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**Abstract**

As important knowledge producers, universities play a critical role in regional smart specialization processes through strategy design, implementation and building long term capacity. This paper highlights the smart specialization concept: What does it mean for regions and HEIs and why did it emerge? What are the six steps of developing and implementing the strategy and what challenges do these steps include? Drawing on practical case studies from six countries, the paper provides a checklist for validating the fitness-for-purpose of the strategy and outlines the role of HEIs in the different pathways to knowledge-based development of regions and the entrepreneurial discovery process. (HRK / Abstract übernommen)