des soins. Il doit tenir compte des avantages, des inconvénients et des conséquences des différentes investigations et thérapeutiques possibles* [225]». This means that physicians, in addition to stop themselves when they lack sufficient knowledge, must also evaluate the degree of pain of their patients and also the potential risks and benefits of the opioid painkillers and prescribing it only in the cases when they are sure that the treatment will be safe and effective. Here, we have a first step to regulate prescription abuse that are one of the cause of opioid problem in France and opioid crisis in the United-States. Article R.4127-8 of CSP could be one of the legal instrument used to, if not regulate alone, support a compliance mechanism such as opioid prescriptions are limited to the strict necessary. Another article of CSP could be used to serve as a basis of opioid regulation, it is the article R.5132-30 which states that, concerning narcotic-registered drugs, the treatment must not be longer than 28 days. In terms of opioids, prescribing limits depends on the substance. Weak opioids like Tramadol, Codeine or Opium Powder cannot be prescribed for more than one year and cannot be delivered for more than 28 days. Oral Morphine and oral Oxycodone cannot be prescribed for more than 28 days. This limit may also be set at 7 days in the cases of injectable Morphine or Oxycodone. Concerning Fentanyl, which is the most powerful legal opioid in France, it cannot be delivered for more than 14 days in case of prolunged action treatment and for more than 7 days in case of fast action treatment. We can see that there alreday is regulation of prescription for opioid. However, this regulation is not sufficient and permit anyway abuse which could blead to addiction and even overdose. We will see in the following what we could do to reinforce this regulation.

Besides obligations concerning prescribing, physicians also have duties concerning informing patients. The duty to inform patient about their health state and also about the treatment that physicians proposes is already contained in the Hippocratic Oath where it is said: « *j'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences. Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences. Je ferai tout pour soulager les*

223 « Medicine must not be practiced as a business » (translation by the author).

224 «Must not, except exceptional circumstances, undertake or pursue a treatment nor make prescribing in fields which overpass his or her knowledge, experience and means » (translation by the author).

225 « The physician must, without neglecting his or her moral assistance duty, limit his or her prescribing and his or her acts to what is necessary for the quality, the security and the efficiency of care. He or she must take into account the advantages, the drawbacks and the consequences of the possible treatments » (translation by the author).

souffrances »[226]. The CSP takes back this obligation of informing and deploys it in different articles. In the article R.4127-35 of CSP, it is said that « *le médecin doit à la personne qu'il examine, qu'il soigne ou qu'il conseille une information loyale, claire et appropriée sur son état, les investigations et les soins qu'il lui propose. Tout au long de la maladie, il tient compte de la personnalité du patient dans ses explications et veille à leur compréhension*[227]». Here, it is clear that physicians must inform the patients over their health state and about the treatment that they propose in order to solve the problem. The CSP, in its article R.4127-13 adds that « *lorsque le médecin participe à une action d'information du public de caractère éducatif et sanitaire, quel qu'en soit le moyen de diffusion, il doit ne faire état que de données confirmées, faire preuve de prudence et avoir le souci des répercussions de ses propos auprès du public. Il doit se garder à cette occasion de toute attitude publicitaire, soit personnelle, soit en faveur des organismes où il exerce ou auxquels il prête son concours, soit en faveur d'une cause qui ne soit pas d'intérêt général* »[228]. Informing does not mean promoting or relaying information. The physician must make sure to remain neutral and intellectually honest. Besides delivering information, the physician must also make sure that this information is understood by the patient. It is not sufficient that the information is given, it is also necessary to make sure that the information understood. Indeed, in the article R.4127-34 of CSP, « *le médecin doit formuler ses prescriptions avec toute la clarté indispensable, veiller à leur compréhension par le patient et son entourage et s'efforcer d'en obtenir la bonne exécution* »[229]. The obligation of informing is reinforced when the physician is prescribing narcotic-registered drugs and therefore when he or she is prescribing opioid painkillers. Indeed, according to article R.5132-29 of CSP, « *les médecins (lorsqu'ils prescrivent des substances classées comme stupéfiants) doivent indiquer sur l'ordonnance, en toute lettres, le nombre d'unités thérapeutiques par dose et le nombre de doses* [230]». This obligation of informing patients for physicians is a way to answer to a growing principle in medical field which is consent of the patient. More and more, the patient is considered as able to understand but also to make decisions about its own health what was not the case few decades ago. This principle of patient's consent is, for instances, present in the article R.4127-36 of CSP where it is mentionned that « *le consentement du patient doit être recherché dans tous les cas*[231] » . The consent of the patient must be what that guides physicians, and health professional in general, in their action.

Besides this obligation of informing patient, physicians also have an other obligation concerning informing but not towards the same actor. In the CSP, it is said that physicians must collaborate with health authorities and with its colleagues. In article R.4127-12 of

226 « I will inform the patients about the decisions considered, about their reasons and their consequences. I will never deceived their trust and I will never exploit the power give by the circumstances to force their consciences. I will do everything to ease the pains » (translation by the author).

227 « The physician must give to the patient a faithful, clear and appropriate information about his or her condition, investigation and treatment. During all the disease, the physician take into account the personality of the patient in his or her explanations ad make sure of their understanding » (translation by the author).

228 « When the physician participate to an action of information, whatever the way of diffusion, he or she must display only confirmed and reliable data, be prudent and be conscious of the resonance of his or her words. He or she must not promote him or herself, his or her organization or a cause that is not of general interest » (translation by the author).

229 « The physician must pronounce his or her prescribing with necessary clearness, make sure of the comprehension of the prescribing by the patient and his or her entourage and do his or her best to obtain the good execution of the prescribing » (translation by the author).

230 « Physicians (when they are prescribing narcotic-registered drugs) must indicate on the prescription, in letters, the number of therapeutic unities per dose and the number of dose » (translation by the author).

231 « The consent of the patient must be researched in every cases » (translation by the author).

CSP, it is said that « *le médecin doit apporter son concours à l'action entreprise par les autorités compétentes en vue de la protection de la santé et de l'éducation sanitaire. La collecte, l'enregistrement, le traitement et la transmission d'informations nominatives ou indirectement nominatives sont autorisés dans les conditions prévues par la loi* [232]». Such a collaboration between physicians and health authorities requires that physicians collect and transfer information to health authorities. Some would say that this circulation of information is detrimental for physicians' professional secret because some personal information from patients is transfered towards health authorities and because physicians are made transparent and accountable. Other would say that this system of sharing of information is absolutely necessary face to the opioid problem and that it is a good first point to build a Compliance system leaning on physicians and on the other health professionals. This obligation of informing is also extended to the physician's colleagues with who he or she is working. For example, article R.4127-59 of CSP: « *le médecin appelé d'urgence auprès d'un malade doit, si celui-ci doit être revu par son médecin traitant ou un autre médecin, rédiger à l'intention de son confrère un compte rendu de son intervention et de ses prescriptions qu'il remet au malade ou adresse directement à son confrère en en informant le malade. Il en conserve le double* »[233]. This general principle of informing interested colleagues is also consacred in article R.4127-64 of CSP where it is said that « *lorsque plusieurs médecins collaborent à l'examen ou au traitement d'un malade, ils doivent se tenir mutuellement informés ; chacun des praticiens assume ses responsabilités personnelles et veille à l'information du malade*[234]». Here again we can ask the question if this obligation of circulation of information between colleagues attacks professional secret which protect patient and physician. In any case, this obligation is anyway necessary to build a compliance system to prevent opioid crisis too.

All of these obligations engaged the liability of the physician. For instance, in 2012, a physician was convicted for not having informed his patient that he was under off-label use of a drug[235]. Physician's liability is regulated by article R.4127-69 of CSP where it is said that « *l'exercice de la médecine est personnel ; chaque médecin est responsable de ses décisions et de ses actes* »[236]. Today, since the law n°2002-303 of 4th of March 2002 which modified the article L.1142-1 of CSP and case law corresponding[237], physician's liability is a fault-based liability which means that physicians can be considered as liable only if they committed a fault. This fault-based liability protects in a way physicians. Before 2002, physicians liability was indeed a strict libaility which means that the physician could be liable even without a fault from him or her.

2- Pharmacists also already have some duties

232 « The physician must participate to the action undertaken by competent authorities to protect health and educate to health. He or she participate to health monitoring. The collection, the registration, the treatment and the transmission of nominative or indirectly nominative information is allowed within the framework designed by law » (translation by the author).

233 « The physician who is called with emergency by a sick person must, if this sick person should be seen again by his or her regular physician or another physician, write a report of his or her intervention and prescribing for the address of his or her colleague, informing the sick person. The physician keep a copy » (translation by the author).

234 « When physicians are collaborating to the examination or to the treatment of a sick person, they must inform each others. Each physician assumes his or her personal responsibilities and makes sure of the information of the patient » (translation by the author).

235 Cass 1ere Civ. 12th of June 2012, n°11-18327

236 « Medicine is personal. Each physician is liable of his or her decisions and acts » (translation by the author).

237 Cass 1ere Civ., 12th of July 2012, n°11-17510

In the same way than medicine, pharmacy is considered as a field to exclude from Competition Law. Indeed, the research of profit should not be the guide of action in pharmacy and some regulations are implemented to make the sector operating differently than under Competition Law. In article R.4235-64 of CSP, it is said that « *le pharmacien ne doit pas, par quelque procédé ou moyen que ce soit, inciter ses patients à une consommation abusive de médicaments* »[238]. A seller in another sector would be allowed to make any effort necessary to convince the potential buyer to buy the good and the pharmacist would even be expected to act like that because it is natural, according to Competition Law, and also because it is necessary to distinguish operators between them and to classify them between those who deserve to remain on the sector and those who are not competitive enough to not fail. But, in pharmacy things are different : it is not permitted to the pharmacist to engage in marketing operations which would enable him or her to artificially increase its market share. For example, article L.5125-28 of CSP prohibites « *toute convention d'après laquelle un pharmacien assure à un médecin praticien, à un chirurgien dentiste ou à une sage-femme un bénéfice d'une nature quelconque sur la vente des produits pharmaceutiques, médicamenteux ou cosmétiques que ceux-ci peuvent prescrire* »[239]. What should govern the sector is trust and honnesty. A patient should be able to trust its physician in every circumstances which is impossible if the possibility that the physician in question is in a convention with a pharmacist exists. In the same way, article L.5125-25 of CSP: forbidds « *aux pharmaciens ou à leurs préposés de solliciter des commandes auprès du public*[240] ».

Because pharmacy is not a business as the others in France, some restrictions are imposed to pharmacists. The first of them is the fact that pharmacists are not perfectly free in their delivering. Article R.4235-62 of CSP says that « *le pharmacien ne peut faire de diagnostique* »[241]. This means that pharmacists connot advice and deliver a drug to a patient according to their own opinion. They are only authorized to deliver drug that was prescribed by a physician. Indeed, according to article L.5125-23 of CSP, « *le pharmacien ne peut délivrer un médicament ou produit autre que celui qui a été prescrit, qu'avec l'accord exprès et préalable du prescripteur, sauf en cas d'urgence et dans l'intérêt du patient* [242]». Pharmacists cannot deliver drugs that they are not prescribed but, however, they must deliver, among prescribed drugs, only the drugs that seems justified. Article R.4235-61 of CSP says that « *lorsque l'intérêt de la santé du patient lui paraît l'exiger, le pharmacien doit refuser de dispenser un médicament. Si ce médicament est prescrit sur une ordonnance, le pharmacien doit informer immédiatement le prescripteur de son refus et le mentionner sur l'ordonnance* »[243]. This means that the pharmacist has a control power over the prescriptions and must not deliver a drug when he or she judges that it is necessary. This also means that a prescribing does not exempt the pharmacist from liability. Indeed, a pharmacist cannot defends that he or she was just delivering a drug which was prescribed by a doctor because it is said in article R.4235-61 of CSP that is in their responsability to check the prescription and to stop the delivering if it is necessary. Narcotic-registered drugs are also subject to reinforced regulations concerning their

238 « The pharmacist must not, whatever the process used, encourage his or her patient to abusively consume a drug » (translation by the author).

239 « All convention between a pharmacist and a physician to ensure to the physician a benefit, whatever its form, over the sale of the products that he or she prescribes" (translation by the author).

240 « The pharmacist to request orders form the public" (translation by the author).

241 « The pharmacist cannot make a diagnostic » (translation by the author).

242 « Pharmacists may deliver another drug that the prescribed drug [...] only with the agreement of the prescriber, expect in case of emergency or for the interest of the patient » (translation by the author).

243 « When the health interest of the patient requires it, the pharmacist must refuse to deliver a medication. If it is a prescribed drug, the pharmacist must immediately inform the prescriber of its refusal and write it on the prescribing paper » (translation by the author).

delivering as concerning their prescription. Indeed, article R.5132-33 of PHC explains that, concerning narcotic-registered drugs, a pharmacist must not deliver the treatment if the prescription is older than 3 days or must deliver only the remaining to compete treatment. A pharmacist must not execute a narcotic-registered drug prescription of the same physician during the duration of the first prescription. Once again, the pharmacist is erected as a controller and a keeper of drug abuse.

As well as the physicians, pharmacists also have a duty to inform patients about the drug they sell to them, about their way of using and the risks taken. This duty to inform is consacred in the article R.4235-2 of CSP where it is stated that the pharmacist « *doit contribuer à l'information et à l'éducation du public en matière sanitaire et sociale* »[244]. This duty to inform is part of the delivering at the same level than the analysing of prescribing and than the preparation of the doses according to the article R.4235-48 of CSP[245]. Moreover, the responsibility of the pharmacist does not stop with the delivery of the drug. Patient should be also able to ask for an additional advice or information afterwards. Indeed, according to article R.5125-46 of CSP, « *avant de délivrer un médicament, le pharmacien doit écrire sur la boîte son nom et adresse et le nom officiel du produit* [246]». This obligation can also permit to guarantee the traceability of the drug and to find the pharmacist and the prescriber of the drug. Such an obligation could be helpful to build a Compliance system leaning on health professionals and so, on pharmacists. Of course, the information furnished by the pharmacist must, in any cases, be exact and relying on verified sources. The article R.4235-30 of CSP especially states that « *toute information ou publicité, lorsqu'elle est autorisée, doit être véridique, loyale et formulée avec tact et mesure* »[247].

This idea that tact and prudence should be the guideline for pharmacist's action could also be found in the article R.4235-62 of CSP saying that « *chaque fois qu'il lui paraît nécessaire, le pharmacien doit inciter ses patients à consulter un praticien qualifié* »[248]. Here, besides ensuring availability of information for the patient, we also join the idea of task sharing and therefore of collaboration between health professionals. Pharmacists are, by the way also expected to share their knowledge with another actor of the system which is the drug manufacturer. As we already said, each drug manufacturer must ensure the presence in its production process of a pharmacist who should evaluate the risks of the drugs and work on their reduction. This pharmacist is also expected to train the employees of the drug manufactory, according to article R.4235-68 of CSP[249]. If this cooperation is essential for the functioning of the current system, it would be even more crucial when we

244 « Must contribute to the information and the education of the public concerning health and social issues » (translation by the author).

245 Article R.4235-48 of CSP : « le pharmacien doit assurer l'acte de délivrance dans son integralité and doit : 1) faire l'analyse pharmaceutique de la prescription, 2) enventuellement, préparer les doses, 3) donner les informations et les conseils nécessaires au bon usage du médicament » (« pharmacist must ensure delivery act in its integrality and must: 1) make the pharmaceutical analyze of the prescribing, 2) eventually prepare the doses, 3) give information and advices necessary to the good use of the drug » (translation by the author)).

246 « Before delivering a drug, the pharmacist must write on the box his or her name and address and the official name of the product » (translation by the author).

247 « Every information when it is allowed, must be true, faithful and given with tact and prudence » (translation by the author).

248 « Each time it seems necessary for him or her, the pharmacist must encourage the patient to refer to a qualified professional » (translation by the author).

249 Article R.4235-68 of CSP: the referent pharmacist in pharmaceutical firms "doit former ses employés à suivre les bonnes pratiques » (« must train [employees] to use good practices » (translation by the author)).

will start thinking to the best way to create a Compliance system, supporting by health professionals, in order to prevent the occurrence of an opioid crisis in France.

But, pharmacists have not only the duty to cooperate with their colleagues but also with the regulator of the sector. Indeed, according to article R.4235-8 of CSP, « *les pharmaciens sont tenus de prêter leur concours aux actions entreprises par les autorités compétentes en vue de la protection de la santé*[250] ». Among other obligations towards ANSM and other health authorities, « *les pharmaciens doivent veiller à maintenir des relations confiantes avec les autorités administratives. Ils doivent donner aux membres des corps d'inspection compétents toutes facultés pour l'accomplissement de leurs missions*[251] »[252]. This means that, for instance, pharmacists should collect every information necessary to the health authority and transfer it as the physician must. Once again, even if this obligation ask questions concerning professional secret, it is also clear that it is a chance for those who want to build a Compliance system leaning on health professionals as we can see. This is particularly reinforced by two articles, both concerning narcotic-registered drugs (like opioids). Article R.5132-35 of CSP states that pharmacists must conserve narcotic-registered drug prescription during at least three years and article R.5132-36 of CSP that pharmacists must register every entry or exit of narcotic-registered drug. Here, we can see that pharmacists are expected, at least concerning narcotic-registered drugs, to collect and save information in relation to their delivering.

In this section, we saw that physicians as pharmacists already have obligations and that this obligations could serve as a basis of as a way of introducing a Compliance system in the sector to prevent opioid crisis. However, the current obligations are not always respected and we have to make some credible proposition to make them effective to permit the prevention of an opioid crisis while preserving some fundamental and essential principles of medicine exercise like professional secret and freedom of prescribing. This is the object of the following section.

B- The existent duties should be made effective

Compliance Law could be used to prevent the occurrence of an opioid crisis in France. Although the United-States have chosen to position the drug manufacturer at the heart of the Compliance system, we have seen that, in France, it is not either reasonable nor efficient to rely on the drug manufacturer which already have a lot of duties and which cannot do much more than it already does. However, we have detected that health professionals – physicians and pharmacists – could play a central role in a Compliance system which would have the « monumental goal » to guarantee the right use of opioid painkillers, since we have shawn that this is the crucial point to avoid a massive crisis. We have explained that health professionals could help to the prevention of opioid crisis in two ways : first, rationalizing their prescriptions or their delivering and second, make sure that the patient gets all the necessary information to rightly use the drug that was prescribed and delivered to him or her. We will so work in these two aspects.

1- A system based on the principle « comply or explain » can force physicians and

250 « Pharmacists are expected to help competent authorities in order to protect health » (translation by the author).

251 « Pharmacists must be careful to maintain trustful relationships with administrative authorities. They must give to the competent inspection corps every faculties necessary to accomplish their missions » (translation by the author).

252 Article R.4235-20 of CSP

pharmacists to rationalize their prescriptions or delivering

The « comply or explain » principle is a regulatory principle especially used in sector as banking or finance since it was introduced for the first time in the Cadbury Report in 1992 to regulate these sectors[253]. According to this principle, the operators are accountable of a determined-in-advance data that they must furnish to a supervisory authority. Two cases are possible since this point : either the data is close to the one expected by the supervisor (close ot the mean of the others operator or close to an objective set by the regulator) and in this case, we say that the operator has *complied,* or, the data is judged by the supervisor not close enough to the one expected and then, the operator has to *explain* why its data is so far from the target. If the operator can give an explanation that is judged acceptable by the supervisor, then the operator is not punished and is, at the worst, just warning that better data is expected from it next time but, if the operator cannot justify the gap between its result and the expected data or if it has no valid explanation to give to the supervisor, then the operator is punished[254].

This system responsabilizes a lot the firm which must reach a gap and, besides, find the way itself to reach this gap, but, at the same time, this system is flexible enough to be fair and to not punish a firm which has a good reason to not having reached the goal. Therefore, a goal is set and firms are liable in Ex Ante for the fulfilment of this objective but, the system is empathic enough and does not punish arbitrarily all the firm who did not reach the goal[255]. This empathy is advantageous in two ways : first, it permits to ease a system which could be seen as brutal (especially because it reverses the charge of the proof and shakes the presumption of innocence by giving to the defendant the duty to justify itself[256]) and also, it permits to work on the improvement of the regulation system because, the justifications given by the non compliant firms permits to understand better the problem and the obstacles to its solving[257]. Some could say that this system is not enough severe with the non compliant firm which are not incentivize enough to comply because they have the alternative to explain (while there should not have the possibility to have an alternative to Compliance). But, we can answer that the punishment for those firms is not really in the sanction that they did not get, but rather in the fact to be force to reveal their data. Since this point, they are already force to show that they are not in the target and this is sometimes sufficient to constitute a punishment in itself. Indeed, in an economy where the market is more and more expecting from the firm, the fact to not being in the right track is a bad signal sent to investors and consumers. The obligation to be transparent is here a kind of « name and shame » in itself[258]. If the supervisor does not punish, the market will do it.

In our case, a « comply or explain » system could be organized according to the following

253 Adrian Cadbury, Financial Aspects of Corporate Governance, ireport issued by "The Committee on the Financial Aspects of Corporate Governance", 1992

254 The « comply or explain » concept is particularly well explained in Fasterling, B. et Duhamel, J.-Ch., Le Comply or Explain : la transparence conformiste en droit des société, *Revue Internationale de Droit International (RIDE)*, 2009, p.129-157.

255 Manella, D., « Le Comply or Explain (enfin) détaillé : proposition de recommendation de l'UE », *Bulletin de Droit économique*, 2014

256 Boncori, A.-L., et Cadet, I. « Le comply or explain, un avatar de l'accountability », *Revue française de gestion*, vol. 237, no. 8, 2013, pp. 35-55.

257 De la Garanderie et al, « Comply or Explain : guide pratique de mise en oeuvre », *Institut français des administrateurs*, 2013

258 De la Garanderie et al, « Comply or Explain : guide pratique de mise en oeuvre », *Institut français des administrateurs*, 2013

way. Physicians could be subject to furnish to a supervisor[259] the number of times they prescribe opioid painkillers to patients every months or every years. The supervisor could determine a range such as the number situating in this interval would be considered as acceptable, either because it would be close to the mean of the other similar doctors or because it would be close to a theoretical average number build from medical and sociological data from the patients living in the region where the physician is operating. If the physicians are situated within this range, the supervisor could consider that they are compliant with the recommendation from health authorities advicing prudence with the prescription of opioid painkillers. If they are not and if they cannot give an acceptable justification to explain their gap from the norm (I operate in a mountaneous region where accident are more frequent or I operate in a manufacturing region where work accident are very frequent or there was a tragic accident in the manufactory just next to my office this month or I am a doctor specialized in the management of pain...), then we can imagine that the supervisor punish the non compliant physician. The system could be very similar for pharmacists who could be « invited » to communicate their data concerning their delivering. If they are in the range determined by the regulator, they would have nothing to scare and if they are not and that they do not have a reason to not being in it, they could be punished by the supervisor.

This system, for physicians and pharmacists, lies on the idea that a doctor who is prescribing or delivering much more opioid painkillers than the others[260] is much more likely to operate as a drug dealer than as a physician or as a pharmacist[261]. Such a Compliance system could permits to push the health professionals to rationalize their prescriptions or delivering either by detecting health professionals who do not take care of the recommendations (even without bad intentions) or those who are deliberately transgressing them because of business reasons. Such a system could inform the former that they are not in the norm and that may be, even if they do not have bad intentions, something goes wrong with their operations and that it would be desirable that they question their practice and change it. Concerning the later, such a system could dissuade them to continue in this way because they are now visible and that they are likely to be detected very rapidely. Such a system is not very costely because a machine or a computer could easily and quickly gather all the data and isolate those who are not corresponding to the norm determined in advance[262]. Obviously, it is necessary that the machine stops there[263] and that human beings take its relay to interpret the results found, to organize a contradictory debate between the operator and the supervisor and to decide if yes or no a sanction is necessary. Therefore, such a system could solve the problem of too massive prescriptions and deliverings by pushing the health professionals to rationalize their practice if they do not want to be punished by the supervisor.

Obviously, it is sure that this kind of system could present some drawbacks and implementing it needs to make choices between different principles as legitimate than each others. Two principles are reduced with this kind of system. The first principle that is

259 We will discuss after which institution is the best positionned to play the role of the supervisor.

260 Jenner Furst and Julia Willoughby Nason, *The Pharmacist*, available on Netflix since February 5th 2020

261 Obradovic, I., " La crise des opioïdes aux Etats-Unis: d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

262 This idea that the machine could play a central role in a Compliance system has been for example defended by General Electrics in a communication published on 6th of August 2019. To have more information about this communication and a criticism of it, please see Frison-Roche, M.-A., « Concevoir la Compliance comme une mécanique, devant être confiée à une machine : la bonne idée de General Electric. Vraimant la bonne voie ? », *The Journal of Regulation and Compliance (JoRC)*, 7 août 2019

263 Supiot, A., « Gouverner par les nombres », *Cours au Collège de France, 2012-2014*, Institut d'études avancées de Nantes, 2015, 520p.

harmed is freedom of prescription. Freedom of prescription is consacred by article R.4127-8 of CSP which states that « *dans les limites fixées par la loi et compte tenu des données acquises de la science, le médecin est libre de ses prescriptions qui seront celles qu'il estime les plus appropriées en la circonstance* »[264]. A great part of medicine is build on the principle according to which the physician is free to prescribe what he or she judges necessary and according to which no one could says to the physician what he or she has to prescribe. Physicians cannot be pursue for their prescriptions. However, with a « comply or explain » system, freedom of prescription could be harmed. Indeed, physicians are invited to reduce their prescription of opioids only to serious cases and they could be hold liable of an amount judged to suspicious of its prescription of opioid painkillers. This principle has two « *raison d'être* ». The first one is that freedom of prescription permits to protect health professionals and indirectly patients of the pressure from external interests. Of course, we can think about drug manufacturers or other authorities that could force health professionals to prescribe a drug or another in certain circumstances. The second « *raison d'être* » of the freedom of prescription is the asymetry of information that, as we repeat since the start of this master thesis, is at the heart of this very specific sector which is medicine and pharmacy. Only physicians have the required knowledge to know what it is necessary to prescribe and even only the physician can know what the patient needs because he or she has physically examined the patients in his or her specificities. The question what is necessary to ask here is not whether the freedom of prescription is needed (very probably it is) but whether the freedom of prescription could be reduced to permit a more efficient fight against opioid crisis. If there was not opioid crisis arriving, then the question won't be asked : freedom of prescription should be the rule and the sole rule. But, the facts are different : the sector is facing a rising risk of sinking into an unprecedent opioid crisis which could cause a lot of deaths or dramatic cases of opioid addiction if not correctly fought. However, as we saw before, the fight against opioid crisis requires, in some extent, the reduction of freedom of prescription. Are we ready to sacrify some of the freedom of prescription to avoid an opioid crisis ? Answering this question needs to decide between values and efficiency, between ideology and pragmatism. In any case, what is proposed in this master thesis is never to sacrify all the freedom of prescription but to limit it a bit to make a place to the fight against opioid crisis which seems as important, perhaps more urgent and unsolvable if freedom of prescription is not a little bit reduced. It is important to note that in a « comply or explain » system, freedom of prescription is partially saved because physicians could still judge which of the patients are needed opioids and public authorities will never forbid the prescription ot opioid to this or this patient. If we compare « comply or explain » system with a strict limitation of prescription, we can observe that in « comply or explain » system, the physician is still free to prescribe more opioids than the norm if he or she judges it necessary as long as he or she is able to justify it, which is not the case in a strict limitation of prescription. Health professional is then still the master of its prescription and can derogate if he or she thinks that it is necessary. Rather, the system invite physician to be aware that opioid prescriptions should be globally rationalized. Freedom of prescriptions are safe at the individual plan, it is freedom of prescription as a collective action which is rationalized.

The second principle that could be reduced with such a « comply or explain » system is professional secret. Professional secret of physicians and pharmacists is consacred by article L.1110-4 of CSP stating that « *toute personne prise en charge par un professionnel de santé (...) a droit au respect de sa vie privée et du secret des informations la*

264 « In the limits of Law and taking into account the current science state of knowledge, the physician is free of prescribing. Those prescribing will be in concordance with what he or she judges appropriate under the circumstances » (translation by the author).

concernant »[265]. However, as we said a « comply of explain » system lies on the transfer of information from the physician to the public authorities which harms medical secret. Professional secret is a duty and a right for the physician. It is a duty regarding to his or her patient who can expect from him or her that the health professional does not diffuse information concerning him or her. Physician must respect the professional secret with regards to their patients. But, professional secret is also a right to the health professionals when their interlocutor and the one expecting something from them is not the patient anymore but anyone else and particularly public authorities here. Physician can claim their professional secret to not divulge information of their patients and Law protects them from these other interlocutors. If professional secret has been created and implemented in medical field it is especially to protect patients and to prevent the constitution of medicial files which could be dangerous if misused as we saw during the World War II, for instance. But, the aim of a « comply or explain » system is especially to create such data to have an overview over the consumption of opioids and to incentivize or punish those who seems to abuse of their power of prescription or delivering. And this reduction of professional secret seems necessary to create such a system (operators should be transparent) and to fight against opioid crisis. Once again we are face to a dilemma between a legitimate principle, which is professional secret, and a as legitimate goal, which is the prevention of an opioid crisis in France, and its solving requires a political choice. But, once again, the solution is not to destroy completely professional secret and to replace it by total transparency. A « comply or explain » system just require that health professional transfer their aggregated data. In this perspective, the personal data of each patient is safe because what the supervisor gets is only the total number of prescription or delivering that a health professional did in the last month or the last year. The supervisor does not need to know that such numbers are those of Mr A. or Mrs B. but just to have a global overview over each professional activity. In the same way, the explanations expected from the non-compliant professional are not to justify every prescription but to give general explanations on why they on average prescribe or deliver more. The arguments required from professionals could be general and should not lie on personal examples. Here, we see that professional secret and « comply or explain » system could be balanced and that professional secret could survive and even be renforced in such a Compliance system.

2- Holding health professionals in Ex Ante of every case of addiction or overdose of their patients could be a solution to push them to inform and follow their patients

If Compliance Law could push health professionals to modify their practice, it could also push health professionals to act in way such as patients change their behavior. As we already said, health professionals are intermediaries who are in position to make sure that patients would act rightly with opioid medications. Indeed, they can inform them and make sure that this information is received and understood. And then, they can also control and continue to advice patients after the prescription and during the treatment. If they act like that, crisis is less likely to occur because all the unvoluntary victims, who sank into opioid addiction because they were not informed enough, will be assisted by an enlightened health professional that will prevent them to arrive at this stage by giving to them more information and by advicing them when they just start to misuse opioids.

However, it is difficult to make sure that health professionals will indeed act like that. The regulator, which is the ANSM, is not able to monitor each physician and each pharmacist to make sure that each of them follows his or her patients. Technically, the regulator cannot enter in each patient-health professional relationship to see how it is happening

265 « Every person taking in charge by a health professional (…) has the right of the respect of his or her private life and of the secret concerning his orher personal data » (translation by the author).

into it. By the way, it is also philosophically not desirable because the patient-health professional relationship is a private and personal relationship[266] which does not concern ANSM and because it seems important to trust and to relie on health professionals how know their job and who retire trust from patients because of their autonomy and because of the trust they have from the regulator. The regulator could set a list of rules and of procedures that the health professionals must respect (and even prepare a speech that the health professional must read to the patient before the prescription and naming all the risks of opioid painkillers or a list of questions that the health professional must ask to his or her patient every week by phone) but as we said, health professionals know their job much more than everybody else. The regulator suffers from asymetry of information[267] and it is difficult as a public authority to really know what the health professionals should do and what the patients needs. Leting some autonomy to the health professional and permitting him or her to elaborate his or her own protocole and to adapt it to each of his or her patient is then necessary to be efficient[268] (and efficiency is what is researched in Compliance Law[269]). But, if we let health professionals free, how can we make sure that they will act in the desirable way and put their knowledge at the service of the prevention of opioid crisis. For the moment, they are free and they do not really act enough. So, what could we do ?

Compliance Law proposes to create a system such as operators are free and autonomous but also such as we could be approximatively sure that they will use their autonomy at the service of the regulator's cause because they have interest to. Interest because they can get something from their compliance (incentives)[270] or interest because they have something to loose if they do not comply (sanction)[271]. By making health professionals liable in Ex Ante for every death due to an overdose, it is reasonable to expect that health professionals will be more responsbilized. ANSM cannot monitor every patient-health professional relationship but it can count the number of overdoses. It cannot monitor the process, which is hidden to him and whose it does not interest nor legitimacy to monitor by the way, but it can monitor the results. Let's imagine that each hospital or police officer is obliged, and this is conceivable, to report to ANSM every case of overdose or of addiction that they encounter during their mission with the name and the corresponding number of the referring physician and pharmacist. Then, the regulator have the choice either to turn towards the patient or towards the health professionals. As we said in the introduction, it is not very reasonable to turn towards the patients who could have been mislead by a lack of information and who suffer already a lot from their situation to be punish twice. However, the supervisor can hold the physician and the pharmacist jointly liable for this damage to the victim, considering that if this situation (addiction or overdose) has occured it is probably because information has not been given rightly or enough or because the following of the patient has not been realized effectively, and asking them some accounts concerning the disaster that occured. For the moment, health professionals could already

266 It is also and especially because this relationship between patient and health professional is considered as private that professional secret exists and is sacralized by article 1110-4 of CSP

267 Ross, S., and Mitnick, B., "Origin of the Theory of Agency", University of Pittsburgh, 2006

268 Greener, I., *Public Management*, Hound mills: Palgrave Macmillan, 2013

269 Frison-Roche, M.-A., « La mesure de l'efficacité et de l'effectivité des Outils de la Compliance », General presentation, Conference du 5 mars 2020

270 Frison-Roche, M.-A., « Compliance et Incitations : un couple à propulser », in Faculté de droit de l'Université Toulouse-Capitole, et Journal of Regulation & Compliance (JoRc), *Les incitations, outils de la Compliance*, 12 décembre 2019, Toulouse.

271 Frison-Roche, M.-A., La sanction comme incitation dans les techniques de compliance, in Faculté de droit de l'Université Toulouse-Capitole, Journal of Regulation & Compliance (JoRc), *Les incitations, outils de la Compliance*, 12 décembre 2019.

be found liable if they do not give sufficient information to their patients[272] but, in the Compliance system that we propose, the engagement of the responsibility of the health professional would not be episodic and led by the victim anymore but systematic and led by Public Authorities (and mainly the supervisor), which could be much more incitative for health professionals who could be sure that any addiction or overdose case will be reproach to him or her. Here, we do not recommend to punish with any empathy every health professional whose the patient does an overdose or fall into addiction but we rather propose to ask some accounts to the practionner in question and, a little bit as in a « comply or explain » system, punish them only if they have no arguments to oppose to the supervisor questions about the reasons why the patients became victim of opioid painkillers. What is expected from health professionals is that they do their best effort not that they avoid any case of absuse (which is impossible or at least too much asking to health professionals. Here, as in the « comply and explain » system, health professionals do not have an obligation of results but rather an obligation of means, which is much more realistic and pretty sufficient. By the way, this Ex Ante liability system would function a little bit as a « comply or explain system » in which every physician or pharmacist would be called to explain every abnormal number of addict or dead patients or will be punished.

The major advantage of holding referring health professionals liable in Ex Ante for the overdoses or the addiction of their patient is that it incentivizes a lot the health professionals to behave in the right way and to do everything they can to avoid such a behavior[273]. Indeed, it is reasonable to expect that physicians and pharmacists do not want to be pursued and judged personally liable for the overdose or for the addiction of their patient. It is the reason why we can expect that they will do everything they could to make sure that this never happen. They will so warn very carefully patients of the posology and of the risks to not following it. Then, they will probably make sure that this information was well received and understood by patients. Moreover, they will probably follow their patients according to the modalities they judge relevant to make sure that their use is conform to their recommendations. Even, they will probably avoid to prescribe/deliver opioids painkillers massively, knowing whether they are likely to be hold liable in case of abuse. In any case of doubt concerning the potential behavior of the patient, they will certainly avoid to prescribe/deliver opioids and each time that an alternative treatment will be possible and effective enough, they will probably prescribe/deliver it instead of opioid medications. We can see here that physicians and pharmacists will internalize the « monumental goal » consisting in guaranteeing right use of opioid painkillers even if this aim was not their aim naturally because they are mechanically forced to adopt it as their principal goal because they are judged according to it and because they could be punished if they do not reach it[274].

However, as for a « comply or explain » system, a Ex Ante liability could be harmful for some current principles in the health care system. Here, freedom of prescription is partially safe. However, it is not really the case for professional secret. Indeed, a holding liable in Ex Ante referring physicians and pharmacists requires two things. First, data from overdoses and addiction must be centralized. Contrary to a « comply or explain » system, aggregated data are not sufficient here. The supervisor needs to know the name of the patient to be able to pursue its referring pharmacist and physician. Second, the supervisor

272 Law n°2002-303 of 4/03/2002 transcript in PHC at article L.1142-1 ; for case law see especially : Cass. 1Ère Civ. 12/07/2012 n°11-17510 and Cass. 1Ère Civ. 12/06/2012 n°11-18327

273 Frison-Roche, M.-A., La sanction comme incitation dans les techniques de compliance, in Faculté de droit de l'Université Toulouse-Capitole, Journal of Regulation & Compliance (JoRc), *Les incitations, outils de la Compliance*, 12 décembre 2019.

274 Frison-Roche, M.-A., « Du Droit de la régulation au Droit de la compliance », in Frison-Roche, M.-A. (dir.), *Régulation, Supervision, Compliance*, Série Régulations, Dalloz, 2017, p.1-14.

should be able to link the name of the patient to the name of its prescribing physician and of its delivering pharmacist. Such an information should be available only if each prescriber and each pharmacist is forced to register every of its prescription or delivering of opioid painkillers in a software with the whole information concerning the prescription or the delivery in question (name of the patient, quantity prescribed or delivered, lenght of the prescription or of the delivering...). In some words, the supervisor should be able to track the drug from its consumer to its prescriber passing through its deliverer[275]. Of course, professional secret is harmed with such a tracking system because the supervisor could be able to check at every moment who is using opioid painkillers and who prescribe/deliver it. The health state of the patient and the activity of the health professionals are not a secret anymore. But, once again, this professional secret has to be balanced by the absolute necessity to fight against the occurrence of a potential opioid crisis similar to those of the United-States. If professional secret is important, this « monumental goal » is as important and legitimate. Politics have to decide[276]. Not necessarily between professional secret and prevention of opioid crisis but perhaps rather what should be the respective place of professional secret and of action against opioid abuse. How should we dose this two aim and balance them to permit to each of them of being effective without hurting too much the other ? Because, after all, in terms of opioids, everything is a matter of dosage.

III- PROFESSIONAL ORDERS SHOULD PLAY THE ROLE OF SUPERVISOR

In the precendent section, we have described what could be a Compliance system in the medical sector, relying on the health professionals and with the « monumental goal » of preventing the opioid crisis in France. This system would lie on two pillars : a « comply and explain » system to force health professionals to rationalize their prescriptions and deliverings, and an Ex Ante liability to push the pharmacists and the physicians to do everything they can to make sure that patients use rightly opioid painkillers. This two pillars permits to avoid two risks : the risks of a health professional abuse and the risk of a patient abuse.

But, we have also shown that the efficiency and the effectivity of such a system is possible only if one actor is present : the supervisor. The supervisor is the actor which monitor the « crucial operator » in its work to achieving the « monumental goal »[277]. « Crucial operators » are totally transparent for the supervisor who can collect every data that it wants for controlling the effective effort of the « crucial operator » to reach the goal. We say that the supervisor has a power of control. In our case, this power of control could take the form of the collection of data concerning the prescribing and the delivering of opioid painkillers and also the gathering of information concerning the patients falling into addiction or into overdose. But the supervisor also have a power of sanction. To make its control efficient, it needs indeed to have the power to punish the deficient « crucial operators ». In our case, the supervisor could have the power to punish health professionals who prescribe or deliver to much opioids without any reasons or those whose the patients fall into addiction or into overdose.

275 Kadri, Y., « Olivier Dupuy (Nasdaq) : « La compliance exige une traçabilité détaillée des actions pour être prêt en cas de contrôle » », in *Décideurs Magazine*, 08/11/2018

276 For Marie-Anne Frison-Roche in Frison-Roche, M.-A., « Il faut construire un dispositif européen de compliance, voilà l'avenir ! », in Actualité/Entretien, *Petites Affiches*, propos recueillis par Olivia Dufour, n° 244, 7 déc. 2017, pp. 4-6, « Compliance is a matter of State » in which Politics has a major role to play.

277 Frison-Roche, M.-A., « Du Droit de la régulation au Droit de la compliance », in Frison-Roche, M.-A. (dir.), *Régulation, Supervision, Compliance*, Série Régulations, Dalloz, 2017, p.1-14.

A- ANSM cannot play the role of the supervisor

But what is exactly the salience of the supervisor ? In the regulated sectors, there is no supervisor. On the contrary, there is a regulator with extended power who has the power to set the goal, to impose obligations but also to control in Ex Ante and in Ex Post the operators and to punish them if their behaviors are not satisfying[278]. In other words, regulator cumulates the fonctions of the regulator who give the obligations and the prerogatives of the supervisor who control and sanction. Such a accumulation has been judged acceptable by the judge[279] and even desirable in the sense that it permits to the actor who accumulates this two functions to be much more effective than two distinct institutions, holding respectively the power of the regulator and the power of the supervisor. As we are looking for efficience in Compliance Law and especially in the fight against opioid crisis, why do not create such a big actor in our medical case ? We have a regulator which is ANSM, which set the goals and the more or less concrete obligations and which organize a Compliance system such as health professionals could help in the prevention of opioid crisis. Why do not giving to the ANSM the power of supervise the operators too ? As we said, this accumulation is already existent in many sectors and especially in regulated sectors and prove too be efficient. In the Banking sector, for instance, the Solving and Prudential Control Authority in France and the European Banking Authority at the European level accumulate the two powers of supervision and regulation[280]. This has good advantages of rapidity and efficiency. However, it would be not the solution that we will propose in this master thesis.

1- To be efficient a supervisor needs to know the operator and this is not enough the case of the ANSM towards health professionals

Entitling the regulator of the drug sector to be also the supervisor would say entitling ANSM to supervise health professionals. If ANSM would be a salient institution to superivise the drug manufacturer if it would be the « crucial operator », this institution seems less appropriate to supervise health professionals. As we have already said it precedenlty in this master thesis, ANSM's privilegied interlocutor is the drug manufacturer. The reason why ANSM talks principally to drug manufacturers is that ANSM regulates pharmaceutical sector[281]. However, if health professionals are in contact with the object « drug » they are not really included in the parmaceutical sector or at its very periphery. ANSM would not be the most pertinent actor to supervise health professionals because it is not its mandate. More precisely, ANSM is not used to be in contact with physicians and pharmacists. For instance, it is reasonable to assume that this regulator does not know them as well as it knows drug manufacturers, especially because it is less in contact with them than with drug manufacturers. However, to supervise an operator well, it is necessary to know it very well[282]. Especially when we implement a « comply or explain » system, for instance. As ANSM does not know very well the health professionals, how can

278 Borga, N., Marin, J.-Cl., Roda, J.-Ch. (dir.), *Compliance : l'entreprise, le régulateur et le juge*, Série Régulations & Compliance, 2018.

279 CC, décision n° 89-260 DC du 28 juillet 1989, loi relative à la transparence et à la sécurité du marché financier about the compliance to Constitution of the concentration of powers of Independant Administrative Authority

280 The powers of the French banking regulator and supervisor are detailled in Frison-Roche, M.-A., « Les régulateur et superviseurs bancaires et financiers », Leçon n°6, *Droit de la Régulation bancaire et financière*, Sciences Po, 2016

281 From Article L. 5311-1 to Article L.5311-3 of CSP

282 Frison-Roche, M.-A., « Régulateur » in *Dictionnaire bilingue du Droit de la Régulation et de la Compliance*, 2016

it appreciate the value of the explanation given by non-compliant health professionals. It will be not able to detect what is manifestly a lie and what is a consistent justification. In this perspective, the ANSM risks to punish health professionals who had a good reason to prescribe more opioids than the mean because it would judge that its justification is not serious enough or, on the contrary, it risks to cover some health professionals who would have been skillfull to disguise their justification in a valid justification to the eyes of the ANSM. To supervise in a Compliance system, it is therefore absolutely necessary to know the operators, the specificities of their activities, their abilities and their weaknesses, what is reasonable to expect from them and what seems too much. But, ANSM, as a regulator focus on drug manufacturers – and which know them particularly well – is not well positionned enough to supervise health professionals that it does not know sufficiently.

2- If the ANSM is at the same time regulator and supervisor, this risks to leads to a confusion of tasks detrimental to the efficiency of the supervision system and to the professional secret

But, the fact that health professionals supervision is not the mandate of ANSM and that in this perspective it risks to suffer of asymetry of information with regards to professionals, for the better as the worst, if it engage in this mission, is not the unique reason why we will not propose that the ANSM supervise health professionals. If ANSM becomes the supervisor of health professionals, it will be at the same time the regulator and the supervisor. However, it is reasonable to think that such a concentration of task would be detrimental to our compliance system. It is not really the fact that such a concentration of task would lead to the fact that ANSM would multiply powers of different sources which seems detrimental. As we have already said, this concentration of powers already exists within regulators who accumulate power of setting the rule, applying the rule, controlling the operators and potentially punishing them[283] and the judge has judged it compliant with constitution as long as this concentration was useful to reach the goal for which regulators were mandated[284]. Which is detrimental is rather the concentration of tasks in itself. This concentration of tasks risks indeed to create a kind of confusion. Health professionals needs clearity and a feeling of justice which are possible only if the supervisor and the regulator are clearly distinct. Indeed, if the regulator and the supervisor are the same institution, a doubt concerning the exact function of the institution and of its objective impartiality (because it is at the same time judge and party[285]), could born in the spirit of the health professional. It is the reason why it seems necessary to organise the system precisely : one task, one institution.

Moreover, the existence of an independant supervisor could also lead to a more efficient supervision. A regulator is entitled with many missions : setting the goal, communicating about it, implementing measures and obligations to the operators in order to maximizing the chances to reach the goal set, controlling in Ex Ante the actions of the operators... If we add, besides, the role of controlling Ex Post and punishing the operators (that should be done according to necessary but heavy and length procedures), we minimize our chances that the regulator is efficient either in the regulation and in the supervision

283 This is the case in the majority of the regulated sectors as we said it before. For example, in the Energetic sector where the Commission de Régulation de l'Energie concentrates powers of setting the rule, applying the rule and judging the operators (from article L131-1 to L135-16 of the Code de l'énergie).

284 CC décision n°86-217 DC du 18 septembre 1986 about the compliance to Constitution to give a regulatory power to Independent Administrative Authority and CC, décision n° 89-260 DC du 28 juillet 1989, loi relative à la transparence et à la sécurité du marché financier about the compliance to Constitution of the concentration of powers of Independant Administrative Authority

285 Objective impartiality is one of the expectations of Article 6 of Convention for the Protection of Human Rights and Fundamental Freedoms guaranteeing the right to a fair trial

mission. It is possible that the supervision would be less efficient. On the contrary, if we entitle one institution just to focus on the supervision, this institution could specialized on one unique mission : supervising efficiently without dispersion[286]. This specialization could also enable the independant supervisor to be more mobile. As a regulator, an insitution should be associated to a State with geographical and political borders while, as a supervisor, an institution could be only associated with an operator who sometimes is present in different countries. How could we supervise a multinational operator if we are constrainted by borders and how thinking extrateritorality of Compliance Law if we are a national regulator ? The supervisor does not have these constraint because it is graft on the « crucial operator » and could follow it around the world without any restrictions[287].

We evoked the necessity to know the operator and to distinguish the tasks of supervision and regulation to be efficient but, one of the most important argument to propose an independant supervisor remains in the fact that the existence of an independant supervisor permits to keep safe professional secret that could be hurt in a Compliance system. The existence of an independant supervisor permits first to keep the regulator away from the professional secret of health professionals. Moreover, it permits to entrust the role of the supervisor to an actor whose the fact to be informed of medical information would not hurt professional secret.

We said precendetly that it seemed paradoxal to have at the same time a centralization of information and a respect of professional secret. Indeed, if health professionals have to transfer the information that they have to keep secret, then there is no professional secret anymore. However, it seems possible to concile both and to have at the same time a transparent Compliance system and to save professional secret if the role of the supervisor in charge of collecting the information is entrusted to an actor who could know medical information without violate professional secret. But this actor should at the same time be external to the health professional and in capacity to punish him or her if he or she does not respect the recommendation in terms of opioids prescribing or delivering. Only one actor seems gather this two conditions (internal enough to keep professional secret and external enough to be able to control and punish health professionals) : the professional order.

B- Professional orders should play the role of the supervisor

The fact that ANSM is not close enough to health professionals let us with the task to find an institution close enough to professionals to understand them but also in capacity to supervise them with firmness. One institution seems fulfill this two conditions : the professional order.

1- Professional orders, besides to know the operators and to be distinct from the regulator, are able to protect physicians' and pharmacists' professional secret

The professional order organizing the profession of physician in France is named *Ordre national des médecins* and gather every physician exercizing in France according to the article L.4121-1 of CSP. The *Ordre national des médecins* has the goal to « *veiller au maintien des principes de moralité, de probité, de compétence et de dévouement indispensables à l'exercice de la médecine ainsi que des règles édictées par le code de*

286 Frison-Roche, M.-A., « Du Droit de la régulation au Droit de la compliance », in Frison-Roche, M.-A. (dir.), *Régulation, Supervision, Compliance*, Série Régulations, Dalloz, 2017, p.1-14.

287 Frison-Roche, M.-A., « Du Droit de la régulation au Droit de la compliance », in Frison-Roche, M.-A. (dir.), *Régulation, Supervision, Compliance*, Série Régulations, Dalloz, 2017, p.1-14.

déontologie prévu à l'article L. 4127-1. Il contribuent à la promotion de la santé publique et de la qualité des soins[288] »[289]. The profession of pharmacist is organized according to the same way by the *Ordre national des pharmaciens* which gather every pharmacist of the country according to Article 4231-1 of CSP and which has for goal to « *l'ordre national des pharmaciens a pour objet : d'assurer le respect des devoirs professionnels ; d'assurer la défense de l'honneur et de l'indépendance de la profession ; de veiller à la compétence des pharmaciens ; de contribuer à promouvoir la santé publique et la qualité des soins, notamment la sécurité des actes professionnels*[290] » according to the same article.

Professional orders have three characteristics that would enable them to be a good supervisor : 1) they are constituted by health professionals[291] and so know them very well and are able to understand them, 2) as they are constituted by health professionals and as their mission is to defend the profession, they are in position to keep medical secret within the medical sphere, and 3) they already have the technical and legal capacity to control and sanction health professionals[292]. Then, professionals orders would be the institution able to concile efficience and secret, as they are at the same time intern to medical body but extern to particular health professionals.

This system of entrusting professional orders with the supervision of professionals has already been implemented for the attorney[293]. In this system proposed by Professor Marie-Anne Frison-Roche, attorneys are accountable only to their chairman while the chairman is accountable to the regulator. It would be too detrimental for attorney's professional secret that attorneys would be directly accountable to the regulator. It is the reason why Professor Frison-Roche proposed that the chairman constitute a filter between the professional and the regulator, to ensure at the same time professional secret and efficiency of the Compliance system. In this perspective, the attorney is liable in Ex Ante to its chairman and the chairman is liable in Ex Ante to the regulator. Holding the supervisor liable towards the regulator could permit to avoid the catching of the sector by professionals[294] and make sure that professional orders encourage operators to act and not protect them from regulator to defend the interest of the profession.

The question that deserves to be asked now is : finally, who really is the « crucial operator » in such a system? We have said that professional orders should be « forced » to supervise health professionals, especially because they are able and in the best positionned to do it. In this perspective, the regulator who will not have direct supervisory contact with the operators will consider the supervisor accountable and therefore liable of every opioid problem in the country, considering that if any opioid crisis would occur, it would be because the supervisor did not control/punish or control/punish enough

288 « Ensure the maintaining of the principles of morality, probity, competency and of devoting vital to the exercize of medicine (…) and ensure the respect by every member, of the professional duties and of the rules edicted by the code of deontology seen at the article L.4127-1 of the CSP. They contribute to the promoting of public health and to the quality of healthcare » (translation by the author).

289 Article L.4121-2 of CSP

290 « Ensure the respect of professional duties, to ensure the defence of the honnor and of the independence of the profession, to monitor the competency of pharmacists, to contribute to promote public health and health care quality, especially of professional acts » (translation by the author).

291 From article L.4121-1 to L.4125-9 of CSP for *Ordre national des médecins* and from article L.4231-1 to article L.4231-9 of CSP for *Ordre national des pharmaciens*

292 From article L.4126-1 to article L.4127-1 of CSP for *Ordre national des médecins* and from article L.4234-1 to article L.4234-10 of CSP for *Ordre national des pharmaciens*

293 Frison-Roche, M.-A., « La gouvernance en question », *Journal des Bâtonniers*, n°9 novembre-décembre-janvier 2010-2011, p. 12-13.

294 Stigler, G., The Citizen and the State : Essays on Regulation, University of Chicago Press, 1975

operators. In this sense, why do we not consider professional orders as the « crucial operator » able to act or to force someone else to act ? If health professionnal are those who are expected to act to prevent an opioid crisis, the question of who is liable for the occurrence of an opioid crisis depends on which institutions we look at. Health professionals are accountable and therefore also liable towards their professional order but professional orders are themselves accountable and so also liable to the regulator finally. In this sense, we are face to a double Compliance system with an operator supervised by a supervisor which is itself supervised by the regulator. This seems a little bit bureaucratic but it seems the best solution to avoid asymetry of information and to ensure that everybody is judged by an institution in capacity to understand him or her, for the best and for the worst.

2- Professional orders could rely on their current disciplinary powers towards professionals to supervise them

We agreed on the necessity to have an independant supervisor from ANSM and to the necessity to entrust supervision of health professionals by physicians and pharmacists professional orders. Now, it is necessary to ask the question : how do professional orders will control and punish health professionals ? After having answered to the question 'who', it seems interesting to detail the different modalities of control and sanction.

Concerning control, professional orders will be force to collect data from physicians and pharmacists to have a look concerning their prescription and delivering and to collect and treat all the data emerging from hospital and police officers concerning detected cases of addiction and overdoses. We can imagine that professional orders entrust this task to a rather simple to implement software which could underline automatically any abnormal data[295]. The threshold of prescribing/delivering or of addiction/overdose cases since that a professional could be judged non compliant could be determined jointly by the supervisor and the regulator[296]. We can imagine that the ANSM consults professional orders who are reputed to know the professional constraints and to have a pretty good idea of the standards because of their habits to control, to ask them what could be a realistic and credible expectation. Then, we can imagine than professional orders enter in contact with the non-compliant practitionner, directly or by numeric or paper letter to ask him or her some explanation regarding this non-compliance. A contradictory dialogue could occur between health professional and his or her order. In this perspective, it seems absolutely necessary that professional orders act in compliance with fair trial rules, especially included in Article 6 of the European Convention of Human Rights (ECHR).

Then, if the explanations furnished by the professionals are judged non satisfying by the professional order, then it should be forced to punish the non-compliant physician or pharmacist. We can imagine that this sanction could go from the simple warning to the bannishment from exercise passing through the financial fine, accrording to the extend of the professional's non-compliance, to the number of non-compliant professionals at the same time, to the gravity of the consequences, to the number of recidives and to the arguments advanced by the professional. In this perspective, it seems obvious that the

295 Such a kind of software has for example already been implemented in the some States of the United States and is named « Prescription Drug Monitoring Program (PDMP) ». For more information, see : Kolodny, Courtwright, Hwang et al., "The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction", Annual Review of Public Health, 2015

296 In Frison-Roche, M.-A., *L'apport du Droit de la Compliance dans la Gouvernance d'Internet* (The contribution of Compliance Law to the Internet Governance), Report asked by the French Government, published the 15th July 2019, 139 pages, Marie-Anne Frison-Roche explains that the regulator and the supervisor could be leads to work hands in hands

sanction should be studied and pronounced by a section of the professional order who must respect the fair trial rules stated in Article 6 of the ECHR.

Concerning control, it would perhaps be necessary to entitle professional orders with more powers. They can ask practionners some counts with regards to their activity but for that it is necessary that a disciplinary procedure would be engaged[297]. To implement our Compliance system where the professional order is a supervisor, it is necessary to entrust the order with the power to ask for information in Ex Ante to health professionals without being forced to engage a discplinary procedure. Here we just talk about controlling and not investigating. But, professional orders only can ask for information to professionals who are suspected of a deontological default and not to every professional. Control is an exception and must be justified while we are looking for it should be the ordinary procedure for every practionner.

However, concerning sanction, professional orders seems already entitled with all the necessary power. According to article L.4124-6 of CSP, « *les peines disciplinaires que la chambre disciplinaire de première instance peut appliquer sont les suivantes : 1° L'avertissement ; 2° Le blâme ; 3° L'interdiction temporaire avec ou sans sursis ou l'interdiction permanente d'exercer une, plusieurs ou la totalité des fonctions de médecin ; 5° La radiation du tableau de l'ordre* »[298]. The power of the *ordre national des pharmaciens* is similar. Indeed, according to article L.4234-6 of CSP, « *la chambre de discipline prononce, s'il y a lieu, l'une des peines suivantes : 1° L'avertissement ; 2° Le blâme avec inscription au dossier ; 3° L'interdiction temporaire ou définitive de servir une ou la totalité des fournitures faites ; 4° L'interdiction, pour une durée maximum de cinq ans avec ou sans sursis, d'exercer la pharmacie ; 5° L'interdiction définitive d'exercer la pharmacie* [299]». Therefore, it seems not necessary to add some supplementary powers to professional orders and the Compliance sytem can just rely on the current legal package.

3- In the United-States, the Compliance system could not lie on the shoulders of health professionals because there were no professional orders structured and powerful enough vis à vis operators to supervise them efficiently

Entrusting professional order with the power to supervise physicians and pharmacists in their mission to prevent an opioid crisis was not really possible in the United States. In the United-States, medical professional orders are very weak. For the physicians, there is the American Medical Association (AMA) which collect the adhesion of physicians and act to defend the profession and its deontology. But, there are two major problems with AMA.

First, AMA is not a professional order as we conceive it in Europe. The United-States are a very liberal and free-market country[300] which bannish absolutely any corporation which

297 From article L.4126-1 to article L.4126-6 and from article R.4126-1 to article R.4126-54 of CSP for *Ordre national des médecins* and from article L.4234-1 to article L.4234-10 and from article R.4234-1 to article R.4234-39 of CSP for *Ordre national des pharmaciens*

298 « The disciplinary sanctions that the disciplinary section (of ordre national des médecins) on first trial cann use are the following : 1) the warning, 2) the official reprimand, 3) the temporary interdiction with or without suspented sentence, or the definitive interdiction of exercizing one, various or the totality of the physician's functions (…), 5) the removal from order's table » (translation by the author).

299 « The disciplinary section pronunces, eventually, the following sanctions : 1) the warning, 2) the official reprimand written on the personal file, 3) the temporary or definitive interdiction to serve (some furnitures), 4) the interdiction, for a maximal lenght of five years with or whithout suspensed sentence, of exercizing pharmacy, 5) the definitive interdiction to exercize pharmacy » (translation by the author).

300 Esping-Andersen, G., *The Three Worlds of Welfare Capitalism*. Cambridge: Polity Press & Princeton: Princeton University Press, 1990.

will be detrimental to competition in a sector. Competition Law is strictly applied in the United-States and its transgression is much more severly punished than in Europe where an anti-competition practice could be eventually understood under certain circumstances, the European Economic Culture being not the same than the American one[301]. In this perspective, it seems normal than AMA does not have much power on professionals themselves who could be free to enter, leave or act approximatively as they want on the medical market. Therefore, AMA does not have a power of control and a power of sanction towards physicians as in France, especially because such a power could be considered as a barrier to market entry for practitioners who would be bannished from medical exercise by the order. The AMA is therefore much more a lobbying group which search to defend physicians' interests nearby the Congress and to promote the exercise of medicine than a discplinary order[302]. This has two consequences : first, as the AMA cannot control and punish physicians, it is non pertinent to entrust them of their supervision in the frame of a Compliance system and, second, as they are more active in the role of the denfence without condition of professionals, it seems more difficult for the regulator to trust them in its mission of supervision. Indeed, in this circumstances, it is more reasonable to expect that AMA will hide or defend non-compliant professionals than control or punish them in the name of a regulator seen as a stranger institution which want to control the profession. A good supervisor should be external enough from the operator which is not the case of AMA whose aim is to defend physicians towards hostiles.

The second major problem with AMA is the fact that it represents only a minority of physicians in the United States. Indeed, if physicians are obliged to register to the *Ordre national des médecins* in France to exercise[303], as it is a disciplinary institution, the American physician is not forced to register to the AMA and could choose or not to adhere to it, as it is a group of interest, a trade union representing the interests of profession. Therefore, the AMA represents only between 15 and 19% of the current American physicians[304]. Entrusting the AMA with the mission to supervise health professionals would not be efficient because more than 80% of physicians would not be submitted to control and sanction.

The situation is pretty the same for pharmacists. The American Pharmacists Association (AphA), the equivalent of AMA for pharmacists, has for unique mission to promote the execise of pharmacists and defend pharmacists. Moreover, the Association counts only 62 000 members over the 305 510 American Pharmacists in 2016[305]. It is therefore reasonable to think that, face to the impossibility to entrust health professionals associations with a supervisory power, the solution found in the United-States to stop and prevent opioid crisis was to build a Compliance system rather relying on drug manufacturers because they were much more compact and much easily supervisable.

301 Esping-Andersen, G.,*The Three Worlds of Welfare Capitalism*. Cambridge: Polity Press & Princeton: Princeton University Press, 1990 ; Combe, Emmanuel. « I. L'essor des politiques de concurrence », Emmanuel Combe éd., *La politique de la concurrence.* La Découverte, 2008, pp. 5-13.

302 "About the American Medical Association - AMA". Ama-assn.org. Retrieved 19 April 2018.

303 Article R.4112-1 of CSP

304 Drum, K., « The AMA represents only one-sixth of all doctors », *Mother Jones*, 27th of December 2016

305 Statista, « Number of Pharmacists in the United-States, from 2001 to 2016 »

CONCLUSION

The purpose of this master thesis was to alert about the existence of a major public health problem to come in the future in France and to propose some concrete solutions to avoid right now the occurrence of such a problem. Indeed, thinking about a problem beforehand is always a great opportunity because it permits to avoid hot reactions that sometimes could be the result of erratic feelings and not of a built reasoning. Moreover, start thinking right beforehand could enables policy-makers to prepare an appropriate response for when the problem will occur or – and this is even better – build a system to prevent the occurrence of the problem.

Since the end of 1990s, France is facing a rising problem with the consumption of opioids by its citizens. Like in the United-States, more and more opiods are consumed and much of the time this increase is more due to a rise in the quantities consumed by patients than to the rise of the quantity of patients using opioids. This increase of consumption is particularly problematic when we are aware that an overconsumption of opioid painkillers can lead to addiction and even to death by overdose.

Even if the French situation is far from those of the United-States, being much less lethal and not presenting a substitution effect towards more powerful and illegal substances for the moment, the American crisis is what we could « expect » in the future in France if no measures are implemented to avoid it. It is the reason why it was salient to look at the solution implemented by Americans. Judge Thad Balkman chose to hold liable in Ex Ante and in Ex Post a drug manufacturer, Johnson and Johnson, for the occurrence of the American opioid crisis.

By doing this, judge Thad Balkman applied Compliance Law. Compliance Law seems interesting when appears principle-based, complicated, urgent and sometimes global « monumental goals » that the Politics and the Regulator are unable to reach because of their national limitations, of their lack of knowledge, of their incapacity to collect necessary information or of their lack of contact with the actor who is expected to change its behavior. Face to this blocked situation, Compliance Law proposes to internalize in an operator judged « crucial » the care of this « monumental goal ». The « crucial operator » is named like that because it is able to reach the goal or at least is in better position than others to realize it. For this reason, the « crucial operator » is forced to make the « monumental goal » his or her, even if this « monumental goal » is completely different or contradictory to his or her initial objective. The « crucial operator » is hold liable in Ex Ante of the concretization of the « monumental goal » but has a huge freedom to choose the more effective and efficient way to achieve it.

In our French opioid problem, the right use of opioid medicines could easily be considered as a « monumental goal ». However, the Regulator, which is the ANSM, lacks of professional knowledge, of more precise information about opioids consumption and of direct and physical contact with patient to make right use of opioids painkillers actual. It is the reason why we have decided to search the existence of a « crucial operator » in the opioid chain on which a Compliance system could relies.

We first choose to look at the drug manufacturer because it is the solution found in the

United-States. The objective was to know if the drug manufacturer could be this crucial actor on which Compliance system could relies like in the United States. We have seen that if Amercian judge choose to build a Compliance system relying on the drug manufacturer it is especially because drug manufacturer in the United-States have only few constraints and are able to do much more than they currently do to avoid the occurrence of an opioid crisis. Indeed, they could play a role by warning directly patients and not only health professional as the learned intermediary doctrine enables them to do and by regulating their advertising such as it would be less misleading and even such as it would include some information, even information that would not be « selling arguments ». In this persepctive, it makes sense to hold drug manufacturer liable in Ex Ante for the prevention of opioid crisis because drug manufacturers are able to do something in that direction.

However, in France, the situation seems different. Drug manufacturer are much more regulated and are already expected to play this informational role that the drug manufacturer do not assume in the United-States. Advertising to patients is forbidden for opioid painkillers and advertising to health professionals for these medications is very regulated. Moreover, drug manufacturers already play an important role in the information of health professional, patients and even of the regulator. Drug manufacturers, in France, are already very solicited and it is difficult to imagine what they can do more, especially when we are aware of the fact that the french opioid situation depends on the behavior of other actors that drug manufacturer cannot control, particularly patients and health professionals. In this perspective, drug manufacturers, it seems inefficient and unfair to build a Compliance system relying on drug manufacturers in France.

The fact that drug manufacturers seem not able to carry a Compliance system does not mean that no « crucial operator » exists. We chose then to look at the other actors of the opioid chain to find one. As we excluded patients because they look like more victims than potential saviour, we choose to look at health professionals. We found that health professional behavior could have a real impact on opioid situation in France. Especially, they could play a role in the prevention of opioid crisis by rationalizing their prescription or their delivering according if they are physicians or pharmacists, by ensuring that patients got all the necessary information before the use of opioid painkillers and by follwing their patients in order to make sure that they indeed respect the recommendations formulated and vulgarized by health professionals. Physicians and pharmacists are far from being free from duties concerning prescription, delivering and information to patients but it is necessary to make them effective creating a appropriate Compliance system.

We have proposed to implement a « comply or explain » system such as health professionals must transfer all their statistics concerning their prescriptions and deliverings on a certain amount of time and could be punished if their are not in the norm jointly defined by the supervisor and the regulator and if they are unable to give a persuasive justification for this gap. We have also proposed to hold health professional accountable for the occurrence of their patients' addiction or overdose registered by hospitals or police officers to make sure that health professionals do all they can to inform and follow their patients. This two solutions could be implemented jointly even if it seems that the later (holding health professionals accountable of any of the behavior of their patients) could do without the former (« comply or explain » system). Indeed, holding health professionals accountable of every addiction or overdose push them indirectly to rationalize their prescriptions/deliverings because they could be afraid that a prescription or a delivering of opioids to the wrong person could lead to an addiction or an overdose that they will be forced to assume afterwards. A contrario, a « comply or explain » system would not push health professionals to make sure that their patients will rightly use opioids painkillers after

their delivering or their prescription as holding them accountable of every addiction or overdose of their patients will do. Indeed, they are just responsible of their prescription/delivering and of nothing else afterwards. In this perspective, it would seem appropiate to ask why proposing in this master thesis a « comply or explain » system if its effect could be included in the second solution. Actually, holding health professionals accountable of every addiction or overdose of their patients is a very radical solution and we know that policy-makers could face problematics that are not those of researchers like lobbying from interested parties, pression from public opinion or necessity to maintain peaceful social climate, etc. It is the reason why we have proposed two solutions. Policy-makers could choose to hold accountable health professionals if they want a pretty simple and radical reform. But, they can also just implement a « comply or explain » system over prescriptions/deliverings if they want a more moderate solution. They also can implement both to be sure to reach the « monumental goal ».

This Compliance system connot work without supervisor. ANSM is unable to play this role because its original mandate was to regulate drug manufacturers and that so they don't know enough health professionals to supervise them efficiently and fairly. Moreover, if ANSM would supervise health professionals they will play at the same time the role of regulator and of supervisor and this cumulation could be detrimental to an efficient supervising and to professional secret. However, professional orders seems the salient insitution to supervise health professional because of their independence from regulator, their understanding of practionners and their ability to keep professional secret. If some new powers should be entrusted to professional orders to control their pairs, professional orders could rely on their current power to sanction non-compliant practionners. American professional orders are much less powerful than their French counterparts and it is probably also the reason why Americans found to rather build a Compliance system relying on drug manufacturers which could be supervise more easily than physicians and pharmacists who do not face disciplinary institutions.

The solution against the appearence of an opioid crisis similar to the American one in France could pass by a Compliance Law system relying on health professionals, either they are physicians or pharmacists. Here, we do not use Compliance Law in order to prevent a systemic risk. An opioid problem, even if it turns to a real public health crisis, is not a systemic risk because a victim of opioid addiction or overdose cannot contaminate people who are not using opioids. Opioid crisis cannot turn to an epidemy because opioid addiction is not contagious and the fall of an individual, even if this fall is terrible for him or her, does not put directly and in itself other people in danger. Therefore, what is problematic with opioid problem, it is not its systemic characteristic but its massive characteristic. Opioid problem could touch a lot of people, independently and it is this fact which is terrifying. Because, here, they are human beings' lives that we are talking about. And Compliance Law could be conceived as the Law which targets to protect persons, and especially those who are the most vulnerable. By taking up the opioid problem, Compliance Law could erect the very principle of Person, constitutive of our Western World, and protect it from the potential aggression of other market principles like the search for profit. Compliance Law could show that the person's live and the person health is as important if not more important than profit making and that the right to live is as valuable than the right to not suffer.

BIBLIOGRAPHY

Texts

European Law

Convention for the Protection of Human Rights and Fundamental Freedoms (Article 6).
Treaty on the Functioning of the European Union (Article 114 and 127, §6).
Council Directive 85/374/EEC of 25 July 1985 on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability fo defective products.
Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community Code relating to medicinal products for human use.

French Law

Code Civil (Article 1109 and 1386-1 to 1386-18).
Code de la Sécurité Sociale (Article L.162-17-4-1).
Code de la Santé Publique (Article L.1110-4 ; L.1142-1 ; L.4121-1 to L.4125-9 ; L.4126-1 to L.4126-6 ; L.4127-1 ; L.4231-1 to L.4231-9 ; L.4234-1 to L.4234-10 ; L.5121-5 ; L.5121-14-3 ; L.5122-1 ; L.5122-6 ; L.5125-23 ; L.5125-25 ; L.5125-28 ; L.5311-1 to L.5311-3 and R.4126-1 to R.4126-54 ; R.4127-4 ; R.4127-8 ; R.4127-12 to R.4127-13 ; R.4127-19 ; R.4127-34 to R.4127-36 ; R.4127-59 ; R.4127-64 ; R.4127-69 to R.4127-70 ; R.4234-1 to R.4234-39 ; R.4235-2 ; R.4235-8 ; R.4235-20 ; R.4235-30 ; R.4235-48 ; R.4235-61 to R.4235-62 ; R.4235-64 ; R.4235-68 ; R.5121-21 ; R.5121-138 ; R.5121-148 to R.5121-149 ; R.5121-152 ; R.5121-162 ; R.5121-164 ; R.5122-8 to R.5122-10 ; R.5125-46 ; R.5132-29 to R.5132-30 ; R.5132-33 ; R.5132-35 to R.5132-36)
Code de l'énergie (Article L.131-1 to L.135-16).
Loi n°98-389 du 19 mai 1998 relative à la responsabilité du fait des produits défectueux.
Loi n°2005-781 of 13th of July 2005 de programme fixant les orientations de la politique énergétique (Article 14 to 17).
Arrêté du 6 mai 2008 en application de l'article R.5121-21 du Code de la Santé Publique.

American Law

Code of Federal Regulations (§21).
Food, Drug and Cosmetic Act of 1938.

Case Law

French Case Law

CE, Ass, 28 juin 1968, Société des établissements Février-Decoisy-Chamion et Société d'assurances mutuelles de la Seine et de la Seine-et-Oise, n°67677-67678

CC, décision n°86-217 DC du 18 septembre 1986
CC, décision n° 89-260 DC du 28 juillet 1989, loi relative à la transparence et à la sécurité du marché financier
CA, Toulouse, 22 février 2000, n°1999/01293
Cass. 1ere Civ., 22 novembre 2007, n°06-14174
Cass. 1ere Civ., 22 mai 2008, n°05-20317, n°06-10967, n°06-14952, n°06-18848 and n°05-10593
Cass. 1ere Civ., 9 juin 2009, n°08-11073
Cass. 1Ère Civ. 12 juin 2012 n°11-18327
Cass. 1Ère Civ. 12 juillet 2012 n°11-17510
Tribunal de Grande Instance de Nanterre, 2ème chambre, 22 Octobre 2015, n°12/07723

American Case Law

Reaves v Territory, 1903 OK 92, 74 P. 951
Ellis v. Ellison, 1921 OK 279, §3, 200 P. at 161
Love v Wolf 38 Cal Rptr. 183 (Cal Dist. Ct App 1964)
Sharpe v Pugh, 155 SE 2nd 108 (NC 1967)
Koury v Follo, 158 SE 2nd 548 (NC 1968)
Schenebeck v Sterling Drug Inc, 423 F 2nd 919 (8th Cir 1970)
Reyes v Wyeth Laboratories, 498 F. 2nd 1264, 1276 (5th Cir. 1974)
Buckner v Allergan Pharmaceutical Inc, Florida 5th District Court of Appeal, 498 F 2nd 1264, 1276 (5th Cir), 419 US 1096 (1974)
Dunkin v Syntex Laboratories Inc. 443 F. Supp. 121, 123 (CWD. Tenn. 1977)
Stone v Smith, Kline and French Laboratories, 447 So 2nd 1301 (Ala 1984)
Singleton v Airco Inc, 314 SE 2nd 680 (Ga Ct App 1984)
Kinney v Hutchinson, 449 So 2nd 696 (La Ct App 1984)
Serna v Roche Laboratories, 684 P 2nd 1187 (NM Ct App 1984)
Ross v Jacob, 684 P 2nd 1211 (Okla Ct App 1984)
Roien v. Burroughs Wellcome Co., 856 S.W.2d 607, 609 (Tex. App.- Waco 1993, writ denied).
District Court of Cleveland County, State of Oklahoma (Judge Thad Balkman), August 26th of 2019, Mike Hunter (Attorney General of Oklahoma) versus Purdue Pharma (et al.), Teva Pharmaceutical (et al.), Johnson and Johnson (et al.), Allergan (et al.), Watson Laboratories (et al.), Case n°CJ-2017-816
Settlement Agreement between Purdue Pharmaceuticals and 24 State Attorneys General, September 15th of 2019

Institutional Reports

« Press Release European Medicines Agency Recommends Withdrawal of Dextropropoxyphene-containing Medicines", *EMEA*, 25 of June 2009
Autorité de la Concurrence , *Enquête sectorielle sur le secteur pharmaceutique,* 2013
Commission européenne, *Enquête sectorielle sur le secteur pharmaceutique,* 2013
« Good Use of Pharmaceuticals: Medicines for Breakthrough Pain Due to Cancer », *Haute Autorité de Santé*, July 2014
"Chronic Pain, in France. Recommendations of the National Academy of Medicine for Better Care of Patients", *National Academy of Medicine's Report*, 2018
Monzon, E., "Etats des lieux de la consommation des antalgiques opioïdes et leurs usages problématiques", *Rapport de l'ANSM,* Février 2019
Bonnet, N., « Médicaments antalgiques opïodes : ce qu'il faut savoir ce qu'il faut faire »,

RESPADD and OFMA, 2018
Feuille de route 2019-2022 du ministère des solidarités et de la santé : prévenir et agir face aux surdoses d'opioïdes

Doctrine

Thompson, D., "The Drug Manufacturer's Duty to Warn – To Whom Does It Extend?, *Florida State University Law Review*, 1985, Article 6, Vol 13, Issue 1
Cadbury A., *Financial Aspects of Corporate Governance*, report issued by "The Committee on the Financial Aspects of Corporate Governance", 1992
Frison-Roche, M.-A., « Le Droit de la Régulation », 2001
Frison-Roche, M.-A., « Le couple Ex ante - Ex Post, justificatif d'un droit spécifique et propre de la régulation », 2006
Frison-Roche, M.-A., "Proposition pour une notion : l'opérateur crucial", *Recueil Dalloz*, n°27, 2006
Fasterling, B. et Duhamel, J.-Ch., « Le Comply or Explain : la transparence conformiste en droit des société » , *Revue Internationale de Droit International (RIDE)*, 2009, p.129-157.
Frison-Roche, M.-A., (dir.), *Concurrence, santé publique, innovation et médicament*, LGDJ, 2010, 480p.
Choi, H.W., Lee, J.H., *Principles and Practice of Pharmaceutical Medicine*, Blackwell Publishing, Third Edition, 2010, Chapter 55 "Pharmaceutical Product Liability"
"La responsabilité médicale en cas de dommage impliquant un produit de santé ou un dispositif médical", *Aredoc*, 2013
Frison-Roche, M.-A., « La gouvernance en question » , *Journal des Bâtonniers*, n°9 novembre-décembre-janvier 2010-2011, p. 12-13.
Boncori, A.-L., et Cadet, I. « Le comply or explain, un avatar de l'accountability », *Revue française de gestion*, vol. 237, no. 8, 2013, pp. 35-55.
De la Garanderie et al, « Comply or Explain : guide pratique de mise en oeuvre », *Institut français des administrateurs*, 2013
Manella, D., « Le Comply or Explain (enfin) détaillé : proposition de recommendation de l'UE », *Bulletin de Droit économique*, 2014
Supiot A., Delmas-Marty M. (dir.), *Prendre la responsabilité au sérieux,* Presses universitaires de France, 2015, 432p.
Frison-Roche, M.A., "Compliance Law", 2016
Frison-Roche, M.-A., « Les régulateur et superviseurs bancaires et financiers », Leçon n°6, Droit de la Régulation bancaire et financière, Sciences Po, 2016
Frison-Roche, M.-A., « Régulateur », *Dictionnaire bilingue du Droit de la Régulation et de la Compliance*, 2016
Frison-Roche M.A., « From Regulation Law to Compliance Law », 2017
Frison-Roche, M.-A., « Il faut construire un dispositif européen de compliance, voilà l'avenir ! », in Actualité/Entretien, *Petites Affiches*, propos recueillis par Olivia Dufour, n° 244, 7 déc. 2017, pp. 4-6
Frison-Roche, M.-A. (dir.), *Régulation, Supervision, Compliance,* Dalloz, 2017
Frison-Roche, M.-A., « Le Droit de la Compliance au-delà du Droit de la Régulation », 2018
Borga, N., Marin, J.-Cl., Roda, J.-Ch. (dir.), *Compliance : l'entreprise, le régulateur et le juge,* 2018
Cabrillac, R., *Droit des obligations*, Dalloz, 2018, Third Edition
Frison-Roche M.A., « Dessiner les cercles du Droit de la Compliance » in *Études en l'honneur de Philippe Neau-Leduc. Le juriste dans la cité*, coll. « Les mélanges »,

LGDJ-Lextenso, 2018, pp. 483-496
Frison-Roche, M-A, « Compliance et Incitations : un couple à propulser » in Faculté de droit de l'Université Toulouse-Capitole et Journal of Regulation & Compliance, *Les incitations, outils de la Compliance*, 12 décembre 2019
Frison-Roche, M.-A., « Concevoir la Compliance comme une mécanique, devant être confiée à une machine : la bonne idée de General Electric. Vrimant la bonne voie ? », *The Journal of Regulation and Compliance (JoRC)*, 7 août 2019
Frison-Roche, M.-A., « Compliance et Incitations : un couple à propulser », in Faculté de droit de l'Université Toulouse-Capitole, et Journal of Regulation & Compliance (JoRc), *Les incitations, outils de la Compliance*, 12 décembre 2019,
Frison-Roche, M.-A., « La sanction comme incitation dans les techniques de compliance », in Faculté de droit de l'Université Toulouse-Capitole, Journal of Regulation & Compliance (JoRc), *Les incitations, outils de la Compliance*, 12 décembre 2019.
Frison-Roche, M.-A., *L'apport du Droit de la Compliance dans la Gouvernance d'Internet* (The contribution of Compliance Law to the Internet Governance), Report asked by the French Government, published on 15th July 2019, 139 pages
Frison-Roche, M.-A.(dir.), *Pour une Europe de la Compliance,* Dalloz, 2019
Samantha Dorn and Staff Writer, "Should Pharmaceutical Companies Be Liable for Deaths Caused by their Drugs?", *Juris Magazine,* 2019
Frison-Roche, M.-A., « La mesure de l'efficacité et de l'effectivité des Outils de la Compliance », Présentation générale, Conference du 5 mars 2020 organisée par le Journal of Regulation and Compliance in Université Panthéon-Assas, Paris

Medical publications

Porter J. and Jick H., « Addiction rare in patients treated with narcotics », *N Engl J Med*, 1980, 302:123
Perry S. and Heidrich G., « Management of pain during debridement : a survey of US burn unites », Pain, 1982, 13, 267-280
Hale M.E., Fleischmann R., Salzman R., et al., « Efficacy and Safety of Controlled Release Versus Immediate Released Oxycodone: Randomized, Double-Blind Evaluation in Chronic Back Pain", *Clin J. Pain*, 1999, 15, pp.179-183
Thurel, C., « « Du mauvais usage » des opioïdes forts dans le traitement des douleurs chroniques bénignes (non cancéreuses) », *Douleurs*, 2007, Vol 8, n°2, pp.101-107
Lohman, D., « S'il vous plait ne nous laissez pas souffrir… L'accès au traitement de la douleur est un droit humain », *Human Right Watch Report*, 2009
Roussin, Doazan d'Ouince, Géniaux, Halberer, « Evaluation of Abuse and Dependence in Addiction Monitoring Systems: Tramadol as an Example", *Thérapie*, 2015, 70(2), pp.213-221
Muller C., Chantrel F., Bazin-Kara D, Ott J., Krummel T., Imhoff O., Richter S., Hannedouche T., Dimitriov Y., « Influence de la lecture des notices des médicaments sur l'adhésion thérapeutique », *Néphrologie & Thérapeutique*, Volume 11, Issue 5, September 2015, Page 401
Muszczak, A., « Enquête sur les pratiques de prescription d'opiacés des médecins généralistes,dans le traitement des douleurs chroniques non cancéreuses: à propos d'une étude de faisabilité dans le Grand-Est. » *Sciences pharmaceutiques,* 2015
Mahut, S., « Comment les patients utilisent-ils la notice des médicaments ? Enquête qualitative compréhensive réalisée auprès des patients des Yvelines et du Val d'Oise », Thèse pour le diplôme d'Etat de docteur en médecine, soutenue en 2016, à l'université de Versailles Saint-Quentin en Yvelines

Barreau, M., Chenaf, C., Kabore, J.L, Bertin, C., Delorme, J., Riquelme-Arbre, M., Eschalier, A., Ardid, D., Delage, N., Authier, N., Pharmacoépidémiologie de l'usage des antalgiques opioïdes en France, Trends in opioid analgesic use, *Lettre du pharmacologue,* 2017*,* Vol. 31

Chenaf, C., Kabore, J.-L., Delorme, J., Pereira, B., Mulliez, A., Zenut, M., Delage, N., Ardid, D., Eschalier, A., Authier N., Prescription opioid analgesic use in France: Trends and impact on morbidity–mortality, *European Journal of Pain,* 2018

Ponté, Lepelley, Boucherie, Mallaret, Lapeyre-Mestre, Pradel, Micallef, « Doctor Shopping of Opioid Analgesic Relative to Benzodiazepines: A Pharmacoepidemiologic Study Among 11,7 million Inhabitants in the French Countries", *Drug and Alcohol Dependence*, 2018, 187, pp. 88-94

Chenaf, C., Kabore, J.-L., Delorme, J., Pereira, B., Mulliez, A., Zenut, M., Delage, N., Ardid, D., Eschalier, A., Authier N., Prescription opioid analgesic use in France: Trends and impact on morbidity–mortality, *European Journal of Pain,* 2018

Chenaf et al., "Prescription des antalgiques opioïdes en France entre 2004 et 2017 : évolution et impact en termes de morbi-mortalité » , *European Journal of Pain,* 2018, Vol 23, Issue 1

Other academic publications

Rousseau, J.-J, *Du Contrat social,* Flammarion, 2011 (original edition: 1762)

Weber, M., *Le savant et le politique*, La Découverte/poche, 2003 (original edition: 1919)

Mancur Olson, *The Logic of Collective Action: Public Goods and the Theory of Groups*, Cambridge, MA: Harvard University Press, 1965

Galbraith J.K., *The Great Crash, 1929*, Pelican, 1961

Stigler, G., « The Theory of Economic Regulation", *Bell Journal of Economics and Management Science*, 1971, Vol 2, Spring, pp.3-21

Stigler, G., *The Citizen and the State : Essays on Regulation*, University of Chicago Press, 1975

Montlibert, C., « Chômage et licenciements. La crise de la Lorraine sidérurgique : Longwy, 1978-1980. » In: *Annales. Économies, Sociétés, Civilisations*. 39e année, N. 5, 1984. pp. 1044-1068

Minsky H., *Stabilizing an Unstable Economy*, Yale University Press, 1986

Esping-Andersen, G., *The Three Worlds of Welfare Capitalism*. Cambridge: Polity Press & Princeton: Princeton University Press, 1990.

Ross, S., and Mitnick, B., "Origin of the Theory of Agency", University of Pittsburgh, 2006

Combe, E., « I. L'essor des politiques de concurrence », Emmanuel Combe éd., *La politique de la concurrence.* La Découverte, 2008, pp. 5-13.

Van Zee, "The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy", *American Journal of Public Health*, 2009, Vol 99, No. 2

Lebeau Leibovici, B., « Drogues : sortir de la prohibition ? », in *Chimères*, 2010 n°74, pp. 113-121

"Le médicament: les dessous d'une marchandise", *Revue Savoir/Agir,* 2010-2011, n°16, p. 9-59

Roth, A. E., *The theory of stable allocations and the practice of market design*, 2012

Greener, I., *Public Management*, Hound mills: Palgrave Macmillan, 2013

King, Faser, Boikos, Richardson, Harper, "Determinants of Increased Opioid Related Mortality in the United-States and Canada, 1990-2013. A Systematic Review", *American Journal of public Health*, 2014, Vol 104, No. 8

Fournier, P., Lomba, C. & Muller, S. *Les travailleurs du médicament: L'industrie pharmaceutique sous observation.* Toulouse, France, 2014

Supiot, A., « Gouverner par les nombres » , *Cours au Collège de France, 2012-2014*, Institut d'études avancées de Nantes, 2015, 520p.
Riggs, Widmer, Planck, "The impact of pharmaceutical industry salesperson regulations, guidance statements, and laws on their sales behaviours: A taxonomy with managerial insights", *International Journal of Pharmaceutical and Healthcare Marketing*, 2015, Vol. 10 No. 2, pp. 161-191
Kolodny, Courtwright, Hwang et al., "The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction", *Annual Review of Public Health*, 2015
Deaton, A., *La Grande Évasion : Santé, richesse et origine des inégalités,* PUF, 2016
Abecassis, P. & Coutinet, N., *Économie du médicament.* Paris: La Découverte. 2018
Obradovic, I., " La crise des opioïdes aux Etats-Unis: d'un abus de prescriptions à une épidémie aiguë", *Potomac Papers*, 2018, n°35, IFRI

Companies' publications

''OxyContin Marketing Plan, 1996-2001.'' Purdue Pharma, Stamford, CN
''OxyContin Marketing Plan, 2002.'' Purdue Pharma, Stamford, CN, 2002
''OxyContin: balancing risks and benefits,'' in Hearing of the Committee on Health, Education, Labor, and Pensions, United States Senate, February 12, 2002, p 87 (testimony of Paul Goldenheim, Purdue Pharma).
Prescription Drugs: OxyContin Abuse and Diversion and Efforts to Address the Problem. Washington, DC: General Accounting Office; December 2003. Publication GAO-04-110
Stolberg SG, Gerth J. High-tech stealth being used to sway doctor prescriptions
Exhibit 99.1 "Johnson & Johnson To Appeal Flawed Opioid Judgement in Oklahoma", New Brunswick, NJ, August 26, 2019

News

Drum, K., « The AMA represents only one-sixth of all doctors » , *Mother Jones*, 27th of December 2016
Kadri, Y., « Olivier Dupuy (Nasdaq) : « La compliance exige une traçabilité détaillée des actions pour être prêt en cas de contrôle » », in *Décideurs Magazine*, 8 of November 2018
Authier, N., "Antidouleurs opioïdes : vers une crise sanitaire en France ?", in *The Conversation,* 13 of September 2018
Authier, N., interviewed in Florian Bardou, "Médicaments : faut-il craindre une crise des opioïdes en France ?" in *Libération*, 23 of February 2019

Fiction

Jenner Furst and Julia Willoughby Nason, *The Pharmacist*, available on Netflix since February 5th 2020