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Together for the greater goods: legitimising social innovation in the pharmaceutical field

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Social innovation initiatives in the pharmaceutical field seek alternative, collaborative ways to address problems with availability and affordability of medicines. However, these experimental initiatives require legitimacy. Formulating goals is a way of creating and contesting legitimacy, also for social innovation initiatives, yet has not been studied in this context. Based on document analysis (policy reports, news articles and websites) and semi-structured interviews, we investigate what form and role goal formulations take in constructing and contesting the legitimacy of two Dutch social innovation initiatives: one novel coverage arrangement for a rare disease drug and one new manufacturing process for a personalised cancer treatment. We find that actors formulate goals to *manage consensus* with powerful, independent governance bodies and with those who reserve their judgement concerning the initiative. They also *manage differences*, highlighting role differentiation within collaborations and emphasising contrasts with outsiders. These findings show the importance of professional identities and the experimental nature of social innovation initiatives. We conclude that formulating goals is used to probe for and attempt to ensure the longevity of social innovation. Working together in diverse partnerships for 'the greater goods' (plural) is thus essential for organising durable social innovation in the European pharmaceutical field .

Keywords: social innovation; governance; pharmaceuticals; health care; legitimacy; goal formulation

Introduction

Acquiring market approval for pharmaceuticals addressing rare diseases is difficult. Standards for clinical trials are challenging to meet due to low patient numbers (Heemstra et al. 2008; Trouiller et al. 2002). The 1999 EU Directive on Orphan Medicinal Products and the 1983 Orphan Drugs Act (USA) attempted to address this problem by incentivising pharmaceutical innovation. Offered incentives include exclusive marketing rights and scientific advice (Boon and Moors 2008; Mikami 2019). These policy instruments have been considered moderately successful given the minor increase in the development of

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orphan drugs over the last decades (Brabers et al. 2011; Braun et al. 2010; Luzzatto et al. 2018). Still, there are many rare disease patients for whom no treatments are available (Schieppati et al. 2008; Tambuyzer et al. 2020). Developed drugs are in turn often prohibitively priced, threatening their affordability and health care systems' sustainability across Europe and worldwide (Côté and Keating 2012; Faulkner 2012; Gombocz and Vogler 2020; Luzzatto et al. 2018; Mestre-Ferrandiz et al. 2019; Moors, Cohen, and Schellekens 2014; Wadmann, Hauge, and Emdal Navne 2023).

One way to address significant societal problems like these is through social innovation (Cajaiba-Santana 2014; Howaldt, Domanski, and Kaletka 2016; Howaldt, Kaletka, and Schröder 2021; Mumford 2002; van der Have and Rubalcaba 2016). Increasingly an EU policy priority (Sabato, Vanhercke, and Verschraegen 2017), social innovation tend to feature alternative actor constellations, such as public-private partnerships and user-led, bottom-up collaborations. In mainstream pharmaceutical policy circles, 'social innovation discourse' is, so far, absent (Galego et al. 2022). Yet, we see increasing evidence of *social pharmaceutical innovations* (SPINs) (Douglas et al. 2022), which may involve citizens, civil society and patient organisations, clinicians, private companies, governments, or other public institutions (Coppens et al. 2020; de Freitas et al. 2017; Farmer et al. 2018; Jensen and Fersch 2019; van Niekerk et al. 2023; van Niekerk, Manderson, and Balabanova 2021). Concrete examples include digital platforms through which patients may gain access to experimental drugs (Bunnik, Aarts, and van de Vathorst 2018) and pharmacist compounding of (personalised) medicines (Schellekens et al. 2017).

For three reasons, social innovations tend to face a legitimacy penalty (Zuckerman 1999). First, social innovations comprise actor partnerships that are novel and thus do not fall inside recognised actor categories with related interests and remits. Second, since these collaborations often cover multiple institutional domains (such as science, policy, and law), and are likely to spring up where these domains overlap, leave gaps, or change, it is harder for other actors to recognise them. Third, many may perceive these initiatives as disruptive, so other actors may not *want* to recognise them. For these reasons, actors involved in social innovation actively construct legitimacy (Bitektine and Haack 2014; Fougère, Segercrantz, and Seeck 2017; Geels and Verhees 2011; Johnson, Dowd, and Ridgeway 2006; Verleye et al. 2019; Weber and Rohracher 2012).

Bridging sociological literature on social innovation and organisational literature on legitimacy construction and drawing on decades of detailed empirical study of the nuts and bolts of research work aimed at practical innovation as well as theoretical reflection on the sociological and epistemological foundations of science and technology studies, we examine the central role goal articulation plays in constructing legitimacy for social innovations. Scholarship is divided over the role goals play in social innovation. Some see social or societal goal formulations as inherent to social innovation (Cajaiba-Santana 2014; Howaldt, Domanski, and Kaletka 2016; Howaldt, Kaletka, and Schröder 2021; Mumford 2002; Solis-Navarrete, Bucio-Mendoza, and Paneque-Gálvez 2021; van der Have and Rubalcaba 2016), whereas others define social innovation as ideas, objects or activities that change social relations and involve new ways of doing, thinking or organising (Avelino et al. 2019; Pel et al. 2020; Wittmayer et al. 2019). We foreground formulating goals as an essential activity of social innovators to advance the innovation's legitimacy. We will define constructing legitimacy as the process of establishing a particular initiative as consonant with what actors assume is a belief or value considered valid in a particular situation.

So far, formulating goals has not been analysed explicitly in relation to social innovation legitimacy (Verleye et al. 2019; Wittmayer et al. 2019). So, the question is, what

is the form and role of goal formulations in constructing and contesting the legitimacy of SPIN initiatives? By exploring two Dutch social pharmaceutical innovation (SPIN) cases, we add Europe-based insight to the emerging literature on social innovation in health care, currently largely studied in low- and middle-income settings (Douglas et al. 2022; van Niekerk, Manderson, and Balabanova 2021; Farmer et al. 2018; van Niekerk et al. 2023), contribute ethnographic understanding on the interplay between governance and social innovation (Campomori and Casula 2022; Galego et al. 2022), and shed further light on the activities of clinicians based at academic hospitals (Gittelman 2016; Thune and Mina 2016), specifically, their collaborations with others engaged in social innovation.

The role of explicated goals in legitimising social innovation

Social innovation has been celebrated over the past decades as an alternative to technological innovation with great potential for societal change. Van der Have and Rubalcaba (van der Have and Rubalcaba 2016) reviewed scholarly literature on social innovation and identified one strand that broadly conceptualises social innovation as novel approaches to solving social challenges. Some authors define social innovations as explicitly oriented toward a social goal, as meeting social needs or creating social value (Cajaiba-Santana 2014; European Commission 2014; Howaldt, Domanski, and Kaletka 2016; Howaldt, Kaletka, and Schröder 2021; Moulaert et al. 2005; Mumford 2002; Verleye et al. 2019; Ziegler 2017). Others describe social innovation as novel ways of organising social interactions, deliberately highlighting that social innovation 'is not always necessarily intentional or oriented towards social goals' (Avelino et al. 2019, 179), also (Haxeltine et al. 2015; Pel et al. 2020; Wittmayer et al. 2019). Either way, social innovations appear to be in the business of formulating goals and most scholars consider the question of goals in light of whether they are reached or not (Cajaiba-Santana 2014; Howaldt, Domanski, and Kaletka 2016; Howaldt, Kaletka, and Schröder 2021; Johnson, Dowd, and Ridgeway 2006; Verleye et al. 2019; Wittmayer et al. 2019). However, goal formulations, though future-oriented in nature, also affect social innovations in the here and now, once statements about the future are articulated and circulated, they become performative and legitimise current work on these social innovations (Borup et al. 2006; Fougère, Segercrantz, and Seeck 2017; Garud, Schildt, and Lant 2014; Geels and Verhees 2011; Konrad 2006; Molecke and Pinkse 2020; Stryker 1994; Verleye et al. 2019; Weber and Rohracher 2012).

Let us start our overview of relevant work with Suchman's well-known definition of legitimacy:

> a generalised perception or assumption that the actions of an entity are desirable, proper, or appropriate within some socially constructed system of norms, values, beliefs and definitions. (Suchman 1995)

Legitimising is a diverse, stratified activity: it may be implicit or explicit, varies across levels and publics, and may take the shape of different modalities or regimes (Suddaby, Bitektine, and Haack 2017). The legitimacy of social innovations is often derived from 'local' or primary goals (Verleye et al. 2019). Johnson, Dowd and Ridgeway (Johnson, Dowd, and Ridgeway 2006) specified that most innovations first address a 'local' need or goal that closely refers to the context for which the social innovation was developed initially, where its meaning and implications are shared among involved local actors

(Pinch and Bijker 1984). For health care, such goals may include making available a drug for a particular patient or patient group treated at a specific hospital. To gain legitimacy beyond the original setting, however, actors must give an explicit account or justification of how their innovation aligns with one or more *societal* goals (Boltanski and Thévenot 2006; Johnson, Dowd, and Ridgeway 2006): a 'translation', to draw other actors in and potentially align (Callon 1984; Latour 2007; Law and Hassard 1999). Societal goals mobilised might include, for instance, 'disruption', 'pioneering' (Drori and Honig 2013; Wittmayer et al. 2019), the sustainability of a particular health care system or the availability and affordability of medicinal products in general.

Broader societal goals contribute to the construction of legitimacy through the beliefs or values that align the work done with such goals, which is also captured by Suchman's definition of legitimacy given above (Oldenhof, Postma, and Putters 2014; van der Have and Rubalcaba 2016). In Boltanski and Thévenot's seminal work 'On Justification' (Boltanski and Thévenot 2006), these beliefs or values are part of repertoires, indicating shared, though frequently contested, commitments. Likewise, in management literature, many argue that beliefs and values must be shared between actors constructing legitimacy together to be effective (Aldrich and Fiol 1994; DiMaggio and Powell 1983; Drori and Honig 2013; Geels and Verhees 2011; Johnson, Dowd, and Ridgeway 2006; Meyer and Rowan 1977; Suchman 1995; Suddaby, Bitektine, and Haack 2017). Much thinking here considers these legitimating beliefs and values as largely exogenous, static elements: 'out there' sources to draw from to increase legitimacy. This is problematic for two reasons.

First, such beliefs and values are not exogenous to action. When actors construct legitimacy by formulating societal goals their innovation may contribute to, they *presume* the underpinning values and beliefs are held by other actors (Gray, Purdy, and Ansari 2015; Johnson, Dowd, and Ridgeway 2006). However, as Weber (Weber 1978) highlighted, values and beliefs may not even be held by the individuals appealing to them – the individuals constructing the legitimacy simply assume they are held widely (Konrad 2006; Stryker 1994). These assumptions about consensus might turn out to be inaccurate and lead to implicit or outright contestation about legitimacy: controversies have for good reason long served as fruitful research sites for science and technology studies scholars from theoretically diverse denominations such as the Strong Program, Social Construction of Technology (SCOT) and Actor-Network Theory (ANT) (Barnes and Bloor 1982; Barnes and Shapin 1979; Bloor 1991; Callon 1984; Collins 1983; Latour 2007; Law and Hassard 1999; Rip 1986).

Most of that work shows that in such contexts, values and beliefs are setting-dependent: only supported and meaningful in a particular time and place (Arts, Buijs, and Verschoor 2018; Connelly, Richardson, and Miles 2006). Bitektine and Haack (Bitektine and Haack 2014) provide another argument for treating beliefs and values as endogenous. They argue that constructing legitimacy by appealing to beliefs and values may not only draw from these beliefs and values but also recursively influence them. Notably, we know little about how this process takes place. One possible reason is that these beliefs and values are not often explicated, they remain 'taken for granted'. As Boltanski and Thévenot (Boltanski and Thévenot 2006) specify, people tend to come to a shared understanding 'without trying to clarify the principle upon which their agreement is founded' *even* when their conceptualisations of the common good clash (Oldenhof, Postma, and Putters 2014). We accordingly define constructing legitimacy as the process of establishing a particular initiative as consonant with what actors assume is a belief or value considered valid in a particular situation. This formulation allows contestation and disagreement on societal goals in legitimacy construction processes.

Second, these beliefs and values are not static – interpretive flexibility remains, i.e. other readings are still possible (Collins 1983). Bitektine and Haack (Bitektine and Haack 2014) argued that this co-constitutive relationship between legitimacy and asserted valid beliefs had not gained much attention because beliefs do not tend to change in times of stability. However, the co-constitutive relationship should become more visible in times of institutional change. After all, legitimacy construction is of particular importance when rules of the game are changing, for instance, when different institutional fields collide or when one invades the other, as Stryker (Stryker 1994) described for scientific rationalities and procedures invading legal practice (Zelditch 2001). As social innovations often span different institutional fields (Anheier, Krlev, and Mildenberger 2019), the intractability of beliefs and values is by no means given.

Summarising, formulated goals are an essential dimension of legitimacy construction as goals, particularly societal goals, are underpinned by beliefs and values that actors presume other actors share. Moreover, for social innovation, beliefs and values are potentially especially situation-dependent because social innovations tend to surface in times of institutional change or the interplay between institutional fields. For this reason, we look at distinct situations where we examine how actors formulate goals to construct and contest legitimacy of social innovations.

Materials and methods

The data collection and analysis were part of the 'Social Pharmaceutical Innovation for Unmet Medical Needs' (SPIN) project, which investigated fourteen distinct SPIN cases in Brazil, Canada, France, and the Netherlands, funded by the Trans-Atlantic Platform for the Social Sciences and Humanities' Social Innovation Call. For this paper, we examined how social pharmaceutical innovations (SPINs) are constructed and contested as legitimate, specifically through the formulation of goals.

To gain greater insight into patterns of goal formulation, we employed a comparative case studies approach (Creswell and Poth 2017; Ragin 2004). This approach was well-adapted to gaining insight into the construction and patterning of legitimacy through the *in situ*, verbalised use of arguments in the process (Lamont and Thévenot 2000; Lee, Spanjol, and Sun 2019). Specifically, we use interviews to reconstruct a timeline of instances of critical legitimacy construction and contestation and of actors formulating their goals (Arts, Buijs, and Verschoor 2018; Lamont 2012; Lamont and Thévenot 2000; Oldenhof, Postma, and Putters 2014).

Regarding our case selection (Table 1), we chose to study SPIN initiatives that concerned new forms of organising pharmaceutical innovation to advance the availability and affordability of medicines in the Netherlands. Social innovations generally feature novel forms of actor constellations (see Background), and we selected cases with a diverse set of involved actors, where clinicians engaged with other medical professionals, patients and their representatives, pharmaceutical companies, and policy actors. Selecting cases involving partnerships between diverse actors was essential because we are interested in legitimacy construction and contestation amongst actors instead of within collaborations (Wittmayer et al. 2019) or institutionally similar organisations (Verleye et al. 2019). As our methodological gaze was drawn to particular situations, i.e. moments in time and space, where actors actively co-construct or contest legitimacy together, we expected that choosing cases with a great diversity of involved actors would put the situational dependency of legitimacy construction into sharp relief. In other words, it would show the setting-specific nature of legitimacy construction and how this works out in practice.

Table 1. Case descriptions.

Case name	Case description
Case 1: Novel reimbursement route for eculizumab	The breakthrough medicine eculizumab (Soliris®) is currently licenced for two rare diseases. After the responsible health care authority, *Zorginstituut Nederland* (ZIN), issued negative reimbursement advice for the first indication Paroxysmal Nocturnal Hemoglobinuria (PNH), clinicians at the Radboud University Nijmegen drafted a research protocol for the second indication, Atypical Hemolytic Uremic Syndrome (aHUS), which aimed to establish whether a 'restrictive treatment regimen' would be feasible (giving patients less medicine, resulting in lower spending). This resulted in ZIN issuing positive reimbursement advice for aHUS patients, as long as the eculizumab was provided under the CUREiHUS research protocol. Afterwards, the protocol was repeatedly called exemplary: it was the 'first ever' orphan drug arrangement and granted the first prestigious Dutch 'Pearl' prize for projects with particularly relevant results, excellent collaboration, or extra care for diversity, patients, or innovation.
Case 2: Hospital-based manufacturing of CAR T cell therapy	Chimeric Antigen Receptor (CAR) T cell therapy is a personalised treatment for a rare, aggressive cancer, whereby immune cells naturally present in the body are 'harvested', modified, and given to the patient, where these modified cells recognise and attack the cancer cells. In May 2020, the Dutch Minister for Health admitted Yescarta® or axi-cel, a CAR T cell therapy, to the benefits package after successful price negotiations. Researchers at the University Medical Center Groningen (UMCG), University of Groningen, sought funding to investigate the comparison of 'in house' generated CAR T cells with CAR T cells produced by the pharmaceutical company. They received a 30 million euro 'Potentially Promising Care' subsidy, and the six-year project started on 1 December 2020.

Although varying on the kind of actors involved, both cases share an essential role for clinicians based at academic hospitals and for the Dutch National Health Care Institute, (*Zorginstituut Nederland*, in this text: ZIN). The latter is an arm's length body tasked with advising the Minister of Health on which treatments should be included in the basic benefits package and thus covered by Dutch collective health insurance. In both cases, pharmaceutical companies were not directly involved.

We held semi-structured interviews (Holstein and Gubrium 2016; King, Horrocks, and Brooks 2018) with clinicians ($n = 3$), patient representatives ($n = 6$), policy makers ($n = 4$), pharmaceutical company employees and representatives ($n = 6$) (see Table 2). All interviewees invited for the interviews gave written consent in advance. We audio-recorded their oral consent to be interviewed and audio-recorded, and their understanding that we would gather their answers as data for academic purposes. The interviewees confirmed that they had been given the opportunity to ask questions before the recording started and had been informed concerning their rights in withdrawing their consent. They have also been given

Table 2. Interviews.

Interviewees	Case 1: Eculizumab	Case 2: CAR T cell therapy
Clinicians	$n = 2$	$n = 1$
Patient representatives	$n = 3$	$n = 2$
Other patient representatives	$n = 1$ across both cases	
ZIN employees	$n = 2$	Contacted three interviewees, all declined to be interviewed (citing time constraints, referring to the 'Potentially Promising Care' subsidy website instead)
Other policy makers	$n = 2$ across both cases	
Pharmaceutical company employees	Contacted three interviewees, all declined to be interviewed (not commenting on individual cases)	$n = 3$
Pharmaceutical representatives	$n = 2$ across both cases	

the opportunity to read the report(s) afterwards. We also analysed relevant policy documents ($n = 11$), news articles ($n = 12$), and various websites ($n = 2$) (see Appendix A) for triangulation purposes.

Our data analysis comprised three steps. We first constructed the timelines for each case (extended case descriptions below) based on the timelines the interviewees provided. We asked the interviewees how the initiative came about and noted which actors and moments the interviewees considered important in the process. For instance, all interviewees highlighted the appraisal committee meeting for the eculizumab case as a critical moment in the development of the SPIN initiative of case 1, the eculizumab case, as was the granting of the subsidy for case 2, the CAR T cell therapy case. We wrote up the resulting 'summary' timelines in a narrative form. Second, we looked at how actors explicated the SPIN initiative's goals across these timelines. To do so, we asked about the SPIN's primary goal and any societal goals the initiative might contribute to. In our dataset, we inductively coded goal formulations and related them, where we were able, to specific situations or moments of legitimacy construction or contestation noted as crucial moments in the timelines by the interviewees. Examples of phrases coded as goals include: 'improving care but also restraining costs'; 'gaining knowledge'; 'time gains'; and 'keeping this medicine available'. Third, we inductively, iteratively, and comparatively analysed these coded goals to determine different ways of formulating goals to construct and contest SPIN legitimacy across these cases, outlined below. The research process was in line with constructivist grounded theory in that the data concern issues of importance to participants, the data are considered co-constructed with the researcher, and the analysis and theorising were kept purposely close to participants' experiences (Charmaz 2000; Mills, Bonner, and Francis 2006).

Results

Let us zoom in on goals formulated in the construction and contestation of legitimacy of the two SPIN initiatives: case 1, the eculizumab case (featuring the CUREiHUS research protocol) and case 2, the CAR T cell therapy case. We start with the timelines of both cases.

Timeline case 1: Eculizumab for aHUS patients

Eculizumab (Soliris®), an orphan drug, is currently licenced for two related indications, namely Atypical Hemolytic Uremic Syndrome (aHUS) and Paroxysmal Nocturnal Hemoglobinuria (PNH). Both are rare diseases where patients suffer from a dysregulated complement system, an essential pathway in the immune system. Eculizumab is considered a breakthrough medicine for both indications but, at an estimated 300,000–500,000 euro per patient per year, a costly one.

Early spring 2016 the Dutch National Health Care Institute (*Zorginstituut Nederland*, in this text: ZIN) issued a negative reimbursement advice concerning eculizumab for PNH patients specifically, offering its high price as the main argument against reimbursement (Rösken, 2016, news article; Zorginstituut Nederland, 2016a, policy document). According to interviewees, this advice 'awakened' some aHUS patients to take action (patient representative 1, group interview). At that time, however, other patients and clinicians were not convinced of the necessity for action. Patients, for instance, often thought they would 'get the medicine from their doctor anyway' (patient representative 1, group interview).

Several aHUS patients then contacted clinicians at the Radboud University Nijmegen (patient representative 3, interview). These clinicians drafted a new research protocol named CUREiHUS (http://cureihus.nl/) starting from the idea based on earlier clinical experiences indicating that lifelong medication might not be necessary for aHUS patients. The idea behind the protocol and the related research was to establish whether a 'restrictive treatment regimen' would be feasible for Dutch aHUS patients. Such a regimen would entail a clear definition of criteria for starting and stopping treatment, and as such, would mean giving less medicine to patients, leading to a cost reduction, a more favourable incremental cost-effectiveness ratio (ICER), and eventually, a positive reimbursement advice from ZIN. The funding to set up the CUREiHUS research protocol came from VGZ Zorgverzekeraar (a health care insurance company) and ZonMw (the Netherlands Organisation for Health Research and Development) (Berkhout, 2017b, news article). The clinicians had received funding for all research activities except for the procurement of the medicinal product.

The reimbursement decision procedure for using eculizumab for aHUS patients as part of the research protocol started with a 'scoping session', an exploratory session and formal part of ZIN procedures, involving all relevant actors. Involved interviewees repeatedly stated that during the scoping session, participants articulated that there was a great perceived necessity to convince ZIN to accept the CUREiHUS research protocol as worthy of positive reimbursement advice, as they thought the medicinal product would otherwise not be reimbursed for the aHUS patients (patient representative 1 and clinician 2, group interviews). The scoping session was followed by the assessment phase: the formal assessment of the scientific evidence, which takes place at ZIN, with reports sent out to involved actors for consultation. The next step was the public meeting of the appraisal committee, consisting of external experts not employed by ZIN. They would perform the 'societal weighing' of the scientific evidence and other input. This meeting, considered an essential point on the timeline by all, included contributions from one patient and two patient representatives and deliberation by the committee. The appraisal committee members considered the CUREiHUS initiative commendable: something that ought to be 'made possible' through a positive decision to reimburse eculizumab, as long as it was provided under the CUREiHUS research protocol (Zorginstituut Nederland, 2016b) (Kleinhout-Vliek 2020; Kleinhout-Vliek, de Bont, and Boer 2021).

ZIN thus decided to advise the Minister for Health positively concerning the reimbursement of eculizumab for patients enrolled in the CUREiHUS research, which was covered by prominent newspapers (Berkhout 2017a, 2017b, news article; De Visser, 2019, news article). Several actors reviewed the research protocol favourably and judged it to be exemplary. In response to ZIN's advice, the Minister of Health mentioned the CUREiHUS protocol in a public letter to the House of Representatives (Schippers, 2016, 3, policy document). The study was cited as the 'first ever' orphan drug arrangement, i.e. a specific arrangement concerning reimbursement pending further data collection. It was also the first time an 'indication committee' of clinicians was set up to review patients' eligibility for joining the research. Finally, it was the first use of start and stop criteria in the Netherlands (Clinician 1 and 2, group interview; ZIN employee 1, interview; policy maker 1, interview; Rösken, 2018, news article; Van der Geest, 2021, news article). Moreover, ZonMw granted the CUREiHUS research protocol the first ever prestigious 'Pearl' prize in 2018 (see case description, ZonMw, 2018, news article; ZonMw, 2018, 2021, policy documents). An international patient conference in 2018 featured the Dutch protocol of the CUREiHUS study (for a summary, see aHUS alliance website, 2018) and was instrumental in convincing patients and clinicians in other countries of this 'Dutch approach'. Before the study ended, doctors beyond the project had already started to use start and stop criteria or re-examine the dosage of eculizumab for aHUS and other medicines (clinician 2, group interview; interviews with ZIN employee 1, patient representatives 3 and 4). At the time of writing, the 5-year study had just been reported as finished. Through better patient selection and applying start and stop criteria the study has led to more efficient prescribing behaviour, with final savings of around 50 million euros in total (Nieber, 2022, news article).

The pharmaceutical company that marketed the medicinal product remained less convinced. A clinician reflected that the pharmaceutical company conducted itself 'arrogantly' during the reimbursement decision process, refusing to contribute (Clinician 2, group interview). When asked, company employees declined to be interviewed, stating the company 'has no involvement with [the CUREiHUS] study, and we cannot comment on independent studies' (personal communication via email, dated 15 February 2021).

Timeline case 2: CAR T cell therapy for lymph node cancer patients

Chimeric Antigen Receptor (CAR) T cell therapy is a personalised treatment method that is, in this case, applied to patients with a rare, aggressive form of non-Hodgkin lymph node cancer (specifically, diffuse large B-cell lymphoma, DLBCL) when other treatments are unsuccessful (Zorginstituut Nederland, 2020b, policy document). The therapy entails 'harvesting' T lymphocytes – a type of immune cell naturally present in the body – from patients, modifying these cells so that they are able to recognise cancer cells, and placing them back in the patient. These CAR T cells then target and destroy the patient's tumours.

In May 2020, the Minister for Health admitted Yescarta® or axi-cel, a CAR T cell therapy, to the Dutch basic benefits package, and thus the collective health insurance, after successful price negotiations based on ZIN advice. The initial reimbursement advice was negative unless the price would be significantly reduced. CAR T cells were until then produced by freezing the harvested cells and sending them to the United States for modification, followed by refreezing, another shipment, and defrosting in the Dutch hospital treating the patient. Researchers at the University Medical Center at the University of Groningen (UMCG), the Netherlands, sought funding to investigate the

comparison of 'in house' generated CAR T cells with CAR T cells produced by the pharmaceutical company. They worked together with partners including *HOVON* (association of medical specialists working on hemato-oncology for adults in the Netherlands), *Hematon* (the patient organisation for patients with blood- or lymph node cancer), *Zorgverzekeraars Nederland* (the umbrella organisation for Dutch health care insurers), and other medical centres. They received a 'Potentially Promising Care' subsidy from ZIN and ZonMw and the six-year project started on 1 December 2020. Dutch newspaper *de Volkskrant* featured an extensive overview of the subsidy granted to the UMCG and other medical centres, interviewed several involved actors, including one quoting that the project is 'unique', and a patient, Pamela Botter (37), previously treated with CAR T cell therapy. She says she is grateful to be given a chance 'to see my two children grow up' (De Visser, 2020, news article).

At the time of writing, the study is ongoing. Next to the actors mentioned above, several others were involved for quality safeguarding, such as the Dutch Medicines Evaluation Board (clinician 3, interview). Since the start of the six-year project certain events have taken place. First, in June 2020, Kite Pharma, part of Gilead Sciences, opened a new manufacturing facility for CAR T cell therapy in Hoofddorp, the Netherlands – currently one of the only ones in Europe. This was considered an important event as this would enable the manufacture of CAR T cells without flying them across the Atlantic: a significant time gain. Another critical point mentioned was the request for information concerning 'policies unregistered pharmaceuticals' between 1 January and 4 June 2021 under the Dutch Government Information Act (request anonymous as always), which showed that the subsidy was significantly contested by pharmaceutical industry representatives (Rijksoverheid, 2021). Like the CUREiHUS research protocol, several interviewees regarded the CAR T cell therapy study as exemplary, in this case an example of the potential of treatment researched and manufactured at an academic hospital (policy maker 1, interview).

In the remainder of this section, we will outline how actors directly involved in both SPIN initiatives and those indirectly involved use goals in legitimising construction or contestation. Inductively, we discern five distinct ways of goal formulation. First, there is *combining goals*, where the SPIN initiative is said to contribute to a combination of goals. Second, we see actors *balance goals*, specifying that the SPIN initiative may contribute to several goals but will not fully reach all. Third, goals can be actively *decoupled*, where actors consider one possible goal of the SPIN initiative more prominent or more feasible. Fourth, *suspending judgement on goals*, where actors wait to see whether the SPIN initiative may or may not contribute to the formulated goals, and fifth, *challenging goals*, or actively questioning whether the SPIN initiative will contribute to this goal.

Combining goals

Across both cases, involved actors formulated different goals to construct legitimacy for the SPIN in question. These goals were very often combined: the SPIN initiative was said to contribute equally to a number of goals. For the eculizumab case, the patient representatives and the clinicians directly involved see the CUREiHUS initiative's 'lower level' goal as getting aHUS patients continued access to eculizumab, but added various other goals. As one involved patient stated, it is about 'improving care but also (…) restraining costs' (Patient representative 1, group interview). When asked, improving care was specified to consider optimal deployment of the medicinal product in practice and avoid side effects for this patient group. One clinician held that the goal was gaining knowledge

about the risk of the disease flaring up again, the effectiveness of various dosages, etc., adding:

> [T]he higher goal is that you really should be able to get the medicine to anyone who needs it [and ensuring that] the one who doesn't need it, doesn't get it. This means that you already save thirty or thirty-five million with these fifty to sixty [aHUS] patients, which can be spent in a different way on better care for the elderly. That's what we've been aiming for. (Clinician 2, group interview)

This respondent thus added the goal of increasing quality of care for other patient groups, in this case elderly patients, as a possible goal of the SPIN initiative. Interviews with ZIN employees, documents, and websites highlighted the CUREiHUS protocol as exemplary due to 'the millions of euros in savings while keeping the quality of care the same' (Zorginstituut Nederland, 2021, 24, policy document). These interviewees thus combine goals like increasing safety, gaining knowledge, continued access to eculizumab, and cost saving.

For the CAR T cell therapy, one goal formulated by a patient representative and a clinician was to prove that academic pharmaceutical research and development is able to 'deliver' (clinician 3, interview; patient representative 6; Zorginstituut Nederland, 2020d, news article). Practically, this would mean showing the feasibility of 'in house' production by proving that the product would be at least as safe and effective as the alternative (clinician 3, interview). A patient representative specified that the 'in house' version might make patients less nauseous and passive, because a certain chemical compound – otherwise needed to freeze and defrost for long-distance transport – could be avoided (patient representative 6, interview). A clinician underlined that especially time gains might mean the therapy would become available for patients for whom a six weeks' wait (for transportation, modification, and return) might be too long, thus serving a potentially as-yet untreated patient group. ZIN phrased it as follows on their website:

> The research group [at the UMCG] wants to produce CD19 CAR T cells inside the hospital without freezing the cells. It is to be expected that this will lead to quality gains. Next to that, it is expected that the on-location produced CAR T cells will be faster to administer and cheaper to produce. (Zorginstituut Nederland, 2020c, news article)

In the same vein, ZIN employees targeted increasing quality, but, as for the eculizumab case, they combined it with the goal of reducing costs and speed of administration.

Balancing goals

Balancing goals was rarer for both cases, but we do analyse it as a distinct mode of goal formulation: two goals may not be fully reached, but both partially. This idea is visible, for example, in this quote by one eculizumab respondent:

> [The CUREiHUS protocol enables finding] a kind of *balance* between quality of life for patients and safety and cost control. (Patient representative 3, interview, emphasis added)

The quote acknowledges that the SPIN initiative may not fully reach both goals, but aiming to reach both is still a worthy pursuit, granting legitimacy to the initiative. The word 'balance' implies that these goals are contrasting, or that reaching one goal fully

means reaching the other hardly if at all. It is therefore related to the fifth mode of goal formulation, namely challenging goals.

Decoupling goals

The third goal formulation mode in legitimacy construction and contestation is that actors may actively decouple goals, i.e. when actors consider one possible goal of the SPIN initiative more prominent or more feasible. One example is a CAR T cell therapy clinician, who noted that hospital production would 'definitely' be cheaper, but explicitly does not want to emphasise that cost and pricing aspects are important goals from her/his professional perspective:

> My goal is definitely not making it cheaper, but (…) the academic production will definitely be cheaper than commercial production, and that is for (…) ZIN and perhaps the health care insurers an important motivation to do the study. (Clinician 3, interview)

When interviewed in the newspaper, one CUREiHUS clinician likewise said:

> "Money is not our primary motive," says [one clinician], "but the price does play a role, of course." [Another clinician]: "If the drug costs nothing, I don't know whether we would take any risks with this type of patient." (Berkhout, 2017b, news article)

Decoupling goals allows these clinicians to strengthen their professional identity, i.e. underlining that price does not play a role in clinical decision-making and, by this, retaining their closeness to the patients.

Suspending judgement on goals

The fourth goal formulation mode we see is several clinicians, patients, and policy actors suspending their judgement. For example, they underscore the fact that the SPIN initiative concerns a research protocol rather than the research itself or even established practice; indicating that they do not possess all the facts yet, so they do not know, and sometimes explicitly question, whether the formulated goals will (all) be reached. As one involved patient representative noted on the eculizumab case:

> I don't think every nephrologist was convinced that stopping [with eculizumab treatment] was a good idea. And why would you let a patient run this risk [if it isn't necessary]? (Patient representative 3, interview)

One cancer patient representative wrote concerning the CAR T therapy case:

> The question is, for instance, whether the [in house production] can save time between collection and return of the cells, a period in which patients sometimes deteriorate so much that they are no longer eligible for therapy. Another question is whether the quality of the cells will improve because they do not have to be frozen before transport. (…) Finally, production by the hospitals is cheaper and given the number of CAR T [cell therapies] that are being developed and the amount of indications, this cost-saving is certainly something that should be taken into account. (Patient representative 5, email)

This respondent frames the SPIN initiative as potentially contributing to the efficacy and safety of the to-be-developed treatment, thus increasing the quality of care and likely contributing to cost-saving. Likewise, another patient representative said a lower price could

mean improved medicine availability (patient representative 6, interview). In line with this, a representative of the pharmaceutical industry, when interviewed, stated that it would be 'ethically interesting, how you would explain it to a patient' that you would give them something that should work just as well as the registered product, 'but we don't know for sure [whether it works]' (Pharma representative 2, interview). In their wording, these respondents conveyed that they were aware of the uncertain outcomes of the initiatives and were, therefore, cautious in their judgment.

Challenging goals

The fifth mode of goal formulation is challenging goals: actively questioning whether the SPIN initiative will contribute achieving the set objectives. In the two cases, challenging goals especially came to light in how pharmaceutical companies and their representatives challenged the goal formulations and the legitimacy of the SPINs – and how involved actors, such as clinicians, patients, and ZIN, but also newspapers, treated the pharmaceutical industry in turn.

Pharmaceutical companies and their representatives challenged the goals formulated by the SPIN initiatives and distanced themselves from them. They actively questioned whether these SPIN initiatives would legitimately reach their goals (pharma representatives 1 and 2, interviews) or refrained from commenting (pharma employees 1, 2 and 3, group interview). The industry's overall discourse is visible in publicly available documentation derived from an anonymous request relating to the Dutch Government Information Act concerning the CAR T cell therapy case. A pharma representative emailed Ministry employees to highlight that several websites and newspapers reported on the subsidy, continuing:

> With this [subsidy to the UMCG], approval by EMA is set aside. (…) [The already-approved therapy] is an innovative treatment that is already included in the basic benefits package in the Netherlands and is produced in Kite/Gilead's brand new CAR T production facility in Hoofddorp. I am convinced that the registration of complex innovative treatments such as this CAR T cell treatment against lymphoma should always be the preferred route. The route to copy a treatment is motivated by cost savings, but does not take into account international agreements and cooperation within the EMA, with all the consequences that this entails for our innovation climate and international credibility. (email sent 24 November 2020 by Managing Director Holland Bio, accessed via Rijksoverheid, 2021, policy document)

This pharma representative sees the SPIN project as illegitimate and probably illegal. The three pharmaceutical company employees interviewed in the CAR T cell therapy case stated they would not comment on this, and that 'the most important thing is for the patient to become number 1, that it benefits the patient, that that is guaranteed' (Pharma employees 1, 2 and 3, group interview).

For the eculizumab case, the company refused to comment altogether. A ZIN employee explained why this might be:

> I can imagine that it is not desirable for this manufacturer that the results in the Netherlands, if they are positive, would be shared internationally (laughs). So yes, (…) I can understand that [they refused to comment]. (ZIN employee 1, interview)

Moreover, the manufacturer's refusal to participate in and comment on the case heightened the initiative's legitimacy, at least in the eyes of others involved. For example,

ZIN does not *want* the company's approval; they have successfully contributed to challenging the industry in this case.

This aligns with newspaper coverage opting to frame both initiatives as different from the wishes (pricing) or existing practices (fabrication or administration) of the pharmaceutical companies. A ZIN report stated that the CUREiHUS research could 'serve as an example of how to get *out of the manufacturer's hold*' (Zorginstituut Nederland, 2016b, policy document, emphasis added). Distancing from the pharmaceutical industry's goals validates and reinforces the legitimacy of the SPIN initiative.

Discussion

Contributions

Legitimacy construction means establishing a particular initiative as consonant with what actors assume is a belief or value considered valid by all those involved in a particular situation. These beliefs and values are, however, often not explicated. What is made explicit are the goals a project might contribute to, particularly the societal goals underpinned by beliefs and values that actors presume others to share (Geurts, Geerdink, and Sprenkeling 2022). In this paper, we answer the question: what is the form and role of goal formulations in constructing and contesting the legitimacy of SPIN initiatives? The actors driving the two SPIN initiatives (Douglas et al. 2022) we studied, i.e. the CUREiHUS research protocol for the eculizumab case and the CAR T cell therapy protocol, constructed and contested legitimacy with doctors and patients, *Zorginstituut Nederland* (ZIN), other policy actors, and pharmaceutical companies and their representatives.

Our data confirm that actors formulate goals when constructing legitimacy for a particular innovation, both prompted and unprompted. Overall, the formulated goals we found in the two cases are heterogeneous (Arts, Buijs, and Verschoor 2018), including both more direct, local goals, such as CAR T cells being 'cheaper to produce', and more societal goals, like 'better care for the elderly' with money saved through the eculizumab case (Bitektine and Haack 2014), further evidencing this as frontline professional's concerns (Wadmann, Hauge, and Emdal Navne 2023). The goals are recognisable: it often concerns some form of quality of care and/or some form of affordability of care. Notably, these well-known goals are to be reached in new, exemplary ways, breaking with old ways of organising (Avelino et al. 2019; Pel et al. 2020). SPIN legitimacy construction and contestation thus means confirming and contesting whether and how this initiative might contribute to the well-known societal goal(s) in question. These formulated goals are thus combined and contrasted in attempts at reconfiguration that might 'stick', and even precipitate in, institutions (van Niekerk et al. 2023).

Through examining and analysing goal formulations across interviews and documents, we have arrived at five distinct but related *forms* in which actors at a greater and lesser distance from these SPIN initiatives formulate goals, namely by (1) combining, (2) balancing and (3) decoupling goals, (4) suspending judgement on goals, and (5) challenging goals. From these five ways of goal formulation, we distil two more general *roles* that goal formulations play in SPIN legitimacy construction, namely managing consensus and managing differences. Let us unpack both.

First, actors aim to *manage consensus*. Combining goals (Gray, Purdy, and Ansari 2015; Suchman 1995) is a known way of managing consensus, especially vis-à-vis important actors (Bitektine and Haack 2014). In our paper, this important actor is primarily ZIN, considered an impartial, independent governing authority and an important source of

legitimacy (Rosanvallon 2011). Actors align their goals with ZIN's goals and activities. In turn, this governing body played an active role, co-producing these medical technologies (Hogarth 2012) by giving support and accreditation. Specifically, for the eculizumab case, this accreditation came in the form of positive reimbursement advice; for the CAR T cell therapy case, the 'Potentially Promising Care' subsidy. The fact that actors combine goals at one moment and decouple them at other moments (like the clinicians in the eculizumab case, who combine the quality of care and cost control when interviewed but decouple them in a newspaper interview by distancing themselves from the cost aspect) shows the managed nature of this consensus. Moreover, involved actors also manage consensus with those who might not be fully convinced and are reserving their judgement on whether the SPIN initiative may contribute to the proposed goal(s). It allows actors to commit themselves yet remain supportive. This suspending of judgement can happen because both cases concern research protocols: the *experimental nature* of the SPIN initiatives enables actors to postpone their judgement. The initiatives are ongoing and cannot as yet deliver on the goals, but that does on preclude legitimation for the on-going innovation process, rather the opposite.

Honing in on the governance angle, especially the eculizumab case features strong participatory dynamics in a deliberative setting, with ZIN as the governance actor listening to the patient community's voice – though retaining the right of decision (Galego et al. 2022; Kleinhout-Vliek, de Bont, and Boer 2021). Moreover, also taking in the CAR T cell therapy case, it is inevitable to note that these processes more or less explicitly align, or are made to align, with cost-effectiveness discourses highly prevalent in Dutch and European pharmaceutical policy settings (Vreman et al. 2020). Cost-effectiveness and system sustainability are particular formulations of public value pursued by these social innovations, but not necessarily one espoused by the initiators themselves. At the same time, to make this happen, these initiators (patients and clinicians primarily) activated social relations with this governing body, a form of empowerment (Avelino et al. 2019). It is also evident that these social innovations, in turn, legitimise and strengthen this governing body's position (Abad and Ezponda 2022).

Second, actors involved in SPIN initiatives seek to *manage differences* – as the flipside of managing consensus – both within and outside the initiative. Clinicians' professional values prioritise patient well-being and quality of care over cost-effectiveness. When they decoupled goals, stating that reducing costs was not one of their goals, they effectively strengthened their professional identities and repositioned themselves closer to the patient (Schuurmans et al. 2023), another vital legitimacy source (Rosanvallon 2011). This dynamic resonates with 'maintaining plurality' (Gray, Purdy, and Ansari 2015): it is productive for actors to be able to agree on what needs to be done without agreeing on the why. Like in discourse coalitions, the heterogeneity of partners needs to be guarded and cultivated to ensure it remains stable and continues to legitimate the innovation process at stake (Hajer 2002).

Involved actors also seek to *manage differences* with others outside the SPIN initiative (here, pharmaceutical companies) and actively create distance in this way. Interestingly, several pharmaceutical company employees and representatives state in the interviews and elsewhere that they are keen on entering the conversation. They do suspend their judgement, stressing that 'we don't know for sure [whether it works]', or directly questioning the goals the SPIN initiatives contribute to and thus their legitimacy. Yet they feel excluded. Notably, in addition to what some see as unethical behaviour complicating relationships (Abraham 2008; Martin 2022), they are likely to remain excluded as this reifies the beliefs held in common by the SPIN actors. Managing differences shows

that creating legitimacy for an initiative is not just about the initiative's goals but also about what *others* do, implicitly or explicitly problematising the status quo (Johnson, Dowd, and Ridgeway 2006). Reflecting the adage 'the enemy of my enemy is my friend': antagonists' rejection of a SPIN initiative can bolster the reputation of that initiative with others.

Many, if not all, SPIN initiatives need protection to thrive (Farmer et al. 2018; Smith and Raven 2012; Witkamp, Raven, and Royakkers 2011). We conclude that by appealing to long-standing, easily-recognisable goals like quality and affordability of care, these SPIN initiatives seek to create continuity in this highly-institutionalised field, noting that common social innovation goals like 'disruption' or 'pioneering' are absent from our dataset (Drori and Honig 2013; Wittmayer et al. 2019). These SPIN initiatives propose to reach these goals in new, exemplary ways, with the ambition to become a recognised 'type' in the future. The eculizumab case is the first successful example of an orphan drug arrangement; the CAR T cell therapy case is an early example of academia-led pharmaceutical research and development. In other words, legitimacy is also created by ensuring that the individual projects are part of a sequence of projects or fall under a larger umbrella that gets recognised and accepted over time. In this sense, the formulation of goals is a strongly future-oriented activity (Borup et al. 2006; Garud, Schildt, and Lant 2014; Konrad 2006), and the response from and interaction with other actors concerning these goals is an essential way to attempt to ensure longevity. Early-stage alignment of goals-to-formulate and higher-level narratives, such as keeping healthcare sustainable and accessible, supports such legitimisation processes.

When it comes to the effects of legitimacy construction, actors present their experimental social pharmaceutical innovations using these goal formulations to strengthen their legitimacy by expanding and stabilising (managing consensus) and diversifying and delineating (managing differences) the social base of its defenders through multiple modes of goal formulation. In these ways, involved actors work hard to guarantee its protected status over time. Douglas et al. (Douglas et al. 2022) highlight two distinguishing factors of SPIN: first, SPINs are characterised by new partnerships, and second, they seek to meet social needs and are not primarily market-driven. We conclude that these two characteristics are essentially intertwined: these new partnerships are formed through multiple goals. In these partnerships, which we show are expressly varied as well as carefully delineated, we see that actors mobilise professional identities, the experimental nature of SPIN initiatives, and multiple goals to keep actors 'on board' and other actors 'out'. These dynamics precipitate the effects of legitimacy construction: the social base is made as large and diverse as possible (with heterogeneous actors responsive to different goal formulations) while excluding antagonists (in this case, the industry), which, in turn, also legitimises the initiative. As part and result of these processes, resources are mobilised and the initiatives are kept 'alive' for the time being. What happens if and when initiatives fail to reach the goals aspired to remains to be seen, though an adjustment of goals seems likely (Borup et al. 2006; Brown and Michael 2003; Garud, Schildt, and Lant 2014; Konrad 2006; van Lente 2012).

Strengths and limitations

In our dataset, the formulation of goals is situation-dependent and, as such, tentative, requiring maintenance. Despite these nimble interactions, it has been relatively easy to trace legitimacy construction through goal usage across different moments and documents, including newspapers. We observe that due to the contested nature of SPIN

initiatives, their participants, supporters and critics have incentives to be articulate about their goals and that these goals have a solid normative and pragmatic force and even news value.

In terms of limitations, the number of interviewees is on the small side, so the extent to which we were able to capture the variety of opinions within each case is uncertain. More cases and more interviews may help to test the conclusions and develop the analytic model. Another open question is whether we see *strategic* mobilisation of goals or that actors 'believe' that the SPIN initiative may indeed contribute to the formulated goal (s). Undeniably, much of the SPIN initiative legitimacy construction works in the interest of the involved actors. ZIN gets to position itself closer to patients and their needs, patients gain continued access to medicine, and clinicians receive recognition for their work, such as a prize or a 30-million-euro subsidy.

More generally, it is vital to stress that it is our analysis that these actors are involved in legitimacy construction: many if not most are seeking pragmatic solutions to immediate problems and are not preoccupied with furthering larger goals until 'circumstances' force their hands – or until an interviewer asks them about goals. We have sought to visualise and analyse legitimisation work by focusing on explicit (hence, fairly easily identifiable) goal formulations and tracing these across different situations. We have analysed legitimacy as a process rather than an outcome (Johnson, Dowd, and Ridgeway 2006; Molecke and Pinkse 2020; Suddaby, Bitektine, and Haack 2017). Analysing whether or not it 'works' requires a legitimacy-as-outcome conceptualisation that depends on the perceptions or judgements of audiences and, potentially, a different set of methods.

Conclusion

Social Pharmaceutical Innovations (SPINs) are potentially disruptive to existing configurations, requiring legitimacy construction to allow space for the alternative proposed (Fougère, Segercrantz, and Seeck 2017; Verleye et al. 2019; Weber and Rohracher 2012). Goal formulations are crucial in this, but little is known about the precise dynamics. We set out to answer the question: what is the form and role of goal formulations in constructing and contesting the legitimacy of SPIN initiatives?

Actors involved in SPIN initiatives employ a plethora of goal formulations: they use both direct, local goals and well-established and well-known goals, such as quality and affordability of care, to manage the disruptive potential of, and thus legitimise, SPIN initiatives. We find that particularly societal goals or purposes favouring the collective good (Geurts, Geerdink, and Sprenkeling 2022) are critical in legitimising SPINs, as these are underpinned by beliefs and values that actors think others consider valid.

Our analytical approach, in line with constructivist grounded theory, has allowed us to establish timelines with specific situations or moments of legitimacy construction or contestation and analyse the goals explicated therein. Based on this analysis, we distinguish five ways actors use goals to construct or contest legitimacy, linking them with widely held 'beliefs' and 'values', and connecting them to the dynamic development of social innovations and the institutional configuration of governance actors involved.

Overall, we observe varied, contested legitimacy construction (Geels and Verhees 2011) by appealing to long-standing societal goals that are well-known to welfare states across Europe as an essential method to legitimise these new ways of organising pharmaceutical innovation and to attempt to ensure their longevity. This sometimes looks like an explicit agreement between actors and strong legitimacy co-construction, especially with governance actors, whereas other moments show actors who give qualified

support to only part of the set of legitimation arguments or lean towards disagreement and questioning legitimacy. Across these situations, actors formulate diverse goals to solidify diverse SPIN partnerships, clearly demarcating who is 'in' and who is 'out'. Working together for the greater goods (plural) is thus essential for organising durable social innovation in the European pharmaceutical field.

Author contributions

TKV was responsible for conceptualisation, data curation, formal analysis, writing of the original draft, and editing. The other authors were involved in funding acquisition, supervision, and reviewing various paper drafts.

Data availability statement

Anonymised interview data will be made available upon request to protect the identity of the interviewees. All analysed documents are available online.

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Data collection and analysis took place in the Netherlands.

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Appendix. Analysed documents.

Case 1: Eculizumab	Title	Source, year
Policy documents	Pearl project – aHUS: treatment with eculizumab can be much more targeted	ZonMw (2018)
	Optimalization of Eculizumab/Soliris® treatment in patients with atypical hemolytic uremic syndrome by means of individually-tailored, personalised therapy	ZonMw (2021)
	Report Meeting Appraisal Committee (18 March 2016)	Zorginstituut Nederland (2016a)
	Report Meeting Appraisal Committee (14 October 2016)	Zorginstituut Nederland (2016b)
	Package recommendation eculizumab (Soliris®) in treatment of aHUS patients	Zorginstituut Nederland (2016c)
	Monitor Orphan Drugs in Practice 2018	Zorginstituut Nederland (2018a)
	Monitor Orphan Drugs in Practice 2019	Zorginstituut Nederland (2019)
	Monitor Orphan Drugs in Practice 2020	Zorginstituut Nederland (2020a)
News articles	Saving lives sometimes too expensive, Thijs Rösken, De Telegraaf (19 March 2016)	Rösken (2016)
	Dosage of expensive drug may be lower than manufacturer says, Karel Berkhout, NRC Handelsblad (24 June 2017)	Berkhout (2017a)
	Swallow or choke? There is another way, Karel Berkhout, NRC Handelsblad (24 June 2017)	Berkhout (2017b)
	Lower dose of expensive drug also works, Ellen de Visser, de Volkskrant (7 March 2019)	De Visser (2019)
	Kidney patient need not take drug for life, Lineke Nieber, NRC Handelsblad (31 October 2022)	Nieber (2022)
	Tailored usage advice for expensive drugs – ZonMw, Pearls for rare disease research	ZonMw (2018)
	Monitor orphan drugs: spending up 45% in 5 years	Zorginstituut Nederland (2018b)
Other websites	CUREiHUS protocol	Radboud Universiteit Nijmegen (no date)
	aHUS Conference: The Dutch Approach	aHUS alliance (2018)
Policy documents	Promising care – Care site-produced CD19 CAR T-cell therapy in patients with relapsed or refractory DLBCL	Zorginstituut Nederland (2020b)
	Decision request policy on unregistered medicines (19 November 2021)	Rijksoverheid (2021)
News articles	Groningen boosts cancer drug, Ellen de Visser, de Volkskrant (24 September 2020)	De Visser, 2020
	€ 30 million grant for UMCG research into promising cancer treatment	Zorginstituut Nederland (2020c)
	Zorginstituut Magazine: At the desk and at the bedside	Zorginstituut Nederland (2020d)

Documents analysed for the two case studies.