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Convergence, Divergence and Hybridity: A Regulatory Governance Perspective on Health Technology Assessment (HTA) in England and Germany

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Abstract
Countries adopt different methods and processes to evaluate the benefits and costs of health technologies. It is important to identify and analyse the factors that influence the uptake and use of these methods and processes across countries. In this paper, we introduce a regulatory governance approach to the analysis of convergence, divergence and hybridity in HTA methods, discussing and critically analysing national processes for HTA in two major European Union (EU) Member States: England and Germany. We argue that any reasonably sophisticated account of national approaches to HTA must recognise that globalisation and the emergence of advanced industrial society involves the potential for widely varying processes, methods and evidential requirements. We suggest that this potentiality also confronts health policy analysts with the challenge of constructing analytical frameworks capable of identifying the diverse institutional, domestic and other factors that shape national approaches to HTA.

Keywords
Health Technology Assessment
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1. Social Science Research and Health Technology Assessment

Social science research is having an increasingly important impact on the development and operation of advanced industrial societies. With the arrival of the digital era, the social sciences are influencing public policy across a wide variety of sectors, contributing to the development of firms and markets, and shaping wider societal understandings of policy problems and debates regarding their solutions. In the healthcare sector, the influence of social science research is evident in government responses to the exponential growth in the availability of new health technologies and treatment options with the capacity to improve health and quality of life. In Europe and around the world, policymakers have attempted to ensure equitable access to novel and often expensive health technologies by establishing independent regulatory agencies (IRAs) for Health Technology Assessment (HTA), such as the Institute for Quality and Efficiency in Health Care (IQWiG) in Germany and the National Institute for Health and Care Excellence (NICE) in England. These agencies produce evaluations of new health technologies, which incorporate economic,epidemiological and public health evidence, among other elements. These assessments support policies on reimbursement, pricing and the use of technologies in clinical practice. In principle, national IRAs for HTA deliver more legitimate, transparent and accountable methods and processes by which governments can respond to the challenge of delivering efficient and equitable public access to new health technologies. For the future, the role of these agencies within national policy making processes is likely to expand as a wider and more sophisticated array of treatment options becomes available to patients, thus placing additional pressure on national health budgets.

Despite their common remits, roles and aims, national IRAs for HTA differ markedly in terms of their structure, operation, use of evidence and methods for the conduct of evaluations. Across the EU, governments also differ with regard to how they employ evidence generated through HTA within national decision-making processes. These variations, and their potential to impact national health policies and practices, hold consequences for the delivery of efficient and equitable health services, and ultimately for the improvement of population health. For these reasons, there has been significant debate and research regarding the most appropriate methods and process for establishing the value of health technologies. For example, some European analysts have advocated initiatives for pursuing a systematic approach to the evaluation health technologies across the EU and for adapting evaluations of individual technologies for cross border use (Dickinson et al 2003; Lothgren and Ratcliffe 2004; Draborg and Andersen 2006; Turner et al 2009). Others have argued for increased levels of cooperation and exchange of HTA evaluations for the purpose of reducing expenditure and the duplication of work programmes (Hutton et al. 2008; Kristensen 2008; EMA 2011). And more specifically, some have suggested that national HTA agencies should collaborate with European regulatory authorities towards the better congruence of licensing and reimbursement requirements to ensure that comparative efficacy data has a formal role in European drug approvals (Sorenson et al 2011). Overall, most health policy analysts have aimed to

smooth and ameliorate instances of national divergence in assessment processes rather than to explain and analyse them in a critical way. As a result, there has been limited amount of research conducted on the broader national contexts within which methods and processes for HTA are embedded, the factors that influence the uptake of different methods and processes and their subsequent impact on policy and practice.

2. Comparative Policy Research and Regulatory Governance

The study of hybridity and divergence in national processes for HTA involves the challenge of constructing an analytical framework capable of identifying the institutional, domestic and other factors that shape national approaches (Klingler et el 2013; Shah et al 2014; Barron et el 2014). Typically, where health policy analysts have conducted studies of varying national approaches to HTA, they have adopted the perspective of comparative policy research. Broadly speaking, the comparative approach involves the comparison and analysis of national health systems with a view to understanding why these behave in certain ways and what policy-makers can do to improve their performance (WHO 2000). Comparative approaches are concerned withthe identification of policy configurations across national borders, with the aim to highlight the factors that produce comparable or dissimilar outcomes in different jurisdictions (Marmor et al 2005). In terms of HTA, some comparative studies offer collections of national case studies and describe various institutions, roles and responsibilities. Others compare national studies and emphasize themes such as competition and privatization. Some offer statistical and largely descriptive reports that highlight data on a number of countries assumed to constitute a coherent class, analyzing the impact of HTA on policymaking across national contexts (Morgan et al 2006; Sorensen et al 2008; Chalkidou 2009). Others evaluate the role of HTAs within a particular therapeutic class, such as oncology or diabetes (Chalkidou et al 2009; Kanavos et al 2010; Sorenson and Chalkidou 2012).

However, comparative approaches are not well suited to the study of divergence and hybridity in national approaches to HTA. Typically, comparative studies deliver largely functional accounts of specific national organizations (e.g. NICE and IQWiG), supposing that these are broadly similar organizations and the sole sources of legitimacy and power within the decision making frame. For example, some analysts assert a distinction between HTA as an evaluation process and a context-specific appraisal process. The former is a process for producing knowledge about new medicines, or the structured analysis of a health-care technology, which is transferable across national contexts; the latter is a process that translates the analysis into policy advice and decision-making (Stevens and Milne 2004). Applying such distinctions, comparative approaches tend to conclude with analytical summations of common policy lessons, core sets of structural, technical, and procedural requirements for the conduct of HTA that apply across jurisdictions. And, in this way, comparative studies remain largely insensitive to the wider range of institutional, contextual and other factors that influence uptake and use of methods and process in various countries.

However, regulatory governance scholarship offers both an additional lens through which to conceptualise the study national methods and process for HTA, and also an appropriate

frame through which to analyse divergence and hybridity. Regulation is a subset of governance scholarship concerned with the analysis of steering and other regulatory activities, as opposed to activity concerned with providing and distributing goods and services (Braithwaite 2008). In conceptualising national divergences for HTA, regulatory scholars would argue that some policy sectors are more likely to exhibit hybridity and divergence at the national level than others (Levi-Faur 2006a, 2006b). Globalisation affects policy sectors, markets, and regulatory regimes to different degrees. In banking and finance, both markets and regulations are global. In the healthcare and other sectors, however, both markets and regulations are national because governments differ with respect to how much and what kind of services and protections they offer. With regard to health technologies, regulations are subject to globalisation, but markets are not (Braithwaite and Drahos 2000). In other words, manufacturing practices for pharmaceuticals have been internationally standardized to a very high degree, but individual nation states remain the monopolistic buyers in the largest markets, and so the regulatory practices for HTA are mostly national (Levi-Faur 2006b). Accordingly, a regulatory governance lens would suggest that there is significant scope, relative to other sectors, for national healthcare policy, and process for HTA, to become more political than technical, and more parochial than structural. Therefore, health policy analysts would expect that national processes for HTA would display major differences withregards to methods, institutions and evidential requirements. In the context of advanced industrial society, health policy analysts might even become more circumspect about the extent to which national process and methods for HTA can be usefully distilled from one national context to another, and perhaps more interested in identifying and critically analysing instances of divergence and hybridity.

Today, 'regulatory space' is an emerging analytical frame through which scholars are beginning to approach the study of national methods and process for HTA (Klingler et al 2013). Regulatory space is a holistic concept within the field of regulatory governance that frames steering and other regulatory activities within a spatially defined context (Hancher and Moran 1989). Compared with the comparative policy lens, a regulatory space approach denies the distinction between HTA as a twofold process of assessment and appraisal (Shah et al 2014; Barron et el 2014). Under a regulatory space frame, appraisal and assessment processes are mutually constitutive (Klingler et al 2013). Accordingly, the wide range of issues to which decisions regarding the use of pharmaceuticals is subjected defines the boundaries of the HTA 'regulatory space'. For example, a regulatory space approach to HTA can involve the analysis of public policy networks, institutions and wider historical trends and cultural preferences. It may draw attention to the multiplicity of actors who do, or have the potential to, participate in the HTA process. In addition, it might also highlight the historical, political and cultural content of the national decision making environment, relating these to the use and mix of particular agencies and methods of operation (Klingler et al 2013). Or, as in the following sections, a regulatory space approach might also focus on the influence of formal organizations and agencies, analysing their structure, their rules and techniques for enforcement and compliance with a view to delineating the nuances, commonalities and divergences of individual regulatory governance systems and improving their operation.

3. Institutions and Process for HTA in England

In the UK, the National Health Service (NHS) offers universal healthcare free at the point of access for the entire population of the UK. In England and Wales, the HTA process is conducted through two institutions: NICE and the Department of Health (DH). NICE is an independent regulatory organisation tasked with providing national guidance on improving health and preventing disease. It produces clinical guidelines and public health recommendations. It is responsible for setting quality standards for healthcare and ensuring equal access to high quality services across the country. NICE also administers a wide range of internationally respected knowledge databases, such as NHS Evidence, the Cochrane Library, British National Formulary (BNF) and the Map of Medicine, which provide access to clinical guidelines, drug information, academic journals and clinical summaries (NICE 2009).

However, NICE is perhaps best known for producinghealth technology assessments, which form the basis of its recommendations to local health authorities on whether or not new medicines, procedures and medical devices should be part of the basic benefits packaged, in others words, whether health technology covered under the NHS.

Established in 1999, NICE is considered to sit at the interface of scientific knowledge and practical policy making, where some commentators suggest it "sets the benchmark for the use of HTA placed at the centre of a transparent and consultative decision-making process", which derives from the discipline of evidence-based medicine (EBM) and, ultimately, from the enlightenment (Stevens and Longson 2013, p. 324; Stevens and Milne 2004). Beyond these plaudits, however, NICE is essentially a decision-making organisation, although in principle, it is classed as an advisory body. A positive NICE recommendation regarding a particular health technology, assuming it is approved by the DH, involves a legal requirement for the NHS to make the technology available for patients. Analysing NICE's role within the NHS, some scholars have asserted a distinction between HTA as an assessment process, or the "analytical process of gathering and summarizing information about health technologies", and HTA as an appraisal process, or the "political process of making a decision about health technologies, taking into account assessment information but also values and other factors" (Stevens and Milne 2004, p. 11).

Utilising this distinction, NICE assessments produce cost-effectiveness and cost-utility data regarding the use of new technologies, which derive from a variety of sources: systematic reviews of published studies; cost-effectiveness modelling based on estimates derived from a systematic review; indirect comparisons, in the absence of head-to-head studies comparing the clinical and cost-effectiveness of new technologies; and, review and critique of and economic models provided by the manufacturer (Stevens and Milne 2004). Today, much of NICE's work program involves review and critique of existing models with a view to providing speedy advice on new medicines, through the single technology appraisal programme. During the course of a technology assessment, NICE appoints an Evidence Review Group, which evaluates the manufacturer's submission and

advises the Appraisal Committee. In producing cost-effectiveness and cost utility data, the group uses the incremental cost-effectiveness ratio (ICER), which defines the marginal health gain for new technologies in terms of quality-adjusted life years (QALY) against the savings attributable to the product. QALYs integrate changes in life years and quality of life into a single benefit measure that applies across therapeutic areas. The derivation of the ICER requires that an economic model is constructed and parameterised from a particular perspective (e.g. health system, third-party payer, societal, etc.). The generation of the model ICER requires a number of inputs, such as a suitable comparator together with acquisition, treatment, administrative and monitoring costs. While these inputs are subject to significantqualitative and quantitative uncertainty, they also heighten the importance attached to the activities of NICE's Appraisal Committees (Rawlins et al 2013)

NICE Appraisal Committees convene a meeting of the assessment panel, clinical experts, and patient representatives. On the basis of their discussions, the Appraisal Committee prepares an initial Consultation Document, on which it seeks feedback from stakeholders, such as patient groups, manufacturers and clinicians. Those wishing to offer comment are invited to return for the final meeting of the appraisal committee, at which a binding decision regarding the technology is made (Stevens and Milne 2004). Throughout this appraisal process, two economic values are critical: firstly, the ICER and the comparator against which it is derived; and secondly, the cost effectiveness threshold to which the ICER is compared. The threshold represents the opportunity cost of health care at which the technology becomes non cost-effective. At present, the implicit threshold is set at a range £20-30,000 (Appleby et al 2007). In other words, as the ICER approaches the threshold it is less likely to receive a positive recommendation from the Appraisal Committee. As the range provides the committee with an element of discretion, its decisions are regularly subject to discussion and challenge. Typically, challenges relate to the inputs into the assessment process, the use of evidence, the methodology, the interpretation of the evidence and the procedures of the Appraisal Committee (Stevens and Longson 2013, p. 322)

However, the HTA process is not directly under NICE's control. Instead, DH and the National Assembly for Wales are responsible for determining NICE's work program (Stevens and Milne 2004). Each year, the DH invites and receives suggestions from the pharmaceutical industry, professional organizations and patient groups on appropriate topics for NICE assessment and appraisal. From this short list, the DH selects appropriate topics. The topic selection process involves two elements: measuring new technologies and treatment areas against a set of selection criteria; and, the subsequent evaluation of identified technologies by a topic selection panel. The DH selection criteria for identifying technologies include issues such as: the appropriateness of the topic to NICE's remit; the potential of the topic to generate improvement in health and well-being; the potential for added value; and the timeliness of the proposed topic (DH 2006). Following Ministerial approval, the topics are forwarded to NICE for evaluation. While NICE is not permitted to remove or to add topics to the list, it conducts a public exercise to determine the comparators for each assessment and the outcomes for each technology that itshould assess (Stevens and Milne 2004).

One particularity of HTA is the UK is that in theory, NICE recommendations do not serve to influence pricing decisions. As described above, NICE decision only seeks to determine the extent to which health technologies will be reimbursed by the NHS. Prices are set freely by the manufacturer within a voluntary statutory framework known as Pharmaceutical Price Regulation Scheme (PPRS), which the DH and the Association of British Pharmaceutical Industry (ABPI) negotiate at regular intervals. Rather than directly controlling the price of individual products, the PPRS aims to provide an overall pricing framework under which it seeks to regulate the profitability levels of individual pharmaceutical companies through 2 levers, 1) Profit control through a % profit on capital employed (e.g R&D allowance) and 2) Price control through initial price agreement, increase restriction and cross-industry price-cuts price cuts (allowing portfolio price modulation) (Habl 2006). If manufacturers exceed pre-agreed upon profitability levels, they must reduce their prices, postpone price increases, or pay back excess profits to the NHS. At present, international price comparisons and cost-effectiveness information do not play a role in pricing decisions, but favour returning any excess profits to the NHA rather than reduce prices.

Whilst HTA in the UK aims to determine reimbursement, it can however be argued NICE also plays an informal role in setting the prices of certain high cost innovative medicines. Indeed, through its use of the ICER which considers both costs and clinical effectiveness and the use of a willingness to pay threshold, NICE can encourage companies to lower their prices so that they fall under the threshold and obtain a positive recommendation. As a result, rather than negotiating prices with manufacturers, NICE engages into an iterative (pricing) process with manufacturers to encourage them to lower the price of their products. However, this process may soon be phased out as the current government is working towards a new pricing system under which the price of a drug will be negotiated directly with the manufacturer and become more closely linked to its clinical value (DH 2010), but the timing of its introduction has been subject to review.

4. Institutionsand Process in Germany

The German process for HTA is markedly different to those of the UK and other countries (Klingler et al 2013). In Germany, the health system functions under a social insurance model. Two institutions dominate the HTA process in Germany: The Federal Joint Committee (G-BA) and the Institute for Quality and Efficiency in Health Care (IQWiG). The G-BA is responsible for determining the benefit catalogue while the IQWiG informs those decisions. Technologies are included on the benefit catalogue by the G-BA when additional clinical benefit compared to the standard intervention is demonstrated; cost-effectiveness data plays only a minor role in those decision-making processes (GBA 2008; Fricke and Dauben 2009). Established in 2004, IQWiG supports the G-BA through the conduct of clinical effectiveness analyses using the methods of evidence-based medicine (Perleth et al. 2009). However, in 2008, a new competition-strengthening law was introduced - *GKV-Wettbewerbsstärkungsgesetz* – that added to its responsibilities the production of 'cost-effectiveness data', meaning the production of assessments which relate health impacts delivered through the use of new technologies to costs (*Kosten-Nutzen-Bewertung*). Those were thought to inform the National

Association of Statutory Health Insurance Funds (*GKV-Spitzenverband*) (IQWiG 2008). With the new law, the GKV-Spitzenverband became responsible for setting the maximum reimbursement prices for innovative pharmaceutical technologies. Pricing decisions of the GVK-Spitzenverband were based on IQWiG's cost-effectiveness studies (IQWiG 2009). Therefore, IQWiG's changing role reflected related changes at the GKV-Spitzenverband. In 2010, the process for determining prices for new pharmaceutical products was altered again with the introduction of the *Arzneimittelneuordnungsgesetz* (AMNOG) law (DB 2010). Under the reform, the GKV-Spitzenverband was given authority to conduct negotiations with the pharmaceutical industry to determine market prices based on IQWiG-generated clinical effectiveness assessments. AMNOG diminished the importance of cost-effectiveness assessments to the decision making process quite significantly. Under AMNOG, IQWiG's cost-effectiveness assessments are consulted when negotiations stall and the intervention of an arbitrator—appointed by the groups involved — fails to deliver an agreement. Under these circumstances, either party may request a cost-effectiveness assessment to determine the adequacy of the price set by the arbitrator. In addition, the pharmaceutical company may also appeal to a formal cost-effectiveness assessment when the G-BA finds no evidence of any additional clinical benefits associated with the new intervention (DB 2010; Klingler et al 2013).

Where assessment becomes necessary, however, IQWiG applies a divergent approach to cost-effectiveness analysis compared with other EU countries. In 2008, following the widening of its remit, IQWiG introduced the "Efficiency Frontier" approach. For any therapeutic area all available interventions need to be identified to construct the Efficiency Frontier. Costs and clinical effects (presented in any context-adequate benefit measure) of all available interventions need to be known before the Efficiency Frontier can be built. Once derived, the data are plotted on a coordinate system in which the y-axis displays clinical effect of the technology and the x-axis displays the costs of the intervention (Caro et al. 2010; Klingler et al 2013). The Efficiency Frontier is constructed on the basis of the most efficient interventions, or in others words, the interventions that deliver the highest benefit for a given cost.

Analysts establish the cost-effectiveness of the new technology by calculating the ICER. The calculations are made analogous to NICE, although IQWiG uses different effectiveness parameter or base for its threshold. In the case of the IQWiG Efficiency Frontier, the cost-effectiveness threshold is set at the ICER of the second most effective intervention. Researchers establish the ICER of the second most effective intervention based on information regarding the costs and clinical benefit of the second and third most effective interventions, which are generated through the Efficiency Frontier. The ICER of the second most effective intervention now serves as a kind of ad-hoc threshold. If the ICER of the intervention under evaluation falls below or on this ad-hoc threshold, the new intervention is deemed cost-effective. Ultimately, prices are set to allow the ICER to fall on or below the threshold. In other words, the Efficiency Frontier deduces an ad-hoc threshold to which the ICER of the new intervention is compared, allowing the price to be adjusted accordingly (IQWiG 2009; Caro et al. 2010; Klingler 2013 et al).

Another important point of divergence from NICE is that IQWiG does not prioritise the use of the QALY (IQWiG 2008, 2009). For IQWiG, any benefit measure that remain relevant to context and fulfil certain criteria, such as changes in risk profile, or changes in mortality measured in life years gained, can be applied. Depending on the intervention under evaluation, IQWiG can use different benefit measures in its different assessments. QALYs can be used where deemed appropriate, but it is no necessary requirement as with NICE's evaluations. It is important to understand that the different decision making remits of IQWiG and NICE do not explain the divergent methodological decisions. Even though IQWiG's assessments are made to inform pricing decisions and NICE, by contrast, makes procurement recommendations, the decision-making frameworks do not forestall the methods employed in HTA. Naturally, NICE is dependent on a benefit measure that can be used across therapeutic areas like the QALY. However, as the value-based pricing movement in the UK will show, IQWiG could have used a method more similar to NICE's for its pricing decisions. It would have been perfectly workable to base pricing decisions on a fixed and not a variable threshold across therapeutic areas.

6. Discussion and Policy Implications

Whereas a comparative perspective on the analysis of national approaches to HTA tends to conclude with core sets of policy lessons and summations of optimum methods and evidential requirements, a regulatory governance perspective is more relaxed about instances of divergence and hybridity, offering a range of insights into the factors that shape national approaches to HTA and the activities of institutions like NICE and IQWiG (Klingler et al 2013). A regulatory governance perspective can also potentially suggest some means by which their operations can be improved.

For example, some UK-based analysts have suggested that NICE sets an international 'benchmark' for theassessment of new technologies, and that its processes derive from the practice of evidence based medicine (Stevens and Longson 2013; Stevens and Milne 2004). From a regulatory governance perspective, however, rather than setting a benchmark, NICE assessments involve a rigorous, and arguably expensive, set of economic analyses necessary to drive a health system that involves universal and free access to health care, and in which the profits and prices of pharmaceuticals are regulated by an initial agreement between industry and government. In the UK, production of these assessments, and the use of the QALY, is necessary to make comparisons of the cost-effectiveness of medicines across individual disease areas. Given the structure of the UK health system, NICE appraisals need to establish whether or not public money is more effectively invested in the latest cancer treatment or the latest diabetes treatment to effectively ration health care.

Currently, the UK DH is considering a new approach to the appraisals of branded medicines that involves value-based pricing (VBP) based on the same cost-per-QALY threshold (£20,000-30,000). Under VBP, products with an ICER significantly higher than the current threshold will not be excluded from reimbursement. Instead, prices will be negotiated and adjusted to allow its ICER to fall below the previously defined threshold, thereby mimicking the decision-making process in Germany, but with a stronger focus on cost-effectiveness data (DH 2010). Here, a possible policy decision focusing on price

setting to ensure efficient resource use instead of exclusion from universal reimbursement is distilled from one context to another (Zentner and Busse 2011). However, it is unclear whether the German method for price setting as is a workable alternative in the UK context, and vice versa. Indeed, the main difference after AMNOG is the focus on effectiveness vs. cost-effectiveness data for price setting.

In Germany, by contrast, where prices are also negotiated, economic analysis has a significantly reduced role. In Germany, the use of the Efficiency Frontier approach responds to an environment characterised by a requirement to deny, or ignore, the need to ration health care, and also an aversion to describing the benefits of health gains in monetary terms (Klingler et al 2013). Therefore, in the German context, NICE's approach to cost-effectiveness assessment based on a fixed threshold making explicit the limited willingness to pay would not have been acceptable to the public and was avoided. The Efficiency Frontier offered the opportunity to make cost-effectiveness analysis – which depends on the definition of a threshold – work in the German context without having to reveal willingness to pay. The solution was a variable ad-hoc threshold different for every therapeutic area that seemed more acceptable (Klingler et al 2013).

In the context of advanced industrial society, any sophisticated account of HTA must recognise that national approaches involve the potential for widely varying processes, methods and evidential requirements. Of course, these divergences will be the consequence of a number of factors, only some of which we have alluded to here. Some factors may be internal to the structure and organisation of national healthcare systems, while others may arise from historical and cultural factors associated with the delivery of healthcare. In all cases, however, the pathway from the regulatory approval of new technologies to their use in clinical practice operates according to diverse national healthcare contexts. Along the way, a wide variety of factors will intervene to influence the use and application of particular assessment methodologies and evidence bases, and also work against the possibilities for policy learning and transferability in any direct and easy fashion. Indeed, it is difficult to see how NICE sets a benchmark for any other national health system than the particular one in which it operates. Accordingly, advocates of more EU-wide collaboration in HTA need to bear in mind that policy makers respond to multiple stimuli in establishing national institutions and process for HTA and 'best practice' methods and optimum evidential requirements are but one element of this wider process. For the future, the key challenge for health policy analysts, organisations like EUNetHTA in particular, is to develop and adopt an analytical framework capable of identifying and critically analysing insistences of divergence and hybridity with a view to improving the operation of individual national HTA systems.

Note:
The introductory sections of the paper draw upon work in other papers published by this research group (Klingler et el 2013; Shah et al 2014; Barron et el 2014). This is due to the fact that we have conducted this research together and have developed and applied the theoretical framework for analysis jointly.

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